Tuberculosis: New Insights for the Healthcare Professional
2013 Edition
Tuberculosis: New Insights for the Healthcare Professional
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General Editor
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Introduction

Tuberculosis: New Insights for the Healthcare Professional / 2013 Edition is a ScholarlyEditions™ book that delivers timely, authoritative, and comprehensive information about Diagnosis and Screening.

The editors have built Tuberculosis: New Insights for the Healthcare Professional / 2013 Edition on the vast information databases of ScholarlyNews™. You can expect the information about Diagnosis and Screening in this book to be deeper than what you can access anywhere else, as well as consistently reliable, authoritative, informed, and relevant. The content of Tuberculosis: New Insights for the Healthcare Professional / 2013 Edition has been produced by the world’s leading scientists, engineers, analysts, research institutions, and companies. All of the content is from peer-reviewed sources (except content about patents), and all of it is written, assembled, and edited by the editors at ScholarlyEditions™ and available exclusively from us. You now have a source you can cite with authority, confidence, and credibility. More information is available at http://www.ScholarlyEditions.com/.
Chapter 1

Clinical Trials and Studies

Sinai Hospital, New York City: What’s in a name? The future of drug-resistant tuberculosis classification

By a News Reporter-Staff News Editor at Clinical Trials Week – Investigators discuss new findings in Mycobacterium Infections. According to news reporting from New York City, New York, by NewsRx journalists, research stated, “Due to a recent resurgence in tuberculosis research focused on drug development, several new antituberculosis drugs are in the pipeline, and the standard of care for tuberculosis might soon change. If new drugs replace the current first-line treatment, then existing classifications of resistance, including multidrug-resistant and extensively drug-resistant tuberculosis, might become less relevant.”

The news correspondents obtained a quote from the research from Sinai Hospital, “When much needed new drugs reach the market, a new classification system for resistance might need to be devised to describe resistance to these novel agents. Many options for such a system exist, each with its own inherent benefits and challenges. The adoption of new terminology for resistance should be guided by outcomes data from clinical trials in progress, and should be accompanied by increased support for drug susceptibility testing in developing countries to be clinically useful.”

According to the news reporters, the research concluded: “Consideration of these issues now will hopefully help foster an informed approach to the classification of drug-resistant tuberculosis in the era of new drugs.”

Our news journalists report that additional information may be obtained by contacting T. Sullivan, Division of Infectious Diseases, Mount Sinai Hospital, New York, NY, United States. (2013 Apr 22)

National Institute for Public Health and the Environment, Bilthoven: Comparative Study of IS6110 Restriction Fragment Length Polymorphism and Variable-Number Tandem-Repeat Typing of Mycobacterium tuberculosis Isolates in the Netherlands, Based on a 5-Year Nationwide Survey

By a News Reporter-Staff News Editor at Health & Medicine Week – Investigators discuss new findings in Clinical Microbiology. According to news reporting originating from Bilthoven, Netherlands, by NewsRx correspondents, research stated, “In order to switch from IS6110 and polymorphic GC-rich repetitive sequence (PGRS) restriction fragment length polymorphism (RFLP) to 24-locus variable-number tandem-repeat (VNTR) typing of Mycobacterium tuberculosis complex isolates in the national tuberculosis control program in The Netherlands, a detailed evaluation on discriminatory power and agreement with findings in a cluster investigation was performed on 3,975 tuberculosis cases during the period of 2004 to 2008. The level of discrimination of the two typing methods did not differ substantially: RFLP typing yielded 2,733 distinct patterns compared to 2,607 in VNTR typing.”

Our news editors obtained a quote from the research from National Institute for Public Health and the Environment, “The global concordance, defined as isolates labeled unique or identically distributed in clusters by both methods, amounted to 78.5% (n=3,123). Of the remaining 855 cases, 12% (n=479) of the cases were clustered only by VNTR, 7.7% (n=305) only by RFLP typing, and 1.8% (n=71) revealed different cluster compositions in the two approaches. A cluster investigation was performed for 87% (n=1,462) of the cases clustered by RFLP. For the 740 cases with confirmed or presumed epidemiological links, 92% were concordant with VNTR typing. In contrast, only 64% of the 722 cases without an epidemiological link but clustered by RFLP typing were also clustered by VNTR typing.”

According to the news editors, the research concluded: “VNTR typing has a discriminatory power equal to IS6110 RFLP typing but is in better agreement with findings in a cluster investigation performed on an RFLP-clustering-based cluster investigation. Both aspects make VNTR typing a suitable method for tuberculosis surveillance systems.”

The news editors report that additional information may be obtained by contacting J.L. de Beer, National Tuberculosis Reference Laboratory, Laboratory for Infectious Diseases and Perinatal Screening (LIS), Centre for Infectious Disease Control (CIB), National Institute for Public Health and the Environment (RIVM), Bilthoven, Netherlands. (2013 Apr 19)

**Johns Hopkins University, Baltimore: Systems approach to tuberculosis vaccine development**

By a News Reporter-Staff News Editor at Life Science Weekly – Data detailed on Mycobacterium Infections have been presented. According to news reporting out of Baltimore, Maryland, by NewsRx editors, research stated, “Tuberculosis is both highly prevalent across the world and eludes our attempts to control it. The current bacillus Calmette-Guerin vaccine has unreliable protection against adult pulmonary tuberculosis.”

Our news journalists obtained a quote from the research from Johns Hopkins University, “As a result, tuberculosis vaccine development has been an ongoing area of research for several decades. Only recently have research efforts resulted in the development of several vaccine candidates that are further along in clinical trials. The majority of the barriers surrounding tuberculosis vaccine development are related to the lack of defined biomarkers for tuberculosis protective immunity and the lack of understanding of the complex interactions between the host and pathogen in the human immune system. As a result, testing various antigens discovered through molecular biology techniques have been only with surrogates of protection and do not accurately predict protective immunity. This review will address new discoveries in latency antigens and new next-generation candidate vaccines that promise the possibility of sterile eradication.”

According to the news editors, the research concluded: “Also discussed are the potentially important roles of systems biology and vaccinomics in shortening development of an efficacious tuberculosis vaccine through utilization of high-throughput technology, computer modelling and integrative approaches.”

Department of Medical Microbiology, Chandigarh: Multiplex polymerase chain reaction using insertion sequence 6110 (IS6110) and mycobacterial protein fraction from BCG of Rm 0.64 in electrophoresis target genes for diagnosis of tuberculous lymphadenitis

By a News Reporter-Staff News Editor at Tuberculosis Week – Fresh data on Mycobacterium Infections are presented in a new report. According to news reporting originating in Chandigarh, India, by NewsRx journalists, research stated, “Tubercular lymphadenitis (TBLA) is a common manifestations of extrapulmonary tuberculosis (EPTB) accounting for 30-40% of cases. Prompt diagnosis and timely initiation of anti-tubercular therapy (ATT) is the key for successful clinical outcome.”

The news reporters obtained a quote from the research from the Department of Medical Microbiology, “This study was carried out to evaluate multiplex polymerase chain reaction (MPCR) using MPB64 and IS6110, and compare with the conventional methods for rapid diagnosis of TBLA. In our study, lymph node fine-needle aspirates of patients were evaluated for TBLA. They were classified as Group I: TBLA group, divided into (a) Confirmed TBLA cases (n0=80): Culture/smear-positive or cytological examination showing presence of epithelioid cell granuloma with or without multinucleate giant cell and caseation necrosis with presence of AFB, and (b) suspected TBLA cases (n=30): Culture/smear-negative and cytological examination showing presence of epithelioid cell granuloma and response to ATT and Group II (Control) (n=25): Patients of lymphadenopathy confirmed to be caused by other diseases such as sarcoidosis, lymphoma, etc., All samples were subjected to conventional tests and MPCR. For MPCR we used Mycobacterium tuberculosis-specific deoxyribonucleic acid sequences specific for the MPB64 and IS6110 region. In the confirmed TBLA group, Ziehl-Neelsen (ZN) smear, cytology, culture, and MPCR positivity was 30%, 70%, 26.3%, and 91.3% respectively. In the suspected TBLA group, smear and culture were negative, and sensitivity of cytology and MPCR was 73.3% and 86.6%, respectively. In the control group all tests were found to be negative, thus giving a specificity of 100% to all the tests in the study.”
According to the news reporters, the research concluded: “Techniques like MPCR with high sensitivity and specificity can play an important role in rapid diagnosis of TBLA.”

For more information on this research see: Multiplex polymerase chain reaction using insertion sequence 6110 (IS6110) and mycobacterial protein fraction from BCG of Rm 0.64 in electrophoresis target genes for diagnosis of tuberculous lymphadenitis. *Indian Journal of Medical Microbiology*, 2013; 31(1):24-8.

Our news correspondents report that additional information may be obtained by contacting K. Sharma, Dept. of Medical Microbiology, PGIMER, Chandigarh, India. *(2013 Apr 15)*

**Isolated posterior instrumentation for selected cases of thoraco-lumbar spinal tuberculosis without anterior instrumentation and without anterior or posterior bone grafting**

By a News Reporter-Staff News Editor at Pain & Central Nervous System Week – Research findings on Spinal Research are discussed in a new report. According to news reporting out of Bangalore, India, by NewsRx editors, research stated, “The aim of this prospective study is the analysis of the clinical and radiological outcomes of active thoraco-lumbar spinal tuberculosis treated with isolated posterior instrumentation without any posterior bone grafting or anterior inter-body bone grafting or anterior instrumentation. The study was a prospective follow-up of 25 patients with active thoraco-lumbar spinal tuberculosis who underwent posterior spinal instrumentation with pedicle screws and rods.”

Our news journalists obtained a quote from the research, “These patients had posterior stabilization of the involved segment of the spine without anterior or posterior bone grafting. The mean duration of follow-up was 3.3 years and the minimum duration of follow-up was 2 years. The mean kyphotic angle improved from 32.4A degrees pre-operatively to 7.2A degrees in the early follow-up period. Following a minor loss of correction during follow-up, the mean kyphotic angle settled at 11.5A degrees at the time of final follow-up. Inter-body bony fusion was noticed at the final follow-up in all patients despite the absence of anterior bone grafting or cages. Posterior instrumented stabilization followed by chemotherapy seems to be adequate for obtaining satisfactory healing of the lesions. Anterior inter-body bony arthrodesis occurs despite the absence of anterior bone grafts or cages.”

According to the news editors, the research concluded: “Careful patient selection is critical for successful outcome with this technique.”
For more information on this research see: Isolated posterior instrumentation for selected cases of thoraco-lumbar spinal tuberculosis without anterior instrumentation and without anterior or posterior bone grafting. *European Spine Journal*, 2013;22(3):624-632. *European Spine Journal* can be contacted at: Springer, 233 Spring St, New York, NY 10013, USA. (Springer - www.springer.com; European Spine Journal - [http://www.springerlink.com/content/0940-6719/](http://www.springerlink.com/content/0940-6719/))

Our news journalists report that additional information may be obtained by contacting M.N. Kumar, Hosmat Hosp, Bangalore 560025, Karnataka, India. (2013 Apr 08)

**Comprehensive tuberculosis screening program in patients with inflammatory arthritides treated with golimumab, a human antitumor necrosis factor antibody, in phase III clinical trials**

By a News Reporter-Staff News Editor at Clinical Trials Week – Investigators discuss new findings in Drugs and Therapies. According to news originating from Spring House, Pennsylvania, by NewsRx correspondents, research stated, “Reactivation of Mycobacterium tuberculosis infection is a major complication in patients treated with antitumor necrosis factor (anti-TNF) agents. We report on the 5 cases of active tuberculosis (TB) that developed in the Golimumab Phase III Program (3 with rheumatoid arthritis, 1 with psoriatic arthritis, and 1 with ankylosing spondylitis) through 1 year among 2,210 patients receiving golimumab.”

Our news journalists obtained a quote from the research, “Data from global studies were used for an in-depth evaluation of the 5 cases of TB through week 52. Integrated safety data were evaluated for potential hepatotoxicity in patients treated with anti-TB therapy. No active TB developed among 317 patients receiving golimumab and treated for latent TB with isoniazid. Active TB occurred in 5 patients not treated with isoniazid by week 52 (in 2 patients by week 24); all of the patients had negative TB screening tests (per the local guidelines) and resided in countries with high background rates of TB. No deaths were due to TB. Across all of the groups (placebo and golimumab), alanine aminotransferase and aspartate aminotransferase elevations occurred in greater proportions of patients treated for latent TB infection versus not treated; elevations were largely mild (<3 times the upper limit of normal). Comprehensive TB screening kept the number of active TB cases relatively low despite conducting the studies in TB-endemic regions. Treatment for latent TB infection appeared effective, since no patients treated for latent TB had TB reactivation. Concurrent treatment with golimumab and anti-TB medication was generally well tolerated.”
According to the news editors, the research concluded: “Clinicians should remain vigilant for development of active TB after initiation of TNF inhibitors, since prompt diagnosis and treatment can improve outcomes.”


The news correspondents report that additional information may be obtained from E.C. Hsia, Janssen Res & Dev LLC, Spring House, PA 19477, United States. (2013 Apr 01)

Imperial College Healthcare NHS Trust, London: Community-based evaluation of immigrant tuberculosis screening using interferon gamma release assays and tuberculin skin testing: observational study and economic analysis

By a News Reporter-Staff News Editor at Economics Week – Researchers detail new data in Mycobacterium Infections. According to news reporting originating from London, United Kingdom, by Vertical-News correspondents, research stated, “UK tuberculosis (TB) notifications are rising due to disease in the immigrant population. National screening guidelines have been revised but cost-effectiveness analyses are hampered by the lack of data on the comparative performance of tuberculin skin tests (TSTs) and interferon release assays (IGRAs) in immigrants.”

Our news editors obtained a quote from the research from Imperial College Healthcare NHS Trust, “Three-way evaluation of TSTs and two IGRAs (QuantiFERON Gold in-tube (QFN-GIT) and T-SPOT. TB) in immigrants aged >= 16 years to quantify test positivity, concordance and factors associated with positivity. Yields were computed at different incidence thresholds and the relative cost-effectiveness of screening was estimated using different latent TB infection (LTBI) screening modalities at varying incidence thresholds with or without port-of-arrival chest x-ray (CXR). Results 231 immigrants were included; median age 29 (IQR 24-37). TSTs were accepted by 80.9%, read in 93.5% and 30.3% were positive - QFN-GIT and T-SPOT. TB positive in 16.6% and 22.5% respectively. Positive TSTs, QFN-GIT and T-SPOT.
TB were independently associated with increasing TB incidence in immigrants’ countries of origin (p=0.007, 0.007, 0.037 respectively). Implementing current guidance (threshold 40/100 000 per year) would identify 98-100% of LTBIIs (depending on test) but entail testing 97-99% of the cohort; screening at 150/100 000 per year would identify 49-71% of LTBIIs but only entail screening half the cohort. The two most cost-effective screening strategies were no port-of-entry chest radiography and screen with single-step QFN-GIT at 250/100 000 per year (incremental cost-effectiveness ratio (ICER)) 21 pound 565.3/case averted; and no port-of-entry CXR and screen with single-step QFN-GIT at 150/100 000 per year (averted additional 7.8 TB cases; ICER 31 pound 867.1/case averted). UK immigrant screening could cost-effectively and safely eliminate mandatory CXR on arrival by emphasising systematic screening for LTBI with single-step IGRA.”

According to the news editors, the research concluded: “Intermediate incidence thresholds balance the need to identify as many imported LTBIIs as possible against limited service capacity.”


The news editors report that additional information may be obtained by contacting M. Pareek, Imperial Coll Healthcare NHS Trust, St. Mary’s Hospital, Chest & Allergy Clin, London W2 1NY, United Kingdom. (2013 Mar 29)

**Autonomous University, Barcelona: Tuberculosis diagnosed in a rural setting in Angola. Accuracy of follow-up sputum smears to predict outcome**

By a News Reporter-Staff News Editor at Tuberculosis Week – Current study results on Pathogens and Global Health have been published. According to news originating from Barcelona, Spain, by NewsRx correspondents, research stated, “To analyze treatment outcome and the accuracy of positive sputum smear at 2 months to predict treatment failure in a cohort of patients with tuberculosis (TB) in a rural setting in Angola. Observational study of patients with TB from January 2009 to August 2010 in Hospital Nossa Senhora da Paz in Angola.”

Our news journalists obtained a quote from the research from Autonomous University, “A multivariate analysis was performed to identify variables associated with treatment failure and death. Sensitivity, specificity, positive and negative predictive values and likelihood
ratios to define the accuracy of a positive sputum smear at 2 months to predict treatment failure were calculated. One thousand four hundred and twenty-five patients were diagnosed with TB. Overall, 526 patients were cured from TB and 419 had treatment completed, so 945 (66.3%) patients achieved treatment success. The outcomes of the remaining patients were: 91 (6.4%) had treatment failure, 100 (7%) died, 49 (3.4%) interrupted treatment, and 240 (16.8%) were transferred out.

Variables associated with a higher risk of treatment failure were previously treated patients (odds ratio, 2.36; 95% confidence interval, 1.32-4.2) and positive sputum smear at 2 months (odds ratio, 9.81; 95% confidence interval, 5.88-16.36). Among the group of 551 patients with sputum smear confirmed at diagnosis and specimens taken at 2 and 5 months, the positive predictive value (31%) and the positive likelihood ratio (3.21) of a positive sputum smear taken at 2 months to predict treatment failure were low. Patients with positive sputum smear at 2 months have a higher risk of treatment failure.”

According to the news editors, the research concluded: “However, this by itself is a poor predictor of treatment failure.”


The news correspondents report that additional information may be obtained from T. Lopez, Autonomous Univ Barcelona, Vall dHebron Hosp, Dept. of Microbiol, Barcelona, Spain. (*2013 Mar 25*)

**University of Otago, Dunedin: Interferon-gamma ELISPOT as a Biomarker of Treatment Efficacy in Latent Tuberculosis Infection A Clinical Trial**

By a News Reporter-Staff News Editor at Clinical Trials Week – Fresh data on Drugs and Therapies are presented in a new report. According to news reporting originating from Dunedin, New Zealand, by NewsRx correspondents, research stated, “Biomarkers that can be used to evaluate new interventions against latent tuberculosis infection (LTBI) and predict reactivation TB disease are urgently required. To evaluate ESAT-6 and CFP-10 (EC) IFN-gamma ELISPOT as a biomarker for treatment efficacy in LTBI.”

Our news editors obtained a quote from the research from the University of Otago, “This was a randomized, blinded, and placebo-controlled trial of INH in EC ELISPOT and Mantoux test positive participants. Participants received a 6-month course of 900 mg INH twice
weekly or a matching placebo. INH acetylator genotypes were determined and urine tested for INH metabolites to confirm adherence. The proportion of positive responders for CFP-10 and ESAT-6 between treatment arms was compared using mixed effects logistic regression models. A Tweedie (compound Poisson) model was fitted to allow for zero inflation and overdispersion of quantitative response. The proportions of EC ELISPOT-positive subjects reduced over time (P < 0.001) but did not differ by study arm (P = 0.36). Median spot-forming units for ESAT-6 and CFP-10 also declined significantly with time (P < 0.001) but did not differ by study arm (P = 0.74 and 0.71, respectively). There was no evidence of an interaction between acetylator status and INH treatment with respect to ELISPOT results over time. In contacts with LTBI, INH therapy plays no role in observed decreases in Mycobacterium tuberculosis antigen specific T-cell responses over time. IFN-gamma ELISPOT is probably not a useful biomarker of treatment efficacy in LTBI.”

According to the news editors, the research concluded: “Clinical trial registered with www.clinicaltrials.gov (NCT 00130325).”


The news editors report that additional information may be obtained by contacting I.M. Adetifa, University of Otago, Sch Med, Dept. of Prevent & Social Med, Center Int Hlth, Dunedin, New Zealand. (2013 Mar 25)

Centers for Disease Control and Prevention, Vancouver:
Therapeutic drug monitoring in the treatment of tuberculosis: a retrospective analysis

By a News Reporter-Staff News Editor at Biotech Week – Research findings on Mycobacterium Infections are discussed in a new report. According to news reporting originating from Vancouver, Canada, by NewsRx correspondents, research stated, “Tuberculosis (TB) in-patient treatment unit in Vancouver, Canada. To examine the results of therapeutic drug monitoring (TDM) in anti-tuberculosis treatment.”

Our news editors obtained a quote from the research from Centers for Disease Control and Prevention, “We performed a retrospective analysis of TDM data from 2000 to 2010. All in-patients treated for TB with TDM performed during their treatment course were included. TDM was performed on 52 patients in 76 treatment episodes from 2000 to 2010. Overall, 103/213 (48.4%) drug levels measured were low, and 5/213 (2.3%) were high. At least one drug level was low in 47/52 (90.3%)
patients. Initial serum levels were low in respectively 76.6% and 68.4% of isoniazid (INH) and rifampicin (RMP) levels. In contrast, only 2.9% of initial pyrazinamide levels were low. Five patients with a susceptible strain on initial presentation later developed drug-resistant disease, with all five patients demonstrating at least one low drug level and two demonstrating multiple low levels. Dose adjustments were made in response to 26 INH and RMP levels, with variable serum responses. In this population with high rates of treatment failure and acquired resistance, we demonstrate that most patients had low drug levels.”

According to the news editors, the research concluded: “Prospective studies are required to examine the relationship between drug levels and clinical outcomes.”


The news editors report that additional information may be obtained by contacting L. Van Tongeren, British Columbia Center Dis Control, Clin Prevent Serv, Vancouver, BC, Canada. (2013 Mar 13)

**Detection of resistance to second-line antituberculosis drugs by use of the genotype MTBDRsl assay: a multicenter evaluation and feasibility study**

By a News Reporter-Staff News Editor at Life Science Weekly – Research findings on Clinical Microbiology are discussed in a new report. According to news originating from Samara, Russia, by NewsRx correspondents, research stated, “The rate of multidrug-resistant (MDR) and extensively drug-resistant (XDR) tuberculosis (TB) has been steadily increasing in countries of the former USSR. The availability of rapid and reliable methods for the detection of drug resistance to second-line drugs is vital for adequate patient management.”

Our news journalists obtained a quote from the research, “We evaluated the performance of the Genotype MTBDRsl assay compared to that of phenotypic drug susceptibility testing (Becton Dickinson Bactec MGIT 960 system) with a test panel of 200 *Mycobacterium tuberculosis* isolates at four sites in Eastern Europe. The interpretability of the Genotype MTBDRsl assay was over 95%. The sensitivity for the detection of resistance to fluoroquinolones, ethambutol, amikacin, and capreomycin varied between 77.3% and 92.3%; however, it was much lower for kanamycin (42.7%). The sensitivity for the detection of XDR TB was 22.6%. The test specificity was over 82% for all drugs. The assay
presents a good screening tool for the rapid detection of resistance to individual second-line drugs and can be recommended for use in countries with a high burden of MDR/XDR TB.”

According to the news editors, the research concluded: “The sensitivity for the detection of kanamycin resistance needs improvement.”


The news correspondents report that additional information may be obtained from O. Ignatyeva, Samara Oblast Tuberculosis Dispensary, Samara, Russia. (2013 Mar 12)

**Oswaldo Cruz Foundation, Rio de Janeiro: Feasibility study of a smoking cessation intervention in Directly Observed Therapy Short-Course tuberculosis treatment clinics in Rio de Janeiro, Brazil**

By a News Reporter-Staff News Editor at Clinical Trials Week – Current study results on Drugs and Therapies have been published. According to news reporting originating in Rio de Janeiro, Brazil, by NewsRx journalists, research stated, “A pilot feasibility study was conducted to determine whether Directly Observed Therapy Short-Course (DOTS) workers could be trained to deliver smoking cessation counseling and referral interventions, identify potential barriers to a full-scale randomized controlled trial on the effectiveness of integrated smoking cessation in DOTS, and determine whether tuberculosis (TB) patients who smoke would agree to participate in such a program. DOTS providers in two Rio de Janeiro primary health clinics received 1-day training in cessation counseling.”

The news reporters obtained a quote from the research from Oswaldo Cruz Foundation, “They completed pre- and post-training surveys and participated in post-program focus groups. Patients were surveyed 3 months after program completion, and semiquantitative urine assays for cotinine were used to confirm cessation. Providers’ mean self-efficacy scores for cessation counseling improved significantly (advise to quit, assess readiness, assist with quitting, and arrange follow-up) from scores (on a scale of 1-5) of 2-3 pre-training to 3-4 post-training (P < 0.05), with only ability to change motivation not significant. Providers’ knowledge about cessation (withdrawal, nicotine replacement therapy, precontemplation) was low before training and did not improve after training (P > 0.1 for all comparisons). Implementation of a smoking cessation intervention by DOTS providers in TB clinics in Brazil is feasible. Randomized controlled trials to test intervention effectiveness in
reducing TB-related morbidity must include cross-training for tobacco control and TB providers.”

According to the news reporters, the research concluded: “Smoking cessation in DOTS programs may be important in reducing the global burden of TB, improving the health of TB patients, and reducing TB transmission in households.”


Our news correspondents report that additional information may be obtained by contacting A.B. Sereno, Fundacao Oswaldo Cruz, Natl Public Hlth Sch, Rio De Janeiro, Brazil. (2013 Mar 11)

National Institutes of Health, Bethesda: SQ109 targets MmpL3, a membrane transporter of trehalose monomycolate involved in mycolic acid donation to the cell wall core of Mycobacterium tuberculosis

By a News Reporter-Staff News Editor at Health & Medicine Week – Current study results on Antimicrobial Agents and Chemotherapy have been published. According to news reporting from Bethesda, Maryland, by NewsRx journalists, research stated, “SQ109, a 1,2-diamine related to ethambutol, is currently in clinical trials for the treatment of tuberculosis, but its mode of action remains unclear. Here, we demonstrate that SQ109 disrupts cell wall assembly, as evidenced by macromolecular incorporation assays and ultrastructural analyses.”

The news correspondents obtained a quote from the research from the National Institutes of Health, “SQ109 interferes with the assembly of mycolic acids into the cell wall core of Mycobacterium tuberculosis, as bacilli exposed to SQ109 show immediate inhibition of trehalose dimycolate (TDM) production and fail to attach mycolates to the cell wall arabinogalactan. These effects were not due to inhibition of mycolate synthesis, since total mycolate levels were unaffected, but instead resulted in the accumulation of trehalose monomycolate (TMM), the precursor of TDM and cell wall mycolates. In vitro assays using purified enzymes showed that this was not due to inhibition of the secreted Ag85 mycolyltransferases. We were unable to achieve spontaneous generation of SQ109-resistant mutants; however, analogs of this compound that resulted in similar shutdown of TDM synthesis with concomitant
TMM accumulation were used to spontaneously generate resistant mutants that were also cross-resistant to SQ109. Whole-genome sequencing of these mutants showed that these all had mutations in the essential mmpL3 gene, which encodes a transmembrane transporter.

According to the news reporters, the research concluded: “Our results suggest that MmpL3 is the target of SQ109 and that MmpL3 is a transporter of mycobacterial TMM.”

For more information on this research see: SQ109 targets MmpL3, a membrane transporter of trehalose monomycolate involved in mycolic acid donation to the cell wall core of Mycobacterium tuberculosis. *Antimicrobial Agents and Chemotherapy*, 2012;56(4):1797-809. (American Society for Microbiology - www.asm.org; Antimicrobial Agents and Chemotherapy - aac.asm.org)

Our news journalists report that additional information may be obtained by contacting K. Tahlan, Tuberculosis Research Section, Laboratory of Clinical Infectious Diseases, National Institute for Allergy and Infectious Disease, National Institutes of Health, Bethesda, Maryland, United States. (2013 Mar 01)

**University of Minnesota, Minneapolis: Population pharmacokinetics of rifampicin in Mexican patients with tuberculosis**

By a News Reporter-Staff News Editor at Biotech Week – A new study on Pharmacy is now available. According to news reporting from Minneapolis, Minnesota, by NewsRx journalists, research stated, “What is known and Objective: Rifampicin (RIF) shows wide variability in its pharmacokinetics. The purpose of this study was to develop and validate a population pharmacokinetic model to characterize the inter- and intra-individual variability in pharmacokinetic parameters of RIF in Mexican patients.”

The news correspondents obtained a quote from the research from the University of Minnesota, “Ninety-four patients receiving antituberculosis therapy participated in this prospective study. Plasma concentration-time data were described using a one-compartment model with lag time, absorption and first-order elimination. The potential influence of demographic and clinical characteristics of the patients, and the pharmaceutical formulation (A, B, C and D) on the pharmacokinetics parameters, was evaluated by non-linear mixed-effect modelling (nonmem). Seventy-seven additional patients participated in the validation of the model. The final population pharmacokinetic model obtained was as follows: apparent clearance CL/F = 8.17 L/h (1.40 as high for males), apparent distribution volume Vd/F = 50.1 L (1.29 as high for males), absorption rate constant KaA = 0.391/h, KaB,C,D = 2.70/h, relative bioavailability FA = 0.468, FB,C,D = 1, lag time in the absorption
phase Tlag = 0.264 h. The final model improved the precision on the parameter estimates (CL/F, Vd/F and Ka by 31.9%, 16.7% and 92.9%, respectively). The residual variability was 27.3%. What is new and Conclusion: Gender was associated with changes in CL/F and Vd/F whereas the pharmaceutical formulation was associated with changes in F and altered the Ka."

According to the news reporters, the research concluded: “The validation data set showed that the model could be used in clinical practice for Bayesian dose adjustment of RIF in TB patients.”


Our news journalists report that additional information may be obtained by contacting R.C.M. Segovia, University of Minnesota, Coll Pharm, Minneapolis, MN 55455, United States. (2013 Feb 13)

**University of Edinburgh, Midlothian: Vitamin D and solar ultraviolet radiation in the risk and treatment of tuberculosis**

By a News Reporter-Staff News Editor at Tuberculosis Week – Investigators publish new report on Infectious Diseases. According to news originating from Midlothian, United Kingdom, by NewsRx correspondents, research stated, “Improved understanding of the association between tuberculosis and vitamin D is needed to inform clinical practice. Vitamin D has both immunostimulatory and immunosuppressive effects relevant to human antimycobacterial responses.”

Our news journalists obtained a quote from the research from the University of Edinburgh, “Ultraviolet radiation, the main source of vitamin D, also induces immunomodulation and could affect the relation between vitamin D and tuberculosis. Clinical trials of vitamin D supplementation in patients with tuberculosis have produced largely negative results, prompting the review of dosing regimens-an explanation for low 25-hydroxyvitamin D status in patients with active tuberculosis is also needed. The reporting of vitamin D deficiency needs to address assay inaccuracies, rising thresholds to define sufficiency, and scarce knowledge of the concentrations needed for optimum immune responses. Future research to measure the effect of the inflammatory setting on serum concentrations of 25-hydroxyvitamin D, at tuberculosis diagnosis and during recovery, could help to account for 25-hydroxyvitamin D changes
in these concentrations in patients with tuberculosis. Studies into the role of vitamin D supplementation in latent tuberculosis justify clinical trials in this population, but pose methodological challenges.”

According to the news editors, the research concluded: “Vitamin D trials in patients with active tuberculosis should be done in well selected populations using adequate vitamin D doses, although such doses remain undefined.”


The news correspondents report that additional information may be obtained from A.R. Ralph, University of Edinburgh, Sch Med, Edinburgh, Midlothian, United Kingdom. (2013 Feb 11)

**Bill and Melinda Gates Foundation, Seattle: Distinct Phases of Blood Gene Expression Pattern Through Tuberculosis Treatment Reflect Modulation of the Humoral Immune Response**

By a News Reporter-Staff News Editor at Biotech Business Week – Researchers detail new data in Drugs and Therapies. According to news reporting out of Seattle, Washington, by NewsRx editors, research stated, “Accurate assessment of treatment efficacy would facilitate clinical trials of new antituberculosis drugs. We hypothesized that early alterations in peripheral immunity could be measured by gene expression profiling in tuberculosis patients undergoing successful conventional combination treatment.”

Our news journalists obtained a quote from the research from Bill and Melinda Gates Foundation, “Ex vivo blood samples from 27 pulmonary tuberculosis patients were assayed at diagnosis and during treatment. RNA was processed and hybridized to Affymetrix GeneChips, to determine expression of over 47 000 transcripts. There were significant &gt;= 2-fold changes in expression of &gt;4000 genes during treatment. Rapid, large-scale changes were detected, with down-regulated expression of 1261 genes within the first week, including inflammatory markers such as complement components C1q and C2. This was followed by slower changes in expression of different networks of genes, including a later increase in expression of B-cell markers, transcription factors, and signaling molecules. The fast initial down-regulation of expression of inflammatory mediators coincided
with rapid killing of actively dividing bacilli, whereas slower delayed changes occurred as drugs acted on dormant bacilli and coincided with lung pathology resolution.”

According to the news editors, the research concluded: “Measurement of biosignatures during clinical trials of new drugs could be useful predictors of rapid bactericidal or sterilizing drug activity, and would expedite the licensing of new treatment regimens.”


Our news journalists report that additional information may be obtained by contacting J.M. Cliff, Bill & Melinda Gates Fdn, Seattle, WA, United States. (2013 Feb 04)

**Shandong University, Jinan: Recent advances in the research of heterocyclic compounds as antitubercular agents**

By a News Reporter-Staff News Editor at Clinical Trials Week – Current study results on Mycobacterium Infections have been published. According to news reporting originating in Jinan, People’s Republic of China, by NewsRx journalists, research stated, “Tuberculosis (TB) is a major health problem, with approximately one-third of the world’s population infected with *Mycobacterium tuberculosis*, eight million people in the active disease state, and two million dying annually. Furthermore, the prevalence of TB/HIV co-infection, and the emergence of multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) have further aggravated the spread of this disease and thus mortality by it.”

The news reporters obtained a quote from the research from Shandong University, “There is an urgent need for novel antitubercular agents with improved properties, such as lower toxicity, shortened duration of therapy, rapid bactericidal action, and enhanced activity against MDR strains. Fortunately, a number of new potential antitubercular candidate drugs with heterocyclic rings, which are most likely to be effective against resistant strains, have entered clinical trials in recent years.”

According to the news reporters, the research concluded: “This review highlights recent advances in the research of novel heterocyclic compounds, with particular focus on their antimycobacterial activity,
mechanisms of action, toxicity, and structure-activity relationships (SARs).”


Our news correspondents report that additional information may be obtained by contacting M. Yan, Dept. of Medicinal Chemistry, Key Laboratory of Chemical Biology (Ministry of Education), School of Pharmaceutical Sciences, Shandong University, 44 West Culture Road, Jinan 250012, People’s Taiwan. (*2013 Feb 04*)

**University of Sao Paulo, Ribeirao Preto:**

*Antigen-presenting cells transfected with Hsp65 messenger RNA fail to treat experimental tuberculosis*

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators publish new report on Medical Research. According to news reporting out of Ribeirao Preto, Brazil, by NewsRx editors, research stated, “In the last several years, the use of dendritic cells has been studied as a therapeutic strategy against tumors. Dendritic cells can be pulsed with peptides or full-length protein, or they can be transfected with DNA or RNA.”

Our news journalists obtained a quote from the research from the University of Sao Paulo, “However, comparative studies suggest that transfecting dendritic cells with messenger RNA (mRNA) is superior to other antigen-loading techniques in generating immunocompetent dendritic cells. In the present study, we evaluated a new therapeutic strategy to fight tuberculosis using dendritic cells and macrophages transfected with Hsp65 mRNA. First, we demonstrated that antigen-presenting cells transfected with Hsp65 mRNA exhibit a higher level of expression of co-stimulatory molecules, suggesting that Hsp65 mRNA has immunostimulatory properties. We also demonstrated that spleen cells obtained from animals immunized with mock and Hsp65 mRNA-transfected dendritic cells were able to generate a mixed Th1/Th2 response with production not only of IFN-gamma but also of IL-5 and IL-10. In contrast, cells recovered from mice immunized with Hsp65 mRNA-transfected macrophages were able to produce only IL-5. When mice were infected with Mycobacterium tuberculosis and treated with antigen-presenting cells transfected with Hsp65 mRNA (therapeutic immunization), we did not detect any decrease in the lung bacterial load or any preservation of the lung parenchyma, indicating the inability of transfected cells to confer curative effects against tuberculosis.”
According to the news editors, the research concluded: “In spite of the lack of therapeutic efficacy, this study reports for the first time the use of antigen-presenting cells transfected with mRNA in experimental tuberculosis.”

For more information on this research see: Antigen-presenting cells transfected with Hsp65 messenger RNA fail to treat experimental tuberculosis. *Brazilian Journal of Medical and Biological Research*, 2012;45(12):1183-1194. *Brazilian Journal of Medical and Biological Research* can be contacted at: Assoc Bras Divulg Cientifica, Faculdade Medicina, Sala 21, 14049 Ribeirao Preto, Sao Paulo, 00, Brazil.

Our news journalists report that additional information may be obtained by contacting C.D. Rocha, University of Sao Paulo, Fac Med Ribeirao Preto, Dept. of Patol, BR-14049900 Ribeirao Preto, SP, Brazil. (*2013 Jan 29*)

**Max-Planck-Institute for Infection Biology, Berlin: Recombinant live vaccine candidates against tuberculosis**

By a News Reporter-Staff News Editor at Biotech Week – Fresh data on Biotechnology are presented in a new report. According to news reporting originating in Berlin, Germany, by NewsRx journalists, research stated, “Tuberculosis (TB) remains among the most deadly health threats to humankind despite availability of several potent antibiotics and a vaccine, bacille Calmette-Guerin (BCG). BCG partially protects children but not adults from the disease.”

The news reporters obtained a quote from the research from Max-Planck-Institute for Infection Biology, “Growing knowledge of the molecular basis of infection, immunity, and pathology in TB has driven various approaches, which strive to complement or replace BCG with more effective vaccines. Three recombinant live TB vaccine candidates have entered clinical trials.”

According to the news reporters, the research concluded: “These candidates have been genetically engineered to be attenuated, to over-express TB antigens and/or to secrete bacterial perforins, ultimately seeking to trigger a robust immune response thereby providing long-lasting protection against TB.”


Our news correspondents report that additional information may be obtained by contacting S.H.E. Kaufmann, Max Planck Inst Infect Biol, Dept. of Immunol, D-10117 Berlin, Germany. (*2013 Jan 23*)
University of Texas, San Antonio: Lessons from a randomised clinical trial for multidrug-resistant tuberculosis

By a News Reporter-Staff News Editor at Clinical Trials Week – Fresh data on Drugs and Therapies are presented in a new report. According to news reporting from San Antonio, Texas, by NewsRx journalists, research stated, “The treatment of multidrug-resistant tuberculosis (MDR-TB) is currently based upon expert opinion and findings from case series, rather than upon randomised clinical trials (RCTs). To describe the challenges encountered during an RCT for the treatment of MDR-TB.”

The news correspondents obtained a quote from the research from the University of Texas, “Tuberculosis Trials Consortium Study 30 was a pilot, Phase I/II, double-blind, placebo-controlled, RCT of the safety and tolerability of 16 weeks of daily, low-dose linezolid treatment for MDR-TB. A total of 36 patients, 56% of the target of 64 patients, consented to participate, for an average of 0.69 enrolments per week. Of the 36 patients enrolled, only 25 (69%) completed at least 90 doses of study treatment. Among the 12 (33%) patients who did not complete all 112 doses of the study treatment, the median time to study withdrawal was 15 days (range 0-92). After the study, we discovered discordance between treatment assignment and study drug for at least 9 (25%) of the 36 patients. Recruitment and retention in this MDR-TB clinical trial posed substantial challenges, suggesting the need for a large, multidisciplinary group of study staff to support the participants. Withdrawal tended to occur early in study treatment.”

According to the news reporters, the research concluded: “The discrepancy in assigned study medication reflects the need for stronger administrative controls for study drugs.”

For more information on this research see: Lessons from a randomised clinical trial for multidrug-resistant tuberculosis. *International Journal of Tuberculosis and Lung Disease*, 2012;16(12):1582-1587. *International Journal of Tuberculosis and Lung Disease* can be contacted at: Int Union Against Tuberculosis Lung Disease (I U A T L D), 68 Boulevard Saint-Michel, 75006 Paris, France.

Our news journalists report that additional information may be obtained by contacting N. Padayatchi, Univ Texas Hlth Sci Center San Antonio, San Antonio, TX 78229, United States. (2013 Jan 21)
User engagement with and attitudes towards an interactive SMS reminder system for patients with tuberculosis

By a News Reporter-Staff News Editor at Life Science Weekly – Researchers detail new data in Telemedicine and Telecare. According to news reporting originating from Karachi, Pakistan, by NewsRx correspondents, research stated, “We conducted a qualitative study to understand user perceptions, acceptability and engagement with an interactive SMS reminder system designed to improve treatment adherence for patients with tuberculosis (TB). Patients received daily reminders and were asked to respond after taking their medication.”

Our news editors obtained a quote from the research, “Non-responsive patients were sent up to three reminders a day. We enrolled 30 patients with TB who had access to a mobile phone and observed their engagement with the system for a one-month period. We also conducted semi-structured interviews with 24 patients to understand their experience with the system. Most patients found the reminders helpful and encouraging. The average response rate over the study period was 57%. However, it fell from a mean response rate of 62% during the first ten days to 49% during the last ten days. Response rates were higher amongst females, participants with some schooling, and participants who had sent an SMS message the week prior to enrolment. Non-responsiveness was associated with a lack of access to the owner of the mobile phone, problems with the mobile phone itself and literacy.”

According to the news editors, the research concluded: “Our pilot study suggests that interactive SMS reminders are an acceptable and appreciated method of supporting patients with TB in taking their medication.”


The news editors report that additional information may be obtained by contacting S. Mohammed, Interactive Research and Development, Suite 508, Ibrahim Trade Tower, Main Sharah-e-Faisal, Karachi, Pakistan. *(2013 Jan 15)*
Research Institute, Lucknow: Biological evaluation of novel substituted chloroquinolines targeting mycobacterial ATP synthase

By a News Reporter-Staff News Editor at Clinical Trials Week – Data detailed on Gram-Positive Bacterial Infections have been presented. According to news originating from Lucknow, India, by NewsRx correspondents, research stated, “The ATP synthase of *Mycobacterium tuberculosis* is a validated drug target against which a diarylquinoline drug is under clinical trials. The enzyme is crucial for the viability both of actively replicating and non-replicating/dormant *M. tuberculosis*.”

Our news journalists obtained a quote from the research from Research Institute, “Enzyme levels drop drastically as the bacilli enter dormancy and hence an inhibitor would make the dormant bacilli even more vulnerable. In this study, a set of 18 novel substituted chloroquinolines were screened against *Mycobacterium smegmatis* ATP synthase; 6 compounds with the lowest 50% inhibitory concentration (IC(50)) values (0.36-1.83M) were selected for further in vitro studies. All six compounds inhibited the growth of *M. tuberculosis* H37Rv in vitro, with minimum inhibitory concentrations (MICs) of 3.12g/mL (two compounds) or 6.25g/mL (four compounds). All of them were bactericidal to non-replicating *M. tuberculosis* H37Rv in hypoxic culture; three compounds caused a 2log(10) reduction in CFU counts in 4 days at concentrations of 16 x or 32 x their MICs, compared with a 0.2log(10) reduction by isoniazid and a 4log(10) reduction by rifampicin at 100 x their MICs. The compounds also contributed to a greater reduction in total cellular ATP of the bacilli compared with isoniazid and rifampicin during an exposure time of 18h. The compounds at 100M caused only 5-35% inhibition of mouse liver mitochondrial ATP synthase, leading to selectivity indices ranging from >55-fold to >278-fold.”

According to the news editors, the research concluded: “In vitro cytotoxicity to the Vero cell line measured as the 50% cytotoxic concentration (CC(50)) of the compounds ranged between 55g/mL and &gt;300g/mL.”


The news correspondents report that additional information may be obtained from S.R. Khan, Division of Microbiology, Council of Scientific and Industrial Research (CSIR)-Central Drug Research Institute, Lucknow 226 001, India. (2013 Jan 14)
University of California, San Francisco: Reducing deaths from tuberculosis in antiretroviral treatment programmes in sub-Saharan Africa

By a News Reporter-Staff News Editor at AIDS Weekly – Research findings on Immune System Diseases and Conditions are discussed in a new report. According to news originating from San Francisco, California, by NewsRx correspondents, research stated, “Mortality rates are high in antiretroviral therapy (ART) programmes in sub-Saharan Africa, especially during the first few months of treatment. Tuberculosis (TB) has been identified as a major underlying cause.”

Our news journalists obtained a quote from the research from the University of California, “Under routine programme conditions, between 5 and 40% of adult patients enrolling in ART services have a baseline diagnosis of TB. There is also a high TB incidence during the first few months of ART (much of which is prevalent disease missed by baseline screening) and long-term rates remain several-folds higher than background. We identify three groups of patients entering ART programmes for which different interventions are required to reduce TB-related deaths. First, diagnostic screening is needed in patients who have undiagnosed active TB so that timely anti-TB treatment can be started. This may be greatly facilitated by new diagnostic assays such as the Xpert MTB/RIF assay. Second, patients with a diagnosis of active TB need optimized case management, which includes early initiation of ART (with timing now defined by randomized controlled trials), trimethoprim-sulphamethoxazole prophylaxis and treatment of comorbidity. Third, all remaining patients who are TB-free at enrolment have high ongoing risk of developing TB and require preventive interventions, including optimized immune recovery (with ART ideally started early in the course of HIV infection), isoniazid preventive therapy and infection control to reduce infection risk. Further specific measures are needed to address multidrug-resistant TB (MDR-TB).”

According to the news editors, the research concluded: “Finally, scale-up of all these interventions requires nationally and locally tailored models of care that are patient-centred and provide integrated healthcare delivery for TB, HIV and other comorbidities.”

For more information on this research see: Reducing deaths from tuberculosis in antiretroviral treatment programmes in sub-Saharan Africa. *Aids*, 2012;26(17):2121-2133. *Aids* can be contacted at: Lippincott Williams & Wilkins, 530 Walnut St, Philadelphia, PA 19106-3621, USA. (Lippincott Williams and Wilkins - www.lww.com; Aids - http://journals.lww.com/aidsonline/pages/default.aspx)

The news correspondents report that additional information may be obtained from S.D. Lawn, University of California, Dept. of Med, San Francisco, CA, United States. (2012 Dec 17)
**University of Melbourne, Parkville: Lipidated promiscuous peptides vaccine for tuberculosis-endemic regions**

By a News Reporter-Staff News Editor at Biotech Week – Current study results on Molecular Medicine have been published. According to news reporting originating in Parkville, Australia, by NewsRx journalists, research stated, “Despite nine decades of Bacillus Calmette Guerin (BCG) vaccination, tuberculosis continues to be a major global health challenge. Clinical trials worldwide have proved the inadequacy of the BCG vaccine in preventing the manifestation of pulmonary tuberculosis in adults.”

The news reporters obtained a quote from the research from the University of Melbourne, “Ironically, the efficacy of BCG is poorest in tuberculosis endemic areas. Factors such as nontuberculous or environmental mycobacteria and helminth infestation have been suggested to limit the efficacy of BCG. Hence, in high TB-burden countries, radically novel strategies of vaccination are urgently required. Here we showcase the properties of lipidated promiscuous peptide vaccines that target and activate cells of the innate and adaptive immune systems by employing a Toll-like receptor-2 agonist, S[2,3-bis(palmitoyloxy)propyl]cysteine (Pam2Cys). Such a strategy elicits robust protection and enduring memory responses by type 1 T helper cells (Th1).”

According to the news reporters, the research concluded: “Consequently, lipidated peptides may yield a better vaccine than BCG.”


Our news correspondents report that additional information may be obtained by contacting U. Gowthaman, University of Melbourne, Dept. of Microbiol & Immunol, Parkville, Vic 3052, Australia. (2012 Dec 12)

**Sapienza-University, Latina: Serial interferon-gamma release assays for screening and monitoring of tuberculosis infection during treatment with biologic agents**

By a News Reporter-Staff News Editor at Life Science Weekly – Current study results on Rheumatology have been published. According to news reporting out of Latina, Italy, by NewsRx editors, research stated, “Screening for latent tuberculosis infection (LTBI) prior to the prescribing of anti-TNF agents and monitoring for infection during treatment are recommended. The feasibility of novel screening tools, including
QuantiFERON-TB Gold In-Tube (QFT-GIT), remains unclear in the setting of immunosuppression.”

Our news journalists obtained a quote from the research from Sapienza-University, “The aim of this study was to evaluate the usefulness of serial QFT-GIT during biologic therapy to assess whether dynamic changes in IFN-gamma levels may be helpful in identifying reactivation of LTBI or newly acquired TB. We conducted a prospective study on patient candidates to TNF inhibitors. QFT-GIT was performed at baseline and after 3 and 6 months since biologic onset. A further follow-up period of 6 months was observed. Among patients enrolled (n = 119; F = 69 %; median age = 47 years, range 18-80), 24 had at least 1 risk factor for LTBI. Ninety-six were taking immunosuppressants at the time of TB testing. At baseline, 5 patients displayed positive, 93 negative, and 21 indeterminate QFT-GIT results. We observed QFT-GIT conversions and reversions in 12 patients with LTBI and in 73 without LTBI. QFT-GIT results changed of 28 % at month 3 and of 21 % at month 6; the greatest change was observed in patients with indeterminate results that became negative (15 %; p< 0.02). No TB cases were detected.”

According to the news editors, the research concluded: “The routine use of both QFT-GIT and TST at screening seems not to give any advantage in the setting of patients awaiting biologics. In addition, the feasibility of serial QFT-GIT during biologic therapy needs definition since changes in IFN-gamma levels may occur without a pathologic connotation.”


Our news journalists report that additional information may be obtained by contacting R. Scrivo, Sapienza Univ Roma Polo Pontino, Fdn Eleonora Lorillard Spencer Cenci, UOC Malattie Infett, Latina, Italy. (2012 Dec 11)

University Hospital, Madrid: Cost-effectiveness of different screening strategies (single or dual) for the diagnosis of tuberculosis infection in healthcare workers

By a News Reporter-Staff News Editor at Life Science Weekly – Fresh data on Hospitals are presented in a new report. According to news reporting originating in Madrid, Spain, by NewsRx journalists, research
stated, “To evaluate the cost-effectiveness of a dual strategy of tuberculin skin test (TST) and QuantiFERON-TB Gold (QFT-G) for screening of latent tuberculosis infection (LTBI) in healthcare workers (HCWs) and, as a secondary objective, to study relationships between TST results, QFT-G results, and sociodemographic factors. Cross-sectional prospective study. University hospital in Madrid.”

The news reporters obtained a quote from the research from University Hospital, “A total of 103 HCWs. QFT-G was requested for all positive TST results; QFT-G results were compared with TST results, and their relationships with sociodemographic factors were analyzed. A cost-effectiveness analysis was conducted for the dual strategy (TST/QFT-G) and for TST or QFT alone, taking into account the indication of and compliance with isoniazid, the risk of hepatotoxicity, and postexposure tuberculosis. Of all HCWs studied, 42.3% showed a positive result by QFT-G, and 49.5% had received bacille Calmette-Guerin (BCG) vaccination; no significant association was detected between BCG and QFT-G results. Increased TST was linked to higher positive QFT-G values (TST of 5-9.9 mm, 27.6%; TST of 15 mm or more, 56.5%; [Formula: see text]). The probability of positive QFT-G results was 1.04 times higher for each year of age (odds ratio, 1.04 [95% confidence interval, 1.01-1.09]; [Formula: see text]). The incremental cost per active TB case prevented was lower for TST/QFT-G than for the other strategies studied (&#8364;14,211 per 1,000 HCWs). The number of people treated for LTBI per case of active TB prevented (number needed to treat) for TST/QFT-G was lower than for TST alone (17.2 vs 95.3 and 88.7 with the 5-and 10-mm cutoff value, respectively) or QFT-G alone (69.6).”

According to the news reporters, the research concluded: “Dual strategy with TST/QFT-G is more cost-effective than TST or QFT-G alone for the diagnosis of LTBI in HCWs.”

For more information on this research see: Cost-effectiveness of different screening strategies (single or dual) for the diagnosis of tuberculosis infection in healthcare workers. Infection Control and Hospital Epidemiology, 2012;33(12):1226-34. (University of Chicago Press - press.uchicago.edu; Infection Control and Hospital Epidemiology - /ucp/journals/journal/iche.html)

Our news correspondents report that additional information may be obtained by contacting M.T. Del Campo, Dept. of Occupational Health and Prevention, Fundacion Jimenez Diaz University Hospital, Universidad Autonoma de Madrid, Madrid, Spain. (2012 Dec 11)
University of East Anglia, Norwich: Implementation and community involvement in DOTS strategy: a systematic review of studies in China

By a News Reporter-Staff News Editor at Asia Business Newsweekly – Data detailed on Mycobacterium Infections have been presented. According to news reporting originating in Norwich, United Kingdom, by VerticalNews journalists, research stated, “To summarise data on the implementation of the DOTS strategy in China in terms of actual observation and treatment adherence, and to review the effectiveness of quality improvement interventions for tuberculosis (TB) control in China. We included survey studies that reported data on the implementation of DOTS in China and controlled studies that evaluated TB care in specified communities.”

The news reporters obtained a quote from the research from the University of East Anglia, “We excluded studies outside mainland China, pharmacological intervention trials and reviews. We included 12 survey studies that reported on the performance of TB control services in China. The pooled analysis showed that more than half of TB patients were treated by self-administration (52%) and that only 20% actually had their treatment observed by health workers. We include 85 intervention studies that evaluated the effect of quality improvement interventions. Treatment observers were family members in 37 studies, and health workers in 20 studies. The pooled odds ratio (OR) for cure was 2.48 (95%CI 1.97-3.11, I-2 = 70.9%, P< 0.001); the pooled OR for treatment completion was 2.87 (95%CI 2.23-3.69, I-2 = 66.3%, P< 0.001). Sensitivity analysis found that the estimated treatment effects in meta-analyses using reported and imputed data were much reduced, but still statistically significant. The proportion of TB patients whose treatment was strictly observed was much lower than reported by official statistics in China. The treatment completion rate was not optimal, which may be an important reason for the reported increases in drug resistance.”

According to the news reporters, the research concluded: “Community health personnel have become the main work force for TB control in China.”


Our news correspondents report that additional information may be obtained by contacting W.L. Hou, University of East Anglia, Norwich Med Sch, Fac Med & Hlth Sci, Norwich NR4 7TJ, Norfolk, United Kingdom. (2012 Dec 11)
University College London: Active case finding for pulmonary tuberculosis using mobile digital chest radiography: an observational study

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – Researchers detail new data in Tuberculosis and Lung Disease. According to news reporting from London, United Kingdom, by NewsRx journalists, research stated, “Mobile digital chest radiography (CXR) is used routinely to screen for pulmonary tuberculosis (PTB) in London among homeless populations, persons accessing drug treatment services and prisoners. 1) To establish the sensitivity and specificity of mobile digital CXR, and 2) to test the hypothesis that actively identified cases have reduced odds of sputum smear positivity vs. those presenting passively to health care services from the same populations.”

The news correspondents obtained a quote from the research from University College London, “Sensitivity and specificity were calculated using a gold standard comparator of culture-confirmed cases of PTB reported to the national surveillance system within 90 days of screening. Logistic regression was used to determine whether actively detected cases had reduced odds of smear positivity compared to passively detected cases after adjustment for confounding. The intervention had a sensitivity of 81.8% (95%CI 64.5-93.0) and a specificity of 99.2% (95%CI 99.1-99.3). After adjusting for confounding, there was evidence that cases identified through screening were less likely to be smear-positive than passively identified cases (OR 0.34, 95%CI 0.14-0.85; likelihood ratio test P = 0.022).”

According to the news reporters, the research concluded: “Digital CXR achieves a high level of sensitivity and specificity in an operational setting; targeted mobile radiographic screening can reduce the risk of onward transmission by identifying cases before they become infectious.”


Our news journalists report that additional information may be obtained by contacting A. Story, UCL, Royal Free London, NHS Fdn Trust, Center Resp Med, London, United Kingdom. (2012 Dec 10)
Amsterdam Center for Drug Research, Leiden: Feasibility of a Fixed-Dose Regimen of Pyrazinamide and Its Impact on Systemic Drug Exposure and Liver Safety in Patients with Tuberculosis

By a News Reporter-Staff News Editor at Clinical Trials Week – Investigators discuss new findings in Mycobacterium Infections. According to news reporting from Leiden, Netherlands, by NewsRx journalists, research stated, “Historically, dosing regimens for the treatment of tuberculosis (TB) have been proposed in an empirical manner. Dose selection has often been the result of efficacy trials in which drugs were administered regardless of the magnitude of the effect of demographic factors on drug disposition.”

The news correspondents obtained a quote from the research from Amsterdam Center for Drug Research, “This has created challenges for the prescription of fixed-dose combinations with novel therapeutic agents. The objectives of this investigation were to evaluate the impact of body weight on the overall systemic exposure to pyrazinamide (PZA) and to assess whether the use of one fixed dose, without adjustment according to weight, would ensure target exposure and safety requirements across the overall patient population. Using a population pharmacokinetic model, simulation scenarios were explored based on population demographics from clinical trials in TB patients and on historical hepatotoxicity data. The systemic drug exposure (area under the concentration-time curve [AUC]), peak concentrations (the maximum concentration of drug in serum [C-max]), the time above the MIC (t &gt; MIC), and the risk of hepatotoxicity were evaluated for the current weight-banded regimen and compared to fixed doses under the assumption that pharmacokinetic differences are the primary drivers of toxicity. Evaluation of the standard weight banding reveals that more than 50% of subjects in the weight range of 45 to 55 kg remain below the proposed target exposure to PZA. In contrast, the use of a fixed 1,500-mg dose resulted in a lower proportion of subjects under the target value, with a 0.2% average overall increase in the risk of hepatotoxicity.”

According to the news reporters, the research concluded: “Our results strongly support the use of a fixed-dose regimen for PZA in combination with novel therapeutic agents.”

Howard Hughes Medical Institute, Chevy Chase: Modeling early bactericidal activity inmurine tuberculosis provides insights into the activity of isoniazid and pyrazinamide

By a News Reporter-Staff News Editor at Anti-Infectives Week – Research findings on Mycobacterium Infections are discussed in a new report. According to news originating from Chevy Chase, Maryland, by NewsRx correspondents, research stated, “Standard tuberculosis (TB) treatment includes an initial regimen containing drugs that are both rapidly bactericidal (isoniazid) and sterilizing (rifampin and pyrazinamide), and ethambutol to help prevent the emergence of drug resistance. Antagonism between isoniazid and pyrazinamide has been demonstrated in a TB treatment mouse model.”

Our news journalists obtained a quote from the research from Howard Hughes Medical Institute, “Because isoniazid’s bactericidal activity is greatest during the initial two treatment days, we hypothesized that removing isoniazid after the second day would increase the effectiveness of the standard regimen. To test this hypothesis, we developed a mouse model to measure the early bactericidal activity (EBA) of drug regimens designed to analyze the essentiality of both isoniazid and pyrazinamide during the first 14 d of therapy. Our results clearly indicate that discontinuation of isoniazid after the second day of treatment increases the EBA of standard therapy in the mouse model, whereas omitting pyrazinamide during the first 14 d was detrimental.”

According to the news editors, the research concluded: “Substitution of moxifloxacin for isoniazid on day 3 did not increase the EBA compared with only removing isoniazid after day 2. Our data show that a mouse model can be used to analyze the EBA of TB drugs, and our findings support pursuing clinical trials to evaluate the possible benefit of removing isoniazid after the first 2 treatment days.”

The news correspondents report that additional information may be obtained from J. Grosset, Howard Hughes Med Inst, Chevy Chase, MD 20815, United States. (2012 Nov 26)

BJ Wadia Hospital for Children, Maharashtra: Clinical profile of drug resistant tuberculosis in children

By a News Reporter-Staff News Editor at Pediatrics Week – Data detailed on Pediatrics have been presented. According to news reporting from Maharashtra, India, by VerticalNews journalists, research stated, “This Cross-sectional observational study was conducted to determine the clinical profile of drug-resistant tuberculosis in children. Patients were classified as monoresistant TB, polyresistant TB, multidrug resistant (MDR)-TB and extensively drug resistant (XDR - TB).”

The news correspondents obtained a quote from the research from BJ Wadia Hospital for Children, “We coined a term called as Partial XDR-TB when isolates of Mycobacterium tuberculosis were confirmed to be resistant in vitro to be MDR along with either a fluoroquinolone or an aminoglycoside resistance (apart from streptomycin). Of 500 children analysed, 34 (6.8%) had drug resistant TB. Mean age of presentation was 6.8 +/- 3.2 years (Male: Female ratio 13:21). 18 (52.9%) children had been treated for tuberculosis in the past (1 defaulted), 7 patients had been in contact with an adult suffering from drug resistant TB and 3 patients (10.3%) were HIV co-infected. Fourteen children (41.2 %) had MDR TB, 11 (32.4 %) had Partial XDR, 1 each (2.9 %) had polyresistant TB and XDR TB. Clinical features of DR-TB are similar in all age groups.”

According to the news reporters, the research concluded: “Past history of TB with treatment with antitubercular agents, and contact with adults suffering with drug-resistant TB are important risk factors in development of drug-resistant -TB in children.”

For more information on this research see: Clinical profile of drug resistant tuberculosis in children. *Indian Pediatrics*, 2012;49(9):741-744. *Indian Pediatrics* can be contacted at: Springer India, 7TH Floor, Vijaya Building, 17, Barakhamba Road, New Delhi, 110 001, India. (Springer - www.springer.com; Indian Pediatrics - http://www.springerlink.com/content/0019-6061/)

Our news journalists report that additional information may be obtained by contacting I. Shah, BJ Wadia Hosp Children, Pediat TB Clin, Bombay, Maharashtra, India. (2012 Nov 17)

By a News Reporter-Staff News Editor at Tuberculosis Week – A new study on Medicinal Chemistry is now available. According to news originating from New York City, New York, by NewsRx correspondents, research stated, “Clofazimine (CFZ), a member of the riminophenazine class, has been studied in clinical trials for the treatment of multidrug-resistant tuberculosis (MDR-TB). CFZ has several side effects which can be attributed to its extremely high lipophilicity.”

Our news journalists obtained a quote from the research from Global Alliance for TB Drug Development, “A series of novel riminophenazine analogues bearing a C-2 pyridyl substituent was designed and synthesized with the goal of maintaining potent activity against Mycobacterium tuberculosis (M. tuberculosis) while improving upon its safety profile by lowering the lipophilicity. All compounds were evaluated for their in vitro activity and cytotoxicity. The results demonstrated that many new compounds had potent activity against M. tuberculosis with MICs of less than 0.03 μg/mL and low cytotoxicity with IC50 values greater than 64 μg/mL. Some compounds were tested for in vivo efficacy against MDR-TB in an experimental mouse infection model.”

According to the news editors, the research concluded: “Two compounds demonstrated equivalent or better efficacy than CFZ in this model with significantly reduced skin discoloration potential.”


The news correspondents report that additional information may be obtained from D.F. Zhang, Global Alliance TB Drug Dev, New York, NY 10005, United States. (2012 Nov 12)
Queen Mary University, London: Vitamin D accelerates resolution of inflammatory responses during tuberculosis treatment

By a News Reporter-Staff News Editor at Clinical Trials Week – Current study results on Mycobacterium Infections have been published. According to news reporting out of London, United Kingdom, by NewsRx editors, research stated, “Calcidiol, the major circulating metabolite of vitamin D, supports induction of pleiotropic antimicrobial responses in vitro. Vitamin D supplementation elevates circulating calcidiol concentrations, and thus has a potential role in the prevention and treatment of infection.”

Our news journalists obtained a quote from the research from Queen Mary University, “The immunomodulatory effects of administering vitamin D to humans with an infectious disease have not previously been reported. To characterize these effects, we conducted a detailed longitudinal study of circulating and antigen-stimulated immune responses in ninety-five patients receiving antimicrobial therapy for pulmonary tuberculosis who were randomized to receive adjunctive high-dose vitamin D or placebo in a clinical trial, and who fulfilled criteria for per-protocol analysis. Vitamin D supplementation accelerated sputum smear conversion and enhanced treatment-induced resolution of lymphopaenia, monocytosis, hypercytokinaemia, and hyperchemokinaemia. Administration of vitamin D also suppressed antigen-stimulated proinflammatory cytokine responses, but attenuated the suppressive effect of antimicrobial therapy on antigen-stimulated secretion of IL-4, CC chemokine ligand 5, and IFN-alpha. We demonstrate a previously unappreciated role for vitamin D supplementation in accelerating resolution of inflammatory responses during tuberculosis treatment.”

According to the news editors, the research concluded: “Our findings suggest a potential role for adjunctive vitamin D supplementation in the treatment of pulmonary infections to accelerate resolution of inflammatory responses associated with increased risk of mortality.”


Our news journalists report that additional information may be obtained by contacting A.K. Coussens, Queen Mary University, Barts &
Chhatrapati Shahuji Maharaj Medical University, Uttar Pradesh: Trends of anti-tuberculosis drug resistance pattern in new cases and previously treated cases of extrapulmonary tuberculosis cases in referral hospitals in northern India

By a News Reporter-Staff News Editor at Life Science Weekly – Fresh data on Postgraduate Medicine are presented in a new report. According to news reporting from Uttar Pradesh, India, by NewsRx journalists, research stated, “Drug-resistant tuberculosis is one of major current challenges to global public health. The transmission of resistant strains is increasing as a burden of multidrug-resistant tuberculosis (MDR-TB) patients in extra pulmonary tuberculosis (EPTB) cases in India.”

The news correspondents obtained a quote from the research from Chhatrapati Shahuji Maharaj Medical University, “Aim and Objectives: The aim was to study trends of anti-tuberculosis drug resistance pattern in new cases and previously treated cases of EPTB in referral hospitals in northern India. A prospectively observational study and referral medical institutions in northern India. All EPTB specimens were processed for Ziehl Neelsen staining, BACTEC culture and BACTEC NAP test for Mycobacterium tuberculosis complex. All M. tuberculosis complex isolates were performed for radiometric-based drug susceptibility pattern against streptomycin, isoniazid, rifampicin and ethambutol using the 1% proportion method. We found that 165/756 (20.5%) isolates were identified as M. tuberculosis complex by the NAP test. We observed that 39.9% were resistant to first-line antitubercular drugs. The resistance rate was higher in previously treated patients: H (30.3%), R (16.3%), E (15.7%) and S (16.3%). MDR-TB was observed in 13.4%, but, in new cases, this was 11.4% and 19.1% of the previously treated patients (p <0.05). MDR-TB is gradually increased in EPTB cases and predominant resistance to previous treated cases of EPTB. The molecular drug sensitivity test (DST) method can be an early decision for chemotherapy in MDR-TB patients.”

According to the news reporters, the research concluded: “The International Standards of TB Care need to be used by the RNTCP and professional medical associations as a tool to improve TB care in the country.”

For more information on this research see: Trends of anti-tuberculosis drug resistance pattern in new cases and previously treated cases of extrapulmonary tuberculosis cases in referral hospitals in northern India.

Our news journalists report that additional information may be obtained by contacting A.K. Maurya, Dept. of Pulmonary Medicine, Chhatrapati Shahji Maharaj Medical University, (Erstwhile King George Medical College), Lucknow, Uttar Pradesh, India. (2012 Oct 23)

**University of Stellenbosch, Cape Town: From Magic Mountain to Table Mountain**

By a News Reporter-Staff News Editor at Clinical Trials Week – Investigators publish new report on Mycobacterium Infections. According to news reporting out of Cape Town, South Africa, by NewsRx editors, research stated, “Prior to the introduction of chemotherapy, tuberculosis management relied upon aerotherapy, heliotherapy and good nutrition. This ‘treatment’, exemplified by the regimen applied in Swiss and other European mountain resorts, is described by Thomas Mann in the book ‘The Magic Mountain.’

Our news journalists obtained a quote from the research from the University of Stellenbosch, “Tuberculosis chemotherapy began in 1944 with the introduction of streptomycin and para- amino-salicylic acid, later augmented by isoniazid. Early experience taught physicians that treatment must be given with multiple drugs to prevent emergence of resistance and that prolonged treatment adherence for 18-24 months was needed for a permanent cure of tuberculosis. Between 1970 and 1980 rifampicin was introduced and with pyrazinamide it made ‘short-course’ treatment possible. For 30 years, a 6-month directly observed treatment short-course (DOTS) based on the three compounds isoniazid, rifampicin and pyrazinamide was the foundation of tuberculosis control strategies world-wide, and in recent years this was supplemented with ethambutol in view of increasing rates of isoniazid resistance. However, even 6 months of treatment is too long to easily ensure the compliance necessary to permanently cure tuberculosis. The recent spread of the HIV/AIDS epidemic has placed tuberculosis programmes under severe pressure and is accompanied by an increase in drug-resistance making tuberculosis virtually untreatable in some instances. In 2004 the first of a new generation of anti-tuberculosis drugs entered clinical evaluation. A series of clinical trials, often conducted at sites in Cape Town, South Africa, has shown them to be efficacious and hold promise of being able to shorten tuberculosis treatment and treat drug-resistant tuberculosis.”

According to the news editors, the researchers concluded: “Development and assessment of these drugs is ongoing but there is renewed hope that these new drugs and regimens will assist in finally conquering
tuberculosis, preventing a return to Magic Mountain where sunshine and fresh air was all that could be offered to patients.”

For more information on this research see: From Magic Mountain to Table Mountain. Swiss Medical Weekly, 2012;142():39-47. Swiss Medical Weekly can be contacted at: E M H Swiss Medical Publishers Ltd, Farnsburgerstr 8, Ch-4132 Muttenz, Switzerland.

Our news journalists report that additional information may be obtained by contacting A.H. Diacon, University of Stellenbosch, Dept. of Paediat & Child Hlth, Cape Town, South Africa. (2012 Oct 08)

Johns Hopkins University School of Medicine, Baltimore: New drugs for the treatment of tuberculosis: hope and reality

By a News Reporter-Staff News Editor at Clinical Trials Week – Current study results on Mycobacterium Infections have been published. According to news reporting originating in Baltimore, Maryland, by NewsRx journalists, research stated, “The objective of this review is to report evidence about the efficacy and potential of currently licensed drugs and new molecules beyond pre-clinical development for improving the chemotherapy of tuberculosis (TB). Rifapentine, a rifamycin with low minimum inhibitory concentration, long half-life and potent sterilizing activity in mice did not confirm its potential in a recent short-term clinical trial and is being extensively re-evaluated.”

The news reporters obtained a quote from the research from the Johns Hopkins University School of Medicine, “Moxifloxacin, a fluoroquinolone, improved the activity of the standard drug regimen when substituted for ethambutol (EMB). It is being studied to shorten the duration of treatment for fully drug-susceptible TB (Remox study). Clofazimine, a fat-soluble dye with experimental activity against TB, but used only for leprosy in the last 50 years, requires further study because it has been included in a successful short 9-month combined drug regimen for the treatment of multidrug-resistant TB. The diarylquinoline TMC207 is the most promising among the new TB drugs because of its experimental and clinical rate of culture conversion. Also exciting, 200 mg daily doses in humans of the nitroimidazo-oxazine PA-824 and the nitro-dihydro-imidazooxazole OPC-67683 were safe and induced a bactericidal effect of respectively 0.098 &± 0.072 log(10) and 0.040 &± 0.056 log(10) per day. The new oxazolidinones PNU-100480 and AZD-5847 might be at least as active as linezolid and much less toxic. SQ109 is an EMB analogue that does not have cross-resistance with EMB and might have synergistic activity in combined regimens.”

According to the news reporters, the researchers concluded: “Benzothiazinones and dinitrobenzamides show exciting in vitro antimicrobial activity and deserve careful attention.”

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Our news correspondents report that additional information may be obtained by contacting J.H. Grosset, Center for Tuberculosis Research, Johns Hopkins University School of Medicine, Baltimore, Maryland 21231, United States. (2012 Sep 24)

University Hospital, Florence: Serial T-spot.tb and quantiferon-tb-gold in-tube assays to monitor response to antitubercular treatment in Italian children with active or latent tuberculosis infection

By a News Reporter-Staff News Editor at Life Science Weekly – A new study on Tuberculosis is now available. According to news reporting originating in Florence, Italy, by NewsRx journalists, research stated, “We performed a prospective study to investigate T-SPOT.TB and QuantiFERON-TB Gold In-Tube (QFT-G-IT) dynamics during antitubercular treatment in active tuberculosis (TB) or latent TB. Eighteen children with latent TB and 26 with TB were enrolled.”

The news reporters obtained a quote from the research from University Hospital, “At 6 months of follow-up reversion rate was 5.88% (95% CI:0-13.79) for QFT-G-IT; 9.09% (95% CI:0.59-17.58) for T-SPOT.TB (p=0.921) in TB cases. Significant decline in quantitative response was observed exclusively in TB cases.”

According to the news reporters, the researchers concluded: “Our results suggest that serial IGRA have limited use in children receiving antitubercular treatment.”

For more information on this research see: Serial T-spot.tb and quantiferon-tb-gold in-tube assays to monitor response to antitubercular treatment in Italian children with active or latent tuberculosis infection. The Pediatric Infectious Disease Journal, 2012;31(9):974-7.

Our news correspondents report that additional information may be obtained by contacting E. Chiappini, From the Dept. of Science for Woman and Child Health, Meyer University Hospital, Florence, Italy. (2012 Sep 04)
University of Michigan, Ann Arbor: Comparison of the Predicted Population Coverage of Tuberculosis Vaccine Candidates Ag85B-ESAT-6, Ag85B-TB10.4, and Mtb72f via a Bioinformatics Approach

By a News Reporter-Staff News Editor at Biotech Week – New research on Immunization is the subject of a report. According to news reporting from Ann Arbor, Michigan, by NewsRx journalists, research stated, “The Bacille-Calmette Guerin (BCG) vaccine does not provide consistent protection against adult pulmonary tuberculosis (TB) worldwide. As novel TB vaccine candidates advance in studies and clinical trials, it will be critically important to evaluate their global coverage by assessing the impact of host and pathogen variability on vaccine efficacy.”

The news correspondents obtained a quote from the research from the University of Michigan, “In this study, we focus on the impact that host genetic variability may have on the protective effect of TB vaccine candidates Ag85B-ESAT-6, Ag85B-TB10.4, and Mtb72f. We use open-source epitope binding prediction programs to evaluate the binding of vaccine epitopes to Class I HLA (A, B, and C) and Class II HLA (DRB1) alleles. Our findings suggest that Mtb72f may be less consistently protective than either Ag85B-ESAT-6 or Ag85B-TB10.4 in populations with a high TB burden, while Ag85B-TB10.4 may provide the most consistent protection.”

According to the news reporters, the researchers concluded: “The findings of this study highlight the utility of bioinformatics as a tool for evaluating vaccine candidates before the costly stages of clinical trials and informing the development of new vaccines with the broadest possible population coverage.”

For more information on this research see: Comparison of the Predicted Population Coverage of Tuberculosis Vaccine Candidates Ag85B-ESAT-6, Ag85B-TB10.4, and Mtb72f via a Bioinformatics Approach. Plos One, 2012;7(7):e40882. (Public Library of Science - www.plos.org; Plos One - www.plosone.org)

Our news journalists report that additional information may be obtained by contacting J. Davila, Dept. of Epidemiology, School of Public Health, University of Michigan, Ann Arbor, Michigan, United States. (2012 Aug 15)
Johns Hopkins University School of Medicine, Baltimore: Dose-ranging comparison of rifampin and rifapentine in two pathologically distinct murine models of tuberculosis

By a News Reporter-Staff News Editor at Clinical Trials Week – Current study results on Mycobacterium Infections have been published. According to news reporting originating from Baltimore, Maryland, by NewsRx correspondents, research stated, “In previous experiments, replacing the 10-mg/kg of body weight daily dose of rifampin with 7.5 to 10 mg/kg of rifapentine in combinations containing isoniazid and pyrazinamide reduced the duration of treatment needed to cure tuberculosis in BALB/c mice by approximately 50% due to rifapentine’s more potent activity and greater drug exposures obtained. In the present study, we performed dose-ranging comparisons of the bactericidal and sterilizing activities of rifampin and rifapentine, alone and in combination with isoniazid and pyrazinamide with or without ethambutol, in BALB/c mice and in C3HeB/FeJ mice, which develop necrotic lung granulomas after infection with Mycobacterium tuberculosis.”

Our news editors obtained a quote from the research from the Johns Hopkins University School of Medicine, “Each rifamycin demonstrated a significant increase in sterilizing activity with increasing dose. Rifapentine was roughly 4 times more potent in both mouse strains. These results reinforce the rationale for ongoing clinical trials to ascertain the highest well-tolerated doses of rifampin and rifapentine.”

According to the news editors, the researchers concluded: “This study also provides an important benchmark for the efficacy of the first-line regimen in C3HeB/FeJ mice, a strain in which the lung lesions observed after M. tuberculosis infection may better represent the pathology of human tuberculosis.”

For more information on this research see: Dose-ranging comparison of rifampin and rifapentine in two pathologically distinct murine models of tuberculosis. Antimicrobial Agents and Chemotherapy, 2012;56(8):4331-40. (American Society for Microbiology - www.asm.org; Antimicrobial Agents and Chemotherapy - aac.asm.org)

The news editors report that additional information may be obtained by contacting I.M. Rosenthal, Center for Tuberculosis Research, Dept. of Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland, United States. (2012 Aug 13)
University of California, San Francisco: Isoniazid vs. rifampin for latent tuberculosis infection in jail inmates: toxicity and adherence

By a News Reporter-Staff News Editor at Clinical Trials Week – Current study results on Mycobacterium Infections have been published. According to news originating from San Francisco, California, by NewsRx correspondents, researchers stated “This open-label randomized trial compared isoniazid (9 months) to rifampin (4 months) on toxicity and completion in a jailed population with latent tuberculosis infection. Rifampin resulted in fewer elevated liver function tests (risk ratio [RR] 0.39, 95% confidence interval [CI] [0.18, 0.86]) and less toxicity requiring medication withdrawal (RR 0.51, 95% CI [0.13, 2.01]), although one participant receiving rifampin experienced an allergic reaction.”

Our news journalists obtained a quote from the research by the authors from the University of California, “Completion was achieved for 33% receiving rifampin compared to 26% receiving isoniazid (p=.10). With careful monitoring rifampin is a safe and less toxic regimen and appears to be a reasonable alternative because of its shorter duration, allowing more people to complete treatment behind bars.”

According to the news editors, the researchers concluded: “Therapy completion in released inmates is unacceptably low and ensuring follow-up after discharge must be part of a decision to treat.”


The news correspondents report that additional information may be obtained from M.C. White, Dept. of Community Health Systems, School of Nursing, University of California, San Francisco, CA 94143, United States.

The publisher’s contact information for the *Journal of Correctional Health Care* is: SAGE Publications, USA, 2455 Teller Road, Thousand Oaks, CA 91320, USA. (2012 Jul 23)
University of Pretoria: Nuclear medicine imaging in tuberculosis using commercially available radiopharmaceuticals

By a News Reporter-Staff News Editor at Biotech Week – Investigators publish new report on HIV/AIDS. According to news reporting originating from Pretoria, South Africa, by NewsRx correspondents, researchers stated “In this paper, data available on nuclear medicine imaging using commercially available radiopharmaceuticals for the differentiation, staging, and prediction or assessment of the response to treatment in tuberculosis (TB) are reviewed. Limited available studies suggest that single photon emission computed tomography (SPECT) using either 201Tl, 99mTc-sestamibi, or 99mTc-tetrofosmin is accurate (=85%) and has a high negative predictive value (=90%) for the differentiation of TB from carcinoma in patients presenting with a solitary pulmonary nodule (SPN).”

Our news editors obtained a quote from the research by the authors from the University of Pretoria, “The criteria for detection of TB on 201Tl SPECT are nondepiction of the suspicious lesion in the delayed image or a negative retention index [washout on the delayed images (3-4 h postinjection) vs. the early image (5-15 min postinjection)] and a comparable-to-background uptake on 99mTc-sestamibi or 99mTc-tetrofosmin SPECT. Another SPECT tracer of potential interest for the differentiation of TB from malignant SPN that warrants further exploration, is N-isopropyl-p-[123I]iodoamphetamine (123I-IMP). In contrast, 18F-fluorodeoxyglucose (18F-FDG) PET is unable to differentiate malignancy from TB and thus cannot be used as a tool to reduce futile biopsy/thoracotomy in these patients. A limited number of studies have reported on the potential of nuclear medicine imaging in assessment of the extent of disease in patients with extrapulmonary TB using 67Ga-citrate SPECT and 18F-FDG PET, respectively. 67Ga-citrate SPECT was shown to be as sensitive as bone scintigraphy for the detection of bone infection and was found to be complementary to computed tomography (CT) imaging. 18F-FDG PET was found to be significantly more efficient when compared with CT, respectively, in over half of patients for the identification of sites of lymph node involvement that were missed by CT and often the only sites of extrapulmonary TB identified. Unfortunately, 18F-FDG PET findings did not lead to alterations in treatment planning in any of the patients under study. Additional studies confirming these findings are urgently required. Similar to the setting of SPN, 18F-FDG PET cannot differentiate malignant lymph node involvement from lymph node involvement by TB. These results and the recent findings of Demura and colleagues using 18F-FDG PET further suggest that nuclear medicine imaging techniques could be used for the evaluation of therapeutic response. Prospective studies,
focusing on specific subgroups of patients in whom such an imaging approach might be clinically relevant, for example in multidrug-resistant TB patients, are warranted. In acquired immunodeficiency syndrome patients, $^{67}$Ga scintigraphy proved to be a reliable and sensitive method for the primary detection and follow-up of opportunistic pneumonias, including TB. Combining $^{201}$Tl scintigraphy with $^{67}$Ga scintigraphy was shown to increase the specificity for both pulmonary and extrapulmonary TB, which is a $^{67}$Ga(+) and $^{201}$Tl(-) mismatch pattern in acquired immunodeficiency syndrome patients that is specific for mycobacterial infections.”

According to the news editors, the researchers concluded: “Finally, the results obtained using both SPECT and PET indicate that nuclear medicine could be an important noninvasive method for the determination of disease activity, detection of extrapulmonary TB, and determination of response to therapy.”

For more information on this research see: Nuclear medicine imaging in tuberculosis using commercially available radiopharmaceuticals. *Nuclear Medicine Communications*, 2012;33(6):581-90. (Lippincott Williams and Wilkins - www.lww.com; Nuclear Medicine Communications - http://journals.lww.com/nuclearmedicinecomm/pages/default.aspx)

The news editors report that additional information may be obtained by contacting M. Sathokge, Dept. of Nuclear Medicine, University of Pretoria, Pretoria, South Africa. (2012 Jul 11)

**Russian Federation, Samara: Performance of the GenoType(®) MTBDRPlus assay in routine settings: a multicenter study**

By a News Reporter-Staff News Editor at Clinical Trials Week – A new study on Tuberculosis is now available. According to news reporting originating from Samara, Russia, by NewsRx correspondents, researchers stated “Former Soviet Union countries including the Baltic States (Latvia, Lithuania, and Estonia) are hot spots for an emerging epidemic of drug resistant tuberculosis (TB). As a part of the development of a co-ordinated network of centers for diagnostic trials across Eastern Europe we conducted a retrospective multicenter analysis of the performance of the GenoType® MTBDRPlus assay for TB identification and susceptibility to isoniazid (INH) and rifampicin (RIF) in routine settings.”

Our news editors obtained a quote from the research by the authors from Russian Federation, “A total of 1,045 primary samples, 1045 TB cultures derived from these specimens and 306 separate *M. tuberculosis* isolates tested in 2007-2010 at four participating sites (Tartu, Estonia; Riga, Latvia; Vilnius, Lithuania; and Samara, Russian Federation)
were included in the analysis. The pooled sensitivity and specificity values for RIF and INH were 95.3% and 95.5%, 89.9 and 87.1%, respectively; there were no statistically significant variations in performance across sites. The proportion of multidrug resistant (MDR) strains in the collections ranged from 21.8% (in Estonia) to 55.9% (in Russia). In a routine non-trial context, the assay reliably detected both rifampicin and isoniazid resistance.”

According to the news editors, the researchers concluded: “The absence of statistically significant differences between sites suggested that the comparable performance obtained using these assays has helped demonstrate the formation of a successful diagnostic trial network.”

For more information on this research see: Performance of the GenoType(®) MTBDRPlus assay in routine settings: a multicenter study. European Journal of Clinical Microbiology & Infectious Diseases, 2012;31(7):1381-7. (Springer - www.springer.com; European Journal of Clinical Microbiology & Infectious Diseases - http://www.springerlink.com/content/0934-9723/)

The news editors report that additional information may be obtained by contacting S. Mironova, Samara Oblast TB Service, 154 Novosadovaya Street, Samara, 443068, Russia. (2012 Jul 02)

University of Pavia: Antituberculars which target decaprenylphosphoryl-β-D-ribofuranose 2’-oxidase DprE1: state of art

By a News Reporter-Staff News Editor at Clinical Trials Week – New research on Tuberculosis is the subject of a report. According to news reporting from Pavia, Italy, by NewsRx journalists, researchers stated “Multidrug resistance is a major barrier in the battle against tuberculosis and still a leading cause of death worldwide. In order to fight this pathogen, two routes are practicable: vaccination or drug treatment.”

The news correspondents obtained a quote from the research by the authors from the University of Pavia, “Vaccination against Mycobacterium tuberculosis with the current vaccine Mycobacterium bovis Bacillus Calmette-Guerin is partially successful, being its efficacy variable. A few new tuberculosis vaccines are now in various phases of clinical trials. The emergence of multidrug-resistant strains of M. tuberculosis gave the impulse to discover new effective antitubercular drugs, a few of which are in clinical development. Here we focus on three different classes of very promising antitubercular drugs recently discovered (benzothiazinones, dinitrobenzamides, and benzoquinoxalines) that share the same cellular target: a subunit of the heteromeric decaprenylphosphoryl-β-D-ribofuranose 2’-epimerase, encoded by the dprE1 (or Rv3790) gene.”
According to the news reporters, the researchers concluded: “This enzyme is involved in the biosynthesis of D- arabinose which is crucial for the synthesis of the mycobacterial cell wall and essential for the pathogen’s survival.”

For more information on this research see: Antituberculars which target decaprenylphosphoryl-\(-\)-ribofuranose 2’-oxidase DprE1: state of art. *Applied Microbiology and Biotechnology*, 2012;94(4):907-16. (Springer - www.springer.com; Applied Microbiology and Biotechnology - http://www.springerlink.com/content/0175-7598/)

Our news journalists report that additional information may be obtained by contacting S. Buroni, Dipartimento di Biologia e Biotecnologie Lazzaro Spallanzani, Universita degli Studi di Pavia, Via Ferrata 9, Pavia, Italy. (2012 Jul 02)

**University of Amsterdam: Knowledge of tuberculosis-treatment prescription of health workers: a systematic review**

By a News Reporter-Staff News Editor at Tuberculosis Week – Fresh data on Tuberculosis are presented in a new report. According to news reporting originating in Amsterdam, Netherlands, by NewsRx journalists, researchers stated “Treating tuberculosis (TB) patients with inappropriate treatment regimens can lead to treatment failure and, thus, patients who have not been cured and/or to the development of (multi)-drug resistance. A systematic review was performed to assess the knowledge of appropriate TB drug regimens among all categories of healthcare workers (HCWs).”

The news reporters obtained a quote from the research by the authors from the University of Amsterdam, “In January 2011, MEDLINE, EMBASE and other databases were searched for relevant articles. Observational studies published as of the year 2000 that assessed HCW knowledge of TB treatment were selected. A treatment regimen, drug dosage or treatment duration was considered inappropriate if it was not recommended by national guidelines or by the World Health Organization (WHO). Of 1,896 studies, 31 were included from 14 different countries. No study was performed in Europe. In all studies, HCWs with inappropriate knowledge of treatment regimens (8-100%) or treatment duration (5-99%) were observed. The few studies providing detailed data showed that HCWs mainly reported giving treatment regimens with too many drugs and for too long. Knowledge of appropriate doses was also insufficient in most studies. The available studies show that there is a lack of knowledge of national or international TB treatment guidelines and recommendations.”
According to the news reporters, the researchers concluded: “Generalisation of the findings to other settings and countries should be done with caution.”


Our news correspondents report that additional information may be obtained by contacting M.J. van der Werf, University of Amsterdam, Academy Med Center, Dutch Cochrane Center, NL-1105 AZ Amsterdam, Netherlands. (2012 Jun 25)

University of Lille: Tuberculosis: The drug development pipeline at a glance

By a News Reporter-Staff News Editor at Tuberculosis Week – Investigators discuss new findings in Tuberculosis. According to news reporting originating from Lille, France, by NewsRx correspondents, researchers stated “Tuberculosis is a major disease causing every year 1.8 million deaths worldwide and represents the leading cause of mortality resulting from a bacterial infection. Introduction in the 60’s of first-line drug regimen resulted in the control of the disease and TB was perceived as defeating.”

Our news editors obtained a quote from the research by the authors from the University of Lille, “However, since the progression of HIV leading to co-infection with AIDS and the emergence of drug resistant strains, the need of new anti-tuberculosis drugs was not overstated. However in the past 40 years any new molecule did succeed in reaching the market. Today, the pipeline of potential new treatments has been fulfilled with several compounds in clinical trials or preclinical development with promising activities against sensitive and resistant Mycobacterium tuberculosis strains. Compounds as gatifloxacin, moxifloxacin, metronidazole or linezolid already used against other bacterial infections are currently evaluated in clinical phases 2 or 3 for treating tuberculosis. In addition, analogues of known TB drugs (PA-824, OPC-67683, PNU-100480, AZD5847, SQ609, SQ109, DC-159a) and new chemical entities (TMC207, BTZ043, DNB1, BDM31343) are under development.”

According to the news editors, the researchers concluded: “In this review, we report the chemical synthesis, mode of action when known,
in vitro and in vivo activities and clinical data of all current small molecules targeting tuberculosis.”


The news editors report that additional information may be obtained by contacting B. Villemagne, Univ Lille Nord France, F-59000 Lille, France. (2012 Jun 25)

Stellenbosch University, Cape Town: Phase II Dose-Ranging Trial of the Early Bactericidal Activity of PA-824

By a News Reporter-Staff News Editor at Biotech Week – Current study results on Tuberculosis have been published. According to news reporting originating from Cape Town, South Africa, by NewsRx correspondents, researchers stated “PA-824 is a novel nitroimidazo-oxazine under evaluation as an antituberculosis agent. A dose-ranging randomized study was conducted to evaluate the safety, tolerability, pharmacokinetics, and early bactericidal activity of PA-824 in drug-sensitive, sputum smear-positive adult pulmonary-tuberculosis patients to find the lowest dose giving optimal bactericidal activity (EBA).”

Our news editors obtained a quote from the research by the authors from Stellenbosch University, “Fifteen patients per cohort received oral PA-824 in doses of 50 mg, 100 mg, 150 mg, or 200 mg per kg body weight per day for 14 days. Eight subjects received once-daily standard antituberculosis treatment with isoniazid, rifampin, pyrazinamide, and ethambutol (HRZE) as a positive control. The primary efficacy endpoint was the mean rate of decline in log CFU of Mycobacterium tuberculosis in sputum incubated on agar plates from serial overnight sputum collections, expressed as log(10) CFU/day/ml sputum (standard deviation). The mean 14-day EBA of HRZE was consistent with previous studies (0.177 ± 0.042), and that of PA-824 at 50 mg, 100 mg, 150 mg, and 200 mg was 0.063 ± 0.058, 0.091 ± 0.073, 0.078 ± 0.074, and 0.112 ± 0.070, respectively. Although the study was not powered for testing the difference between arms, there was a trend toward significance, indicating a lower EBA at the 50-mg dose. Serum PA-824 levels were approximately dose proportional with respect to the area under the time-concentration curve. All doses were safe and well tolerated with no dose-limiting adverse events or clinically significant QTc changes.”
According to the news editors, the researchers concluded: “A dose of 100 mg to 200 mg PA-824 daily appears to be safe and efficacious and will be further evaluated as a component of novel antituberculosis regimens for drug-sensitive and drug-resistant tuberculosis.”


The news editors report that additional information may be obtained by contacting A.H. Diacon, Division of Physiology, Dept. of Medical Biochemistry, Faculty of Health Sciences, Stellenbosch University, Cape Town, South Africa. (2012 Jun 13)

Stellenbosch University, Tygerberg: Randomized Pilot Trial of Eight Weeks of Bedaquiline (TMC207) Treatment for Multidrug-Resistant Tuberculosis: Long-Term Outcome, Tolerability, and Effect on Emergence of Drug Resistance

By a News Reporter-Staff News Editor at Biotech Week – Investigators publish new report on Tuberculosis. According to news reporting from Tygerberg, South Africa, by NewsRx journalists, researchers stated “The 2-year follow-up results for a randomized placebo-controlled study of 47 patients with multidrug-resistant pulmonary tuberculosis treated with either the new diarylquinoline TMC207, recently renamed bedaquiline, or placebo, added to the first 8 weeks of a background regimen, are presented. Bedaquiline significantly reduced the time to culture conversion over 24 weeks (hazard ratio, 2.253; 95% confidence interval, 1.08 to 4.71; p=0.031).”

The news correspondents obtained a quote from the research by the authors from Stellenbosch University, “With the exception of nausea reported in 26% of patients receiving bedaquiline and none receiving placebo, adverse events occurred at similar frequencies in both groups of patients: bilateral hearing impairment, extremity pain, acne, and noncardiac chest pain occurred in 13 and 21%, 17 and 13%, 9 and 17%, and 4 and 17% of patients, respectively, receiving bedaquiline or placebo. Excluding resistance to ethambutol and ethionamide, only one patient receiving bedaquiline acquired resistance to companion drugs, but five patients receiving placebo (4.8% versus 21.7%; p=0.18) acquired resistance to companion drugs, and resistance to ofloxacin was acquired in four patients receiving placebo and none receiving bedaquiline (0% versus 22%; 0=0.066). In all, 23 patients (49%), including 13 receiving placebo (54%) and 10 receiving bedaquiline (44%), discontinued the
study prior to its completion, 12 during the first 24 weeks of treatment. Eight subjects were withdrawn for noncompliance or default, and seven withdrew consent, citing the rigorous program of investigations for safety and pharmacokinetic monitoring.”

According to the news reporters, the researchers concluded: “Bedaquiline may contribute to the management of multidrug-resistant tuberculosis by effecting more rapid sputum culture negativity and by preventing acquired resistance to companion drugs.”

For more information on this research see: Randomized Pilot Trial of Eight Weeks of Bedaquiline (TMC207) Treatment for Multidrug-Resistant Tuberculosis: Long-Term Outcome, Tolerability, and Effect on Emergence of Drug Resistance. Antimicrobial Agents and Chemotherapy, 2012;56(6):3271-6. (American Society for Microbiology - www.asm.org; Antimicrobial Agents and Chemotherapy - aac.asm.org)

Our news journalists report that additional information may be obtained by contacting A.H. Diacon, Faculty of Health Sciences, Stellenbosch University, Tygerberg, South Africa. (2012 Jun 13)

Comenius University, Bratislava: Antituberculars which target decaprenylphosphoryl-beta-D-ribofuranose 2’-oxidase DprE1: state of art

By a News Reporter-Staff News Editor at Clinical Trials Week – A new study on Tuberculosis is now available. According to news reporting originating from Bratislava, Slovakia, by NewsRx correspondents, researchers stated “Multidrug resistance is a major barrier in the battle against tuberculosis and still a leading cause of death worldwide. In order to fight this pathogen, two routes are practicable: vaccination or drug treatment.”

Our news editors obtained a quote from the research by the authors from Comenius University, “Vaccination against Mycobacterium tuberculosis with the current vaccine Mycobacterium bovis Bacillus Calmette-Guerin is partially successful, being its efficacy variable. A few new tuberculosis vaccines are now in various phases of clinical trials. The emergence of multidrug-resistant strains of M. tuberculosis gave the impulse to discover new effective antitubercular drugs, a few of which are in clinical development. Here we focus on three different classes of very promising antitubercular drugs recently discovered (benzothiazinones, dinitrobenzamides, and benzoquinoxalines) that share the same cellular target: a subunit of the heteromeric decaprenylphosphoryl-beta-d-ribose 2’-epimerase, encoded by the dprE1 (or Rv3790) gene.”

According to the news editors, the researchers concluded: “This enzyme is involved in the biosynthesis of d-arabinose which is crucial
for the synthesis of the mycobacterial cell wall and essential for the pathogen’s survival.”

For more information on this research see: Antituberculars which target decaprenylphosphoryl-beta-D-ribofuranose 2’-oxidase DprE1: state of art. *Applied Microbiology and Biotechnology*, 2012;94(4):907-916. *Applied Microbiology and Biotechnology* can be contacted at: Springer, 233 Spring St, New York, NY 10013, USA. (Springer - www.springer.com; Applied Microbiology and Biotechnology - http://www.springerlink.com/content/0175-7598/)

The news editors report that additional information may be obtained by contacting S. Buroni, Comenius Univ, Dept. of Biochem Mlynska Dolina, Bratislava 84215, Slovakia. (2012 Jun 11)

**University of Amsterdam: Prevalence of inappropriate tuberculosis treatment regimens: a systematic review**

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – Investigators publish new report on Tuberculosis. According to news reporting from Amsterdam, Netherlands, by NewsRx journalists, researchers stated “A potential threat to the success of new tuberculosis (TB) drugs is the development of resistance. Using drugs in appropriate regimens, such as those recommended in the World Health Organization (WHO) treatment guidelines, prevents the development of resistance.”

The news correspondents obtained a quote from the research by the authors from the University of Amsterdam, “We performed a systematic review to assess the prevalence of inappropriate prescription of TB drugs for the treatment of TB. MEDLINE, EMBASE and other databases were searched for relevant articles in January 2011. Observational studies published from 2000 that included TB patients receiving treatment were selected. A treatment regimen was considered inappropriate if the regimen was not a WHO recommended regimen. 37 studies were included. Inappropriate treatment regimens were prescribed in 67% of studies. The percentage of patients receiving inappropriate regimens varied between 0.4% and 100%. In 19 studies the quality of treatment regimen reporting was low. Despite the fact that assessment of inappropriate treatment was hampered by low quality of reporting, our data indicate a reasonable amount of inappropriate prescription of TB treatment regimens. Thus, there is a risk that new drugs will be used in inappropriate treatment regimens, even with WHO guidelines in place, introducing the risk of resistance development.”

According to the news reporters, the researchers concluded: “This article highlights the need to improve implementation of the WHO treatment of TB guidelines.”

Our news journalists report that additional information may be obtained by contacting M.W. Langendam, Dutch Cochrane Centre, Academic Medical Center, University of Amsterdam, Amsterdam, Netherlands. *(2012 Jun 04)*

**Patent Issued for Tuberculosis Vaccines Comprising Antigens Expressed during the Latent Infection Phase**

By a News Reporter-Staff News Editor at Biotech Week – According to news reporting originating from Alexandria, Virginia, by NewsRx journalists, a patent by the inventors Aagaard, Claus (Copenhagen, DK); Vingsbo-Lundberg, Carina (Hollviken, SE); Andersen, Peter (Bronshoj, DK), filed on December 22, 2011, was cleared and issued on October 23, 2012.

The assignee for this patent, patent number 8293250, is Statens Serum Institut (Copenhagen S, DK).

Reporters obtained the following quote from the background information supplied by the inventors: “Human tuberculosis caused by *Mycobacterium tuberculosis* (M. tuberculosis) is a severe global health problem, responsible for approximately 3 million deaths annually, according to the WHO. The worldwide incidence of new tuberculosis (TB) cases had been falling during the 1960s and 1970s but during recent years this trend has markedly changed in part due to the advent of AIDS and the appearance of multidrug resistant strains of M. tuberculosis.

“The only vaccine presently available for clinical use is BCG, a vaccine whose efficacy remains a matter of controversy. BCG generally induces a high level of acquired resistance in animal models of TB, and in humans it is protective against disseminated forms of tuberculosis such as meningitis and miliary tuberculosis. When given to young children it is protective against tuberculosis for years but then the efficacy wanes. Comparison of various controlled trials revealed that the protective efficacy of BCG in adults varied dramatically with an efficacy range from ineffective to 80% protection. This makes the development of a new and improved vaccine against M. tuberculosis an urgent matter, which has been given a very high priority by the WHO.

“Many attempts to define protective mycobacterial substances have been made, and different investigators have reported increased resistance after experimental vaccination. M. tuberculosis holds, as well as secretes, several proteins of potential relevance for the generation of a new M. tuberculosis vaccine. The search for candidate molecules has primarily focused on proteins released from dividing bacteria. Despite the characterization of a large number of such proteins only a few of
these have been demonstrated to induce a protective immune response as subunit vaccines in animal models, most notably ESAT-6 and Ag85B (Brandt et al 2000). However, the demonstration of a specific long-term protective immune response with the potency of BCG or the capability of boosting in a BCG vaccinating person has not yet been achieved. At best, boost of BCG with BCG has no effect [Colditz, 1994]. Boosting of BCG has been done with Ag85A (Brooks et al IAI 2001; WO0204018) in an inbred mouse strain leading to some protection, although compared to BCG alone it was not significantly better. Since BCG needs to divide and secrete proteins in order to induce a protective immune response, the lack of booster effect is primarily due to either sensitization with environmental mycobacteria or a residual immune response from the primary BCG vaccination. Both events lead to a rapid immune response against BCG and therefore quick inhibition of growth and elimination of BCG.

“The course of a M. tuberculosis infection runs essentially through 3 phases. During the acute phase, the bacteria proliferate in the organs, until the immune response increases. Specifically sensitized CD4 T lymphocytes mediate control of the infection, and the most important mediator molecule seems to be interferon gamma (IFN-gamma). The bacterial loads starts to decline and a latent phase is established where the bacterial load is kept stable at a low level. In this phase M. tuberculosis goes from active multiplication to dormancy, essentially becoming non-replicating and remaining inside the granuloma. In some cases, the infection goes to the reactivation phase, where the dormant bacteria start replicating again. It has been suggested that the transition of M. tuberculosis from primary infection to latency is accompanied by changes in gene expression (Honer zu Bentrup, 2001). It is also likely that changes in the antigen-specificity of the immune response occur, as the bacteria modulates gene expression during its transition from active replication to dormancy. The full nature of the immune response that controls latent infection and the factors that lead to reactivation are largely unknown. However, there is some evidence for a shift in the dominant cell types responsible. While CD4 T cells are essential and sufficient for control of infection during the acute phase, studies suggest that CD8 T cell responses are more important in the latent phase.

“In 1998 Cole et al published the complete genome sequence of M. tuberculosis and predicted the presence of approximately 4000 open reading frames (Cole et al 1998) disclosing nucleotide sequences and putative protein sequences. However importantly, this sequence information cannot be used to predict if the DNA is translated and expressed as proteins in vivo. It is known that some genes of M. tuberculosis are upregulated under conditions that mimic latency. However, these are a limited subset of the total gene expression during latent infection. Moreover, as one skilled in the art will readily appreciate, expression
of a gene is not sufficient to make it a good vaccine candidate. The only way to determine if a protein is recognized by the immune system during latent infection with M. tuberculosis is to produce the given protein and test it in an appropriate assay as described herein. A number of proteins are of particular importance and have potential for being late antigens (antigens recognized during latent infection) since they are mainly expressed a relatively long time after infection where the immune system has mounted the first adaptive defense and the environment has turned more hostile for the mycobacteria. In vitro hypoxic culture conditions, which mimic the conditions of low oxygen tension have previously been suggested as relevant in this regard and have been used to analyze changes in gene expression. A number of antigens have been found that are induced or markedly upregulated under these conditions e.g. the 16 kDa antigen alpha-crystallin (Sherman 2001), Rv2660c and Rv2659c (Betts, 2002). (our own application) Another environmental stimuli which may be of particular interest is starvation designed to reflect that nutrients are restricted in the granuloma (the location of the latent infection) and that products expressed by genes upregulated under starvation therefore may be of particular interest as antigen targets during the latent stage of infection.

“Of the more than 200 hundred antigens known to be expressed during primary infection, and tested as vaccines, less than a half dozen have demonstrated significant potential. So far only one antigen has been shown to have any potential as a therapeutic vaccine (Lowrie, 1999). However this vaccine only worked if given as a DNA vaccine and has proved controversial, with other groups claiming that vaccination using this protocol induces either non-specific protection or even worsens disease (Turner, 2000). In contrast, the fusion polypeptides described in the invention may be incorporated in a vaccine that use well-recognized vaccination technology, as demonstrated in provided examples.

“Further, since TB vaccines do not result in sterilizing immunity but rather control the infection at a subclinical level (thereby resulting in the subsequent establishment of latent infection), a multiphase vaccine which combines components with prophylactic and therapeutic activity is described in this invention. After conventional prophylactic vaccination, the evasion of the primary immune response and the subsequent development of latent disease is probably at least in part due to the change in the antigenic profile of the invading bacteria. Thus, vaccinating with antigens associated with latent TB should prevent or reduce the establishment of latent infection and therefore, a vaccine incorporating antigens expressed by the bacteria both in the first logarithmic growth phase and during latent disease should improve long-term immunity when used as a prophylactic vaccine. Such a multiphase vaccine will obviously also be efficient as a therapeutic vaccine thereby
addressing the problem that the majority of the population in the third world who would receive a future TB vaccine would be already latently infected.”

In addition to obtaining background information on this patent, NewsRx editors also obtained the inventors’ summary information for this patent: “The invention is related to an immunogenic composition, vaccine or pharmaceutical composition for preventing (including booster vaccination and multiphase vaccines) or/and treating infection caused by a species of the M. tuberculosis complex (M. tuberculosis, M. Bovis, M. africanum etc.), the immunogenic composition, the vaccine or pharmaceutical composition comprising starvation induced antigen or a fusion polypeptide which comprises one or more starvation induced M. tuberculosis antigens, the units of the fusion polypeptide being M. tuberculosis antigens. Also, the invention relates to the fusion polypeptides as such and to a nucleic acid sequence encoding such a fusion polypeptide. Further, the invention relates to the use of short or long overlapping or non-overlapping peptide(s) made synthetically or recombinant. Further, the invention relates to the use of a starvation induced antigen or a fusion polypeptide sequence or nucleic acid sequence of the invention for preparing said immunogenic composition, vaccine, or pharmaceutical composition and the vaccine or pharmaceutical composition produced in this way. Further, the invention relates to the use of a vaccine comprising a starvation induced antigen or a fusion polypeptide sequence or nucleic acid sequence of the invention given at the same time as BCG, either mixed with BCG or administered separately at different sites or routes for preparing said immunogenic composition, vaccine, or pharmaceutical composition. Further the invention relates to the use of a vaccine comprising a starvation induced antigen or a fusion polypeptide sequence or nucleic acid sequence given as a BCG booster. Furthermore, by including antigens that are expressed both early and late during a natural infection the vaccine will lead to a two step immune response allowing the immune system to combat the pathogen with whatever epitopes are most efficient at a certain timepoint including during latency.”

Chapter 2

Diagnosis and Screening

University of Buenos Aires: Rapid and biosecure diagnostic test for tuberculosis

By a News Reporter-Staff News Editor at Life Science Weekly – Fresh data on Cell Biochemistry and Biophysics are presented in a new report. According to news originating from Buenos Aires, Argentina, by NewsRx correspondents, research stated, “Early and rapid detection of the causative organism is necessary in tuberculosis. We present here an integrated and dedicated molecular biology system for tuberculosis diagnosis.”

Our news journalists obtained a quote from the research from the University of Buenos Aires, “One hundred and eighty-nine (189) biologic specimens from patients strongly suspected by clinical parameters of tuberculosis were studied by Ziehl-Neelsen staining, cultivation on a solid medium, and by a balanced heminested fluorometric PCR system (Orange G3TB) that preserves worker safety and produces a rather pure material free of potential inhibitors. DNA amplification was carried out in a low cost using a tuberculosis thermocycler-fluorometer. The double stranded DNA produced is fluorometrically detected. The whole reaction is carried out in one single tube which is never opened after adding the processed sample, thus minimizing the risk of cross contamination with amplicons. The assay is able to detect 30 bacilli/ml of sample having a 99.8 % inter-assay coefficient of variation. PCR was positive in 36 (18.9 %) tested samples (33 of them were smear-negative). In our study, it yields a preliminary overall sensitivity of 97.4 %. In addition, its overall specificity is 98.7 %. The total run time of the test is 4 h with two and a half real working hours. All PCR-positive samples also had a positive result by microbiological culture and clinical criteria. The results obtained showed that it could be a very useful tool to increase
efficiency in detecting the tuberculosis disease in low bacillus inoculum samples.”

According to the news editors, the research concluded: “Furthermore, its low cost and friendly usage make it feasible to be used in regions with poor development.”


The news correspondents report that additional information may be obtained from J. Garberi, Laboratory of Molecular Biology and Pathology, School of Medicine, Buenos Aires University, Buenos Aires, Argentina.

The publisher’s contact information for the journal Cell Biochemistry and Biophysics is: Springer, 233 Spring Street, New York, NY 10013, USA. (2013 Apr 23)

Kyungpook National University, Taegu: Comparison of whole-blood interferon-gamma assay and flow cytometry for the detection of tuberculosis infection

By a News Reporter-Staff News Editor at Tuberculosis Week – A new study on Infection Research is now available. According to news reporting originating from Taegu, South Korea, by NewsRx correspondents, research stated, “Limited data exist about the performance of the intracellular cytokine flow cytometry (ICCFC) with respect to that of the commercial interferon-gamma release assay for the detection of tuberculosis (TB) infection. Here, we compared the diagnostic accuracy of an ICCFC with that of the QuantiFERON-TB Gold In-Tube (QFT-IT) test for the detection of TB in a clinical setting.”

Our news editors obtained a quote from the research from Kyungpook National University, “Eighty-nine patients suspected of having TB were prospectively included. Both the QFT-IT test and ICCFC were performed for all subjects (TB [n = 65] and non-TB [n = 24]). Ten healthy controls who tested negative by QFT-IT were also assessed by ICCFC. The sensitivity of the ICCFC was significantly superior to that of the QFT-IT test (91% vs. 78%, p = 0.021). The clinical characteristics of patients in whom the ICCFC exhibited superior sensitivity compared to the QFT-IT test included advanced age, lymphocytopenia, hypoalbuminemia, increased C-reactive protein level, a positive acid-fast bacilli smear of respiratory specimens, and radiographically more extensive disease.”
According to the news editors, the research concluded: “ICCFC might be a preferable technique for the detection of TB infection, particularly in patients with conditions associated with impaired performance of the QFT-IT test.”


The news editors report that additional information may be obtained by contacting J. Lee, Kyungpook National University, Dept. of Clin Pathol, Sch Med, Taegu 700842, South Korea. (2013 Apr 22)

**Massachusetts General Hospital, Boston: Is Passive Diagnosis Enough? The Impact of Subclinical Disease on Diagnostic Strategies for Tuberculosis**

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – A new study on Respiratory Research is now available. According to news reporting from Boston, Massachusetts, by NewsRx journalists, research stated, “Tuberculosis (TB) is characterized by a subclinical phase (symptoms absent or not considered abnormal); prediagnostic phase (symptoms noticed but diagnosis not pursued); and clinical phase (care actively sought). Diagnostic capacity during these phases is limited.”

The news correspondents obtained a quote from the research from Massachusetts General Hospital, “To estimate the population-level impact of TB case-finding strategies in the presence of subclinical and prediagnostic disease. We created a mathematical epidemic model of TB, calibrated to global incidence. We then introduced three prototypical diagnostic interventions: increased sensitivity of diagnosis in the clinical phase by 20% (‘passive’); early diagnosis during the prediagnostic phase at a rate of 10% per year (‘enhanced’); and population-based diagnosis of 5% of undiagnosed prevalent cases per year (‘active’). If the subclinical phase was ignored, as in most models, the passive strategy was projected to reduce TB incidence by 18% (90% uncertainty range [UR], 11-32%) by year 10, compared with 23% (90% UR, 14-35%) for the enhanced strategy and 18% (90% UR, 11-28%) for the active strategy. After incorporating a subclinical phase into the model, consistent with population-based prevalence surveys, the active strategy still reduced 10-year TB incidence by 16% (90% UR, 11-28%), but the passive and enhanced strategies’ impact was attenuated to 11% (90% UR, 8-25%) and 6% (90% UR, 4-13%), respectively. The degree of attenuation depended
strongly on the transmission rate during the subclinical phase. Subclinical disease may limit the impact of current diagnostic strategies for TB.”

According to the news reporters, the research concluded: “Active detection of undiagnosed prevalent cases may achieve greater population-level TB control than increasing passive case detection.”


Our news journalists report that additional information may be obtained by contacting D.W. Dowdy, Massachusetts General Hospital, Dept. of Med, Div Infect Dis, Boston, MA 02114, United States. (2013 Apr 08)

Department of Medicine, New Delhi: Diagnostic dilemma: Kikuchi’s disease or tuberculosis?

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators publish new report on Tuberculosis. According to news originating from New Delhi, India, by NewsRx correspondents, research stated, “Any patient from a tuberculosis (TB) endemic area such as India with classical clinical features of fever, weight loss and lymphadenopathy, making a diagnosis of Kikuchi’s disease (KD) prior to waiting for the 6-week culture is not appropriate. KD or histiocytic necrotising lymphadenitis is a rare self-limiting cervical lymphadenitis, often a diagnosis of exclusion.”

Our news journalists obtained a quote from the research from the Department of Medicine, “One needs to exclude TB, sarcoidosis, lymphoma and autoimmune diseases to make such a diagnosis. The patient here with classical clinical presentation of TB with lymph node biopsy mimicking KD (biopsy and immunohistochemistry) posed a big diagnostic dilemma. However, culture of the biopsied lymphatic tissue was confirmed to be mycobacterium TB after the 6th week of incubation. The patient was treated with antitubercular drugs initially, and later, steroid was added in view of his persistent symptoms and he responded. One should wait for the tissue culture report to confirm or exclude the diagnosis of TB. Exclusion should not be based only on laboratory criteria.”

According to the news editors, the research concluded: “Histopathogically, TB can mimic any other granulomatous disorder.”
For more information on this research see: Diagnostic dilemma: Kikuchi's disease or tuberculosis? *Bmj Case Reports*, 2013;2013(). (BMJ Publishing Group - http://group.bmj.com/; Bmj Case Reports - http://casereports.bmj.com/)

The news correspondents report that additional information may be obtained from H.K. Nayak, Dept. of Medicine, LN Hospital, New Delhi, Delhi, India. *(2013 Apr 02)*

**Veterinary Laboratories Agency, Surrey: The consequences of vaccination with the Johne’s disease vaccine, Gudair, on diagnosis of bovine tuberculosis**

By a News Reporter-Staff News Editor at Life Science Weekly – Fresh data on Life Science are presented in a new report. According to news originating from Surrey, United Kingdom, by NewsRx correspondents, research stated, “The single intradermal comparative cervical tuberculin skin-test (SICCT) remains the primary surveillance tool to diagnose bovine tuberculosis (BTB) in the UK. Therefore, understanding the potential confounding influences on this test is important.”

Our news journalists obtained a quote from the research from Veterinary Laboratories Agency, “This study investigated the effects of vaccination against Johne’s disease (JD) on the immunodiagnostics of BTB using a *Mycobacterium bovis* BCG vaccination model as a surrogate of *M* bovis infection. Calves were vaccinated with either BCG (an attenuated live vaccine) or the JD vaccine, Gudair (a heat-inactivated suspension of *Mycobacterium avium* subspecies paratuberculosis), or a combination of both, and SICCT responses were measured approximately six and 12 weeks postvaccination. Animals vaccinated with Gudair only were negative to the SICCT test, thus supporting the specificity of the SICCT test following Gudair vaccination. However, while animals vaccinated with BCG-only demonstrated a bovine tuberculin-biased response as expected, covaccination with Gudair resulted in a bias towards avian tuberculin in the SICCT test. Therefore, our model demonstrates the potential of the Gudair vaccine to reduce the sensitivity of the SICCT.”

According to the news editors, the research concluded: “In addition, while we also demonstrate that Gudair vaccination can compromise the specificity of serological tests to detect JD, the specificity of defined *M* bovis antigens in serological or interferon gamma-based blood assays was not compromised by the vaccine.”

For more information on this research see: The consequences of vaccination with the Johne’s disease vaccine, Gudair, on diagnosis of bovine tuberculosis. *The Veterinary Record*, 2013;172(10):266.

The news correspondents report that additional information may be obtained from M. Coad, Dept. of Bovine Tuberculosis, Animal Health
and Veterinary Laboratories Agency, New Haw, Addlestone, Surrey KT15 3NB, UK. (2013 Apr 02)

University of Hong Kong: Point-of-care diagnosis of tuberculosis: Past, present and future

By a News Reporter-Staff News Editor at Tuberculosis Week – A new study on Mycobacterium Infections is now available. According to news reporting originating from Hong Kong, People’s Republic of China, by NewsRx correspondents, research stated, “Diagnosis represents only one aspect of tuberculosis (TB) control but is perhaps one of the most challenging. The drawbacks of current tools highlight several unmet needs in TB diagnosis, that is, necessity for accuracy, rapidity of diagnosis, affordability, simplicity and the ability to generate same-day results at point-of-care (POC).”

Our news editors obtained a quote from the research from the University of Hong Kong, “When a return visit is required to access test results, time to treatment is prolonged, and default rates are significant. However, a good diagnostic tool is also critically dependent on obtaining an adequate biological sample. Here, we review the accuracy and potential impact of established and newer potential POC diagnostic tests for TB, including smear microscopy, the Xpert MTB/RIF assay (Cepheid) and the Determine TB lipoarabinomannan antigen test (Alere). Novel experimental approaches and detection technologies for POC diagnosis of active TB, including nucleic acid amplification tests, detection of volatile organic compounds or metabolites, mass spectroscopy, microfluidics, surface-enhanced Raman spectroscopy, electrochemical approaches, and aptamers among others, are discussed. We also discuss future applications, including the potential POC diagnosis of drug-resistant TB and presumed latent TB infection.”

According to the news editors, the research concluded: “Challenges to the development and roll-out of POC tests for TB are also reviewed.”


The news editors report that additional information may be obtained by contacting K. Dheda, University of Hong Kong, Dept. of Microbiol, Queen Mary Hospital, Hong Kong, Hong Kong, People’s Republic of China. (2013 Mar 18)
Rollins School of Public Health, Atlanta: Prescribed and self-medication use increase delays in diagnosis of tuberculosis in the country of Georgia

By a News Reporter-Staff News Editor at Tuberculosis Week – Investigators publish new report on Tuberculosis and Lung Disease. According to news reporting originating in Atlanta, Georgia, by NewsRx journalists, research stated, “Georgia has a high burden of tuberculosis (TB), including multidrug-resistant TB. Enhancing early diagnosis of TB is a priority to reduce transmission.”

The news reporters obtained a quote from the research from the Rollins School of Public Health, “To quantify delays in TB diagnosis and identify risk factors for delay in the country of Georgia. In a cross-sectional study, persons with newly diagnosed, culture-confirmed pulmonary TB were interviewed within 2 months of diagnosis and medical and laboratory records were abstracted. Among 247 persons enrolled, the mean and median total TB diagnostic delay was respectively 89.9 and 59.5 days. The mean and median patient delay was 56.2 and 23.5 days, while health care system delay was 33.7 and 14.0 days. In multivariable analysis, receipt of a medication prior to TB diagnosis was associated with increased overall diagnostic delay (adjusted odds ratio [aOR] 2.28, 95%CI 1.09-4.79); antibiotic use prior to diagnosis increased the risk of prolonged health care delay (aOR 4.16, 95%CI 1.97-8.79). TB cases who had increased patient-related diagnostic delay were less likely to have prolonged health care diagnostic delay (aOR 0.38, 95%CI 0.19-0.74). Prolonged delays in detecting TB are common in Georgia.”

According to the news reporters, the research concluded: “Interventions addressing the misuse of antibiotics and targeting groups at risk for prolonged delay are warranted to reduce diagnostic delays and enhance TB control.”


Our news correspondents report that additional information may be obtained by contacting A.S. Rabin, Emory Rollins Sch Public Hlth, Atlanta, GA, United States. (2013 Mar 11)
New York City Department of Health & Mental Hygiene, Queens: Delay in diagnosis leading to nosocomial transmission of tuberculosis at a New York City health care facility

By a News Reporter-Staff News Editor at Tuberculosis Week – Investigators publish new report on Mycobacterium Infections. According to news reporting originating in Queens, New York, by NewsRx journalists, research stated, “Demographic changes have increased the number of elderly individuals for whom age-related immunosenescence may increase latent tuberculosis (TB) infection (LTBI) activation risk. As TB rates decline, maintaining clinical suspicion for TB is challenging.”

The news reporters obtained a quote from the research from the New York City Department of Health & Mental Hygiene, “Timely identification, isolation, and treatment of infectious patients are especially important in settings with vulnerable individuals. An outbreak investigation was conducted at a long-term care facility/hospital complex after a prolonged TB exposure associated with delayed diagnosis in a tuberculin skin test (TST)-negative cancer patient resulted in a secondary TB case along with other evidence of transmission. Investigators identified 64 patient and 239 staff contacts. Among those tested with TST, 7 (23%) patients and 5 (8%) staff at the long-term care facility had conversions. Because of evidence of transmission, concerns about TST anergy, and the high number of patients with illnesses such as cancer and diabetes that increase TB risk, LTBI treatment was recommended for all exposed long-term care facility patients regardless of TST results once active TB was ruled out. After the investigation concluded, a former patient who tested TST-negative and did not receive LTBI treatment developed active TB. When evaluating symptomatic patients, especially elderly individuals, clinicians should ‘think TB’ regardless of a negative test for TB infection.”

According to the news reporters, the research concluded: “After known exposure and when transmission evidence exists, clinicians should consider providing LTBI treatment to elderly contacts with co-morbidities regardless of LTBI test results.”

For more information on this research see: Delay in diagnosis leading to nosocomial transmission of tuberculosis at a New York City health care facility. American Journal of Infection Control, 2013;41(2):155-160. American Journal of Infection Control can be contacted at: Mosby-Elsevier, 360 Park Avenue South, New York, NY 10010-1710, USA.

Our news correspondents report that additional information may be obtained by contacting T.G. Harris, New York City Dept. of Hlth & Mental Hyg, Bur TB Control, Queens, NY 11101, United States. (2013 Mar 04)
University of Washington, Seattle: Diagnostic accuracy of same-day microscopy versus standard microscopy for pulmonary tuberculosis: a systematic review and meta-analysis

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – Investigators discuss new findings in Infectious Diseases. According to news reporting from Seattle, Washington, by NewsRx journalists, research stated, “Sputum smear microscopy is the most widely available diagnostic test for pulmonary tuberculosis in countries with a high burden of the disease. Improving its accuracy is crucial to achievement of case-detection targets established by the Millennium Development Goals.”

The news correspondents obtained a quote from the research from the University of Washington, “Unfortunately, many patients are unable to submit all of the specimens needed for examination or to return for treatment because standard sputum collection and reporting requires several clinic visits. To inform policy recommendations by a WHO-convened Expert Group, we aimed to assess the accuracy of sputum smear examination with strategies for obtaining sputum on 1 day compared with strategies for obtaining sputum over 2 days. We did a systematic review and meta-analysis of research articles comparing the accuracy of front-loaded or same-day microscopy and standard sputum smear microscopy for diagnosis of culture-confirmed pulmonary tuberculosis. We searched Medline, Embase, Biosis, and Web of Science for articles published between Jan 1, 2005, and Feb 14, 2012. Two investigators identified eligible articles and extracted data for individual study sites. We generated pooled summary estimates (95% CIs) for sensitivity and specificity by use of random-effects meta-analysis when four or more studies were available. We identified eight relevant studies from five articles enrolling 7771 patients with suspected tuberculosis in low-income countries. Compared with the standard approach of examination of two smears with Ziehl-Neelsen light microscopy over 2 days, examination of two smears taken on the same day had much the same sensitivity (64% [95% CI 60 to 69] for standard microscopy vs 63% [58 to 68] for same-day microscopy) and specificity (98% [97 to 99] vs 98% [97 to 99]). We noted similar results for studies employing light-emitting diode fluorescence microscopy and for studies examining three smears, whether they were compared with two-smear strategies or with one another. Same-day sputum smear microscopy is as accurate as standard smear microscopy.”

According to the news reporters, the research concluded: “Data from tuberculosis programmes are needed to document the changes required in the health system to successfully implement the strategy and understand its effects.”
CHAPTER 2  DIAGNOSIS AND SCREENING


Our news journalists report that additional information may be obtained by contacting J.L. Davis, University of Washington, Sch Public Hlth, Dept. of Hlth Serv, Seattle, WA 98195, United States. (2013 Mar 04)

G.N. Ramachandran Knowledge Center for Genome Informatics, Delhi: Computational screening for new inhibitors of M. tuberculosis mycolyltransferases antigen 85 group of proteins as potential drug targets

By a News Reporter-Staff News Editor at Biotech Week – Investigators publish new report on Mycobacterium Infections. According to news originating from Delhi, India, by NewsRx correspondents, research stated, “The group of antigen 85 proteins of *Mycobacterium tuberculosis* is responsible for converting trehalose monomycolate to trehalose dimycolate, which contributes to cell wall stability. Here, we have used a serial enrichment approach to identify new potential inhibitors by searching the libraries of compounds using both 2D atom pair descriptors and binary fingerprints followed by molecular docking.”

Our news journalists obtained a quote from the research from G.N. Ramachandran Knowledge Center for Genome Informatics, “Three different docking softwares AutoDock, GOLD, and LigandFit were used for docking calculations. In addition, we applied the criteria of selecting compounds with binding efficiency close to the starting known inhibitor and showing potential to form hydrogen bonds with the active site amino acid residues. The starting inhibitor was ethyl-3-phenoxybenzylbutylphosphonate, which had IC(50) value of 2.0 M in mycolyltransferase inhibition assay. Our search from more than 34 million compounds from public libraries yielded 49 compounds. Subsequently, selection was restricted to compounds conforming to the Lipinski rule of five and exhibiting hydrogen bonding to any of the amino acid residues in the active site pocket of all three proteins of antigen 85A, 85B, and 85C. Finally, we selected those ligands which were ranked top in the table with other known decoys in all the docking results. The compound NIH415032 from tuberculosis antimicrobial acquisition and coordinating facility was further examined using molecular dynamics.
simulations for 10 ns. These results showed that the binding is stable, although some of the hydrogen bond atom pairs varied through the course of simulation. The NIH415032 has antitubercular properties with IC(90) at 20 g/ml (53.023 M).

According to the news editors, the research concluded: “These results will be helpful to the medicinal chemists for developing new antitubercular molecules for testing.”

For more information on this research see: Computational screening for new inhibitors of M. tuberculosis mycolyltransferases antigen 85 group of proteins as potential drug targets. *Journal of Biomolecular Structure & Dynamics*, 2013;31(1):30-43.

The news correspondents report that additional information may be obtained from S. Gahoi, GN Ramachandran Knowledge Centre for Genome Informatics, CSIR-Institute of Genomics and Integrative Biology, Mall Road, Delhi, 110 007, India. (2013 Feb 20)

**Ohio State University, Columbus: Can social history variables predict prison inmates’ risk for latent tuberculosis infection?**

By a News Reporter-Staff News Editor at Life Science Weekly – A new study on Tuberculosis is now available. According to news originating from Columbus, Ohio, by NewsRx correspondents, research stated, “Improved screening and treatment of latent tuberculosis infection (LTBI) in correctional facilities may improve TB control. The Ohio Department of Rehabilitation and Correction (ODRC) consists of 32 prisons.”

Our news journalists obtained a quote from the research from Ohio State University, “Inmates are screened upon entry to ODRC and yearly thereafter. The objective of the study was to determine if social history factors such as tobacco, alcohol, and drug use are significant predictors of LTBI and treatment outcomes. We reviewed the medical charts of inmates and randomly selected age-matched controls at one ODRC facility for 2009. We used a conditional logistic regression to assess associations between selected social history variables and LTBI diagnosis. Eighty-nine inmates with a history of LTBI and 88 controls were identified. No social history variable was a significant predictor of LTBI. Medical comorbidities such as asthma, rheumatoid arthritis, and hepatitis C were significantly higher in inmates with LTBI. 84% of inmates diagnosed with LTBI had either completed or were on treatment. Annual TB screening may not be cost-effective in all inmate populations. Identification of factors to help target screening populations at risk for TB is critical. Social history variables did not predict LTBI in our inmate population.”

According to the news editors, the research concluded: “Additional studies are needed to identify inmates for the targeted TB testing.”
For more information on this research see: Can social history variables predict prison inmates’ risk for latent tuberculosis infection? *Tuberculosis Research and Treatment*, 2012;2012():132406. (Hindawi Publishing - www.hindawi.com; Tuberculosis Research and Treatment - http://www.hindawi.com/journals/trt/)

The news correspondents report that additional information may be obtained from T.E. Weant, Division of Epidemiology, College of Public Health, The Ohio State University, Columbus, OH 43210, United States. (2013 Feb 05)

**Yonsei University, Wonju: Interferon gamma mRNA quantitative real-time polymerase chain reaction for the diagnosis of latent tuberculosis: a novel interferon gamma release assay**

By a News Reporter-Staff News Editor at Life Science Weekly – Research findings on Mycobacterium Infections are discussed in a new report. According to news originating from Wonju, South Korea, by NewsRx correspondents, research stated, “The interferon gamma (IFN-gamma) release assay (IGRA) is widely used as a diagnostic method for latent tuberculosis infection (LTBI). The QuantiFERON-TB Gold and QuantiFERON-TB Gold In-tube (QFT-IT) tests measure plasma IFN-gamma levels using enzyme-linked immunosorbent assay (ELISA), and T-SPOT.TB counts IFN-gamma-producing cells using enzyme-linked immunosorbent spot assay.”

Our news journalists obtained a quote from the research from Yonsei University, “IFN-gamma mRNA was evaluated as an indicator of IGRA in comparison with QFT-IT IFN-gamma ELISA in 46 subjects with active TB and in 73 at low risk for TB. Significant IFN-gamma mRNA expression was detected from 30 min and peaked 4 h after stimulation with MTB antigens or mitogen. This was defined as the optimal time point for IFN-gamma mRNA real-time polymerase chain reaction (PCR). The sensitivities of IFN-gamma mRNA real-time PCR and IFN-gamma ELISA were 84.8% (39/46) and 89.1% (41/46), respectively (no significant difference). Although the specificities of IFN-gamma ELISA was 4.1% higher than that of IFN-gamma mRNA real-time PCR (60.3% versus 56.2%), the difference was not statistically significant. The overall agreement between IFN-gamma mRNA real-time PCR and IFN-gamma ELISA was 79.8% (kappa = 0.475).”

According to the news editors, the research concluded: “Whilst there was no difference in the performance of IFN-gamma mRNA real-time PCR and IFN-gamma ELISA, IFN-gamma mRNA real-time PCR was superior to IFN-gamma ELISA in terms of the time required for detection of MTB infection.”

The news correspondents report that additional information may be obtained from S. Kim, Yonsei University, Wonju Coll Med, Dept. of Lab Med, Wonju, South Korea. (2013 Feb 05)

Makerere University College of Health Sciences, Kampala: Evaluation of in-house PCR for diagnosis of smear-negative pulmonary tuberculosis in Kampala, Uganda

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – Current study results on Biology and Medicine have been published. According to news reporting out of Kampala, Uganda, by NewsRx editors, research stated, “Nucleic acid amplification tests (NAATs) have offered hope for rapid diagnosis of tuberculosis (TB). However, their efficiency with smear-negative samples has not been widely studied in low income settings.”

Our news journalists obtained a quote from the research from the Makerere University College of Health Sciences, “Here, we evaluated in-house PCR assay for diagnosis of smear-negative TB using Lowenstein-Jensen (LJ) culture as the baseline test. Two hundred and five pulmonary TB (PTB) suspects with smear-negative sputum samples, admitted on a short stay emergency ward at Mulago Hospital in Kampala, Uganda, were enrolled.”

According to the news editors, the research concluded: “Two smear-negative sputum samples were obtained from each PTB suspect and processed simultaneously for identification of MTBC using in-house PCR and LJ culture.”


Our news journalists report that additional information may be obtained by contacting L. Nakiyingi, Infectious Diseases Institute, Makerere University College of Health Sciences, Mulago Hospital Complex, Kampala, Uganda. (2013 Jan 28)
Autonomous University, Bellaterra: Effects of vaccination against paratuberculosis on tuberculosis in goats: diagnostic interferences and cross-protection

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators discuss new findings in Veterinary Research. According to news reporting out of Bellaterra, Spain, by NewsRx editors, research stated, “Most countries carrying out campaigns of bovine tuberculosis (TB) eradication impose a ban on the use of mycobacterial vaccines in cattle. However, vaccination against paratuberculosis (PTB) in goats is often allowed even when its effect on TB diagnosis has not been fully evaluated.”

Our news journalists obtained a quote from the research from Autonomous University, “To address this issue, goat kids previously vaccinated against PTB were experimentally infected with TB. Evaluation of interferon-gamma (IFN-gamma) secretion induced by avian and bovine tuberculins (PPD) showed a predominant avian PPD-biased response in the vaccinated group from week 4 post-vaccination onward. Although 60% of the animals were bovine reactors at week 14, avian PPD-biased responses returned at week 16. After challenge with M. caprae, the IFN-gamma responses radically changed to show predominant bovine PPD-biased responses from week 18 onward. In addition, cross-reactions with bovine PPD that had been observed in the vaccinated group at week 14 were reduced when using the M. tuberculosis complex-specific antigens ESAT-6/CFP-10 and Rv3615c as new DIVA (differentiation of infected and vaccinated animals) reagents, which further maintained sensitivity post-challenge. Ninety percent of the animals reacted positively to the tuberculin cervical comparative intradermal test performed at 12 weeks post-infection. Furthermore, post-mortem analysis showed reductions in tuberculous lesions and bacterial burden in some vaccinated animals, particularly expressed in terms of the degree of extrapulmonary dissemination of TB infection. Our results suggest a degree of interference of PTB vaccination with current TB diagnostics that can be fully mitigated when using new DIVA reagents.”

According to the news editors, the research concluded: “A partial protective effect associated with vaccination was also observed in some vaccinated animals.”

For more information on this research see: Effects of vaccination against paratuberculosis on tuberculosis in goats: diagnostic interferences and cross-protection. *BMC Veterinary Research*, 2012;8():1-11. *BMC Veterinary Research* can be contacted at: Biomed Central Ltd, 236 Grays Inn Rd, Floor 6, London WC1X 8HL, England. (BioMed Central - http://www.biomedcentral.com/; BMC Veterinary Research - http://www.biomedcentral.com/bmcvetres/)
University of Sassari: Usefulness of ultrasound in the diagnosis of peritoneal tuberculosis

By a News Reporter-Staff News Editor at Life Science Weekly – Data detailed on Infection Research have been presented. According to news reporting out of Sassari, Italy, by NewsRx editors, research stated, “The peritoneum is one of the most common extrapulmonary sites of tuberculous infection. We report a case of peritoneal tuberculosis (TB) in a 25-year-old man.”

Our news journalists obtained a quote from the research from the University of Sassari, “In this case, ultrasound of the abdomen played an important role in the diagnostic process. The diagnosis of this disease, however, remains a challenge because of its insidious nature, the variability of its presentation, and the limitations of available diagnostic tests. A high index of suspicion should be considered, particularly in high-risk patients with unexplained ascites.”

According to the news editors, the research concluded: “In our case ultrasound guided the diagnosis by rapidly identifying abnormal signs, which in high-prevalence settings are extremely suggestive of peritoneal tuberculosis.”

For more information on this research see: Usefulness of ultrasound in the diagnosis of peritoneal tuberculosis. Journal of Infection In Developing Countries, 2012;6(12):886-90.

Institute for Global Health, Amsterdam: Role of the QuantiFERON &#174;-TB Gold In-Tube assay in screening new immigrants for tuberculosis infection

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – New research on Respiratory Research is the subject of a report. According to news reporting originating from Amsterdam, Netherlands, by NewsRx correspondents, research stated, “This study aimed to estimate the risk of progression to active tuberculosis (TB) within 2 yrs after entry in newly arriving immigrants who were screened with the QuantiFERONI &#174;-TB Gold In-Tube assay (OFT-GIT; Cellestis,
Carnegie, Australia). In a case-base design, we determined the prevalence QFT-GIT-positive subjects among a representative sample of immigrants aged &gt;= 18 yrs who arrived between April 2009 and March 2011 (the base cohort).”

Our news editors obtained a quote from the research from Institute for Global Health, “Active TB patients (cases) within 2 yrs post-arrival in 2005, 2006 or 2007 were extracted from the Netherlands Tuberculosis Register. The risk of progression to active TB was estimated using Bayesian analyses to adjust for the sensitivity of QFT-GIT. Among the base cohort, 20% of 1,468 immigrants were QFT-GIT positive. Stratified by TB incidence in the person’s country of origin as low (&lt;100 cases per 100,000 population), intermediate (100-199 cases per 100,000) or high (&gt;= 200 cases per 100,000), the risk of progression to active TB per 100,000 arriving immigrants if QFT-GIT positive (95% credibility interval) was 456 (95% CI 307-589), 590 (397-762) and 386 (259-499), respectively, compared with 18 (0-46), 38 (0-97) and 28 (0-71) if OFT-GIT negative.”

According to the news editors, the research concluded: “Screening newly arriving immigrants with QFT-GIT contributes to detecting those at high risk of subsequent TB reactivation within 2 yrs after entry, which offers opportunities for prevention by targeted interventions.”


The news editors report that additional information may be obtained by contacting C. Mulder, Amsterdam Inst Global Hlth & Dev, Amsterdam, Netherlands. (2013 Jan 21)

Medical College, Vadodara: Lichen scrofulosorum: A diagnosis overlooked

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators discuss new findings in Tuberculosis. According to news reporting originating from Vadodara, India, by NewsRx correspondents, research stated, “Lichen scrofulosorum, also known as ‘tuberculosis cutis lichenoides,’ is a rare tuberculid that presents as a lichenoid eruption of minute papules in children and adolescents with tuberculosis. The lesions are usually asymptomatic, closely grouped, skin-colored to reddish-brown papules, often perifollicular, and are mainly found on the abdomen, chest, back, and proximal parts of the limbs.”
Our news editors obtained a quote from the research from Medical College, “The eruption is usually associated with a strongly positive tuberculin reaction. Diagnosis of these lesions can be difficult, as they resemble many other dermatological conditions that are often primarily considered. We report a case of lichen scrofulosorum in an adult male without any focus of tuberculosis.”

According to the news editors, the research concluded: “He responded promptly to antitubercular therapy with complete clearance of lesions in one month.”

For more information on this research see: Lichen scrofulosorum: A diagnosis overlooked. Indian Dermatology Online Journal, 2012;3(3):190-2.

The news editors report that additional information may be obtained by contacting P. Singhal, Dept. of Skin-VD, Medical College and SSG Hospital, Vadodara, Gujarat, India. (2012 Dec 25)

University of Witwatersrand, Wits: Implementation of Xpert MTB/RIF for routine point-of-care diagnosis of tuberculosis at the primary care level

By a News Reporter-Staff News Editor at Life Science Weekly – Data detailed on Medical Research have been presented. According to news reporting out of Wits, South Africa, by NewsRx editors, research stated, “Xpert MTB/RIF (Xpert) offers rapid detection of Mycobacterium tuberculosis and rifampicin resistance. However, little is known about routine point-of-care (POC) use in high TB/HIV burden settings.”

Our news journalists obtained a quote from the research from the University of Witwatersrand, “We describe our experiences of launching Xpert as the POC, initial diagnostic for all TB suspects at a primary healthcare clinic in Johannesburg, South Africa. Noted important benefits of POC Xpert were fewer clinic visits, rapid detection of TB and rifampicin resistance, real-time assessment of accompanying household members of new TB cases, and increased staff motivation for TB screening. While Xpert results are available within 2 hours, actual turnaround time was longer for most patients because of sample preparation time and clinic congestion. Consequently, a GX4 instrument did not result in a 16-test capacity during an 8-hour working day, and some patients did not receive same-day results. Loss to follow-up was an unforeseen challenge, overcome by clinic flow changes, marking of clinic files, documenting patients’ physical description and locating patients in the clinic by cell phone. Staff with high school education successfully performed the assay after minimal training. Human resource requirements were considerable, with a minimum of 2 staff needed to supervise sputum collection, process sputum, perform assays, and document
results for an average of 15 TB suspects daily. POC placement of the instrument transferred logistical responsibilities to the clinic, including quality assurance, maintenance, stock control and cartridge disposal.”

According to the news editors, the research concluded: “POC use of Xpert is feasible at the primary healthcare level but must be accompanied by financial, operational and logistical support.”


Our news journalists report that additional information may be obtained by contacting K. Clouse, University of Witwatersrand, Dept. of Mol Med & Haematol, Sch Pathol, ZA-2050 Wits, South Africa. (2012 Dec 18)

**University Nova of Lisboa, Lisbon: Tuberculosis diagnosis after bleach processing for early stage tuberculosis laboratory capacity building**

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators discuss new findings in Tuberculosis and Lung Disease. According to news reporting originating from Lisbon, Portugal, by NewsRx correspondents, research stated, “The diagnosis of tuberculosis is seriously hampered in the absence of standard biosafety laboratory facilities for specimen concentration and Mycobacterium tuberculosis culture.”

Our news editors obtained a quote from the research from the University Nova of Lisboa, “Within a laboratory twinning arrangement, heat-fixed direct smear and sediment from 74 bleach-processed and 20 non-processed specimens from Cumura Hospital, Guinea-Bissau, were sent to Lisbon for molecular evaluation of rifampicin resistance. Sequence analysis of a 369 base-pair ppoB locus detected 3.2% (3/94) resistant specimens.”

According to the news editors, the research concluded: “To our knowledge, this represents the first report on the molecular analysis of M. tuberculosis from bleach-processed sputum, an alternative to current diagnostic practice in low-resource settings.”

For more information on this research see: Tuberculosis diagnosis after bleach processing for early stage tuberculosis laboratory capacity building. *International Journal of Tuberculosis and Lung Disease*, 2012;16(11):1535-1537. *International Journal of Tuberculosis and Lung Disease* can be contacted at: Int Union Against Tuberculosis Lung Disease (I U A T L D), 68 Boulevard Saint-Michel, 75006 Paris, France.
Fiocruz, Rio de Janeiro: Russian “Successful” Clone B0/W148 of Mycobacterium tuberculosis Beijing Genotype: a Multiplex PCR Assay for Rapid Detection and Global Screening

By a News Reporter-Staff News Editor at Tuberculosis Week – Researchers detail new data in Clinical Microbiology. According to news reporting originating in Rio de Janeiro, Brazil, by NewsRx journalists, research stated, “We describe a multiplex PCR assay to detect the Mycobacterium tuberculosis Beijing genotype variant B0/W148, which is considered a ‘successful’ clone of M. tuberculosis, widespread in Russia.”

The news reporters obtained a quote from the research from Fiocruz, “Specificity and sensitivity of the assay were 100% based on the analysis of a collection of 516 M. tuberculosis isolates of different genotypes and origins.”

According to the news reporters, the research concluded: “This assay may be used for accurate and simple detection and surveillance of this clinically and epidemiologically important variant of M. tuberculosis.”


Our news correspondents report that additional information may be obtained by contacting I. Mokrousov, Fiocruz MS, Inst Oswaldo Cruz, Lab Mol Biol Appl Mycobacteria, BR-21045900 Rio De Janeiro, Brazil. (2012 Dec 03)
Nanjing Medical University: Evaluation of interferon-gamma release assays for the diagnosis of tuberculosis: an updated meta-analysis

By a News Reporter-Staff News Editor at Life Science Weekly – Data detailed on Clinical Microbiology have been presented. According to news reporting from Nanjing, People’s Republic of China, by NewsRx journalists, research stated, “The objective of this investigation was to systematically evaluate the diagnostic accuracy of interferon-gamma release assays (IGRAs) for tuberculosis disease. Both English and Chinese databases were searched for relevant articles through January 2012.”

The news correspondents obtained a quote from the research from Nanjing Medical University, “We included studies that were restricted to diagnostic applications of IGRAs in patients with active tuberculosis and excluded studies performed in the immune-compromised population. We used Meta-DiSc software to handle the data. We calculated the sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), diagnostic odds ratio (DOR), and 95% confidence interval (CI) for each study. We also calculated the pooled sensitivity, specificity, PLR, NLR, DOR, and produced forest plots and summary receiver operating characteristic (SROC) curves. A total of 61 papers (73 studies) were eligible for meta-analysis, including 36 published in English and 25 published in the Chinese language. The overall sensitivity, specificity, PLR, NLR, DOR, and 95% CI of IGRAs were 0.85 (95% CI: 0.84-0.86), 0.84 (95% CI: 0.83-0.85), 7.82 (95% CI: 6.01-10.19), 0.17 (95% CI: 0.14-0.21), and 59.27 (95% CI: 40.19-87.42), respectively. For ten studies evaluating T-SPOT.TB in China, the combined sensitivity, specificity, PLR, NLR, DOR, and 95% CI were 0.88 (95% CI: 0.86-0.91), 0.89 (95% CI: 0.86-0.92), 8.86 (95% CI: 5.42-14.46), 0.13 (95% CI: 0.10-0.17), and 88.15 (95% CI: 41.76-186.07), respectively. The SROC area under the curve (AUC) was 0.9548 (95% CI: 0.9323-0.9773).”

According to the news reporters, the research concluded: “Though IGRAs showed good sensitivity and specificity for the detection of tuberculosis in this meta-analysis, the decision to use an IGRA should be based on the local prevalence of the disease and the country guidelines, as well as resources and logistical considerations.”


Our news journalists report that additional information may be obtained by contacting Y. Dai, Dept. of Epidemiology and Biostatistics,
Diagnostic potential of 16 kDa (HspX, alpha-crystalline) antigen for serodiagnosis of tuberculosis

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – Data detailed on Medical Research have been presented. According to news reporting from Delhi, India, by NewsRx journalists, research stated, “Tuberculosis (TB) is a public health problem worldwide. Rapid and accurate diagnosis of tuberculosis is crucial to facilitate early treatment of infectious cases and to reduce its spread.”

The news correspondents obtained a quote from the research, “The present study was aimed to evaluation of 16 kDa antigen as a serodiagnostic tool in pulmonary and extra-pulmonary tuberculosis patients in an effort to improve diagnostic algorithm for tuberculosis. In this study, 200 serum samples were collected from smear positive and culture confirmed pulmonary tuberculosis patients, 30 tubercular pleural effusions and 21 tubercular meningitis (TBM) patients. Serum samples from 36 healthy, age matched controls (hospital staff), along with 60 patients with non-tubercular respiratory diseases were also collected and evaluated. Humoral response (both IgG and IgA) was looked for 16 kDa antigen using indirect ELISA. Sensitivity of detection in various categories of pulmonary TB patients ranged between 73.8 and 81.2 per cent. While in the extra-pulmonary TB samples the sensitivity was 42.8 per cent (TBM) and 63.3 per cent (tubercular pleural effusion). The test specificity in both the groups was high (94.7%). All of the non-disease controls were negative. Among non-tubercular disease controls, five patients gave a positive humoral response against 16 kDa. Serodiagnostic tests for TB have always had drawbacks of suboptimal sensitivity and specificity. The antigen used in this study gave encouraging results in pulmonary TB only, while in extra-pulmonary TB (tubercular meningitis and tubercular pleural effusion), this has shown a limited role in terms of sensitivity.”

According to the news reporters, the research concluded: “Further work is required to validate its role in serodiagnosis of TB especially extra-pulmonary TB.”

For more information on this research see: Diagnostic potential of 16 kDa (HspX, alpha-crystalline) antigen for serodiagnosis of tuberculosis. Indian Journal of Medical Research, 2012;135(5):771-777. Indian Journal of Medical Research can be contacted at: Indian Council Medical Res, PO Box 4911 Ansari Nagar, New Delhi 110029, India.

Our news journalists report that additional information may be obtained by contacting A. Kaushik, Rajan Babu Inst Pulm Med & TB, Delhi, India. (2012 Nov 05)
University of Minnesota, Minneapolis: A high-throughput screening fluorescence polarization assay for fatty acid adenylating enzymes in Mycobacterium tuberculosis

By a News Reporter-Staff News Editor at Tuberculosis Week – A new study on Analytical Biochemistry is now available. According to news reporting originating in Minneapolis, Minnesota, by NewsRx journalists, research stated, “Mycobacterium tuberculosis, the etiological agent of tuberculosis (TB), encodes for an astonishing 34 fatty acid adenylating enzymes (FadDs), which play key roles in lipid metabolism. FadDs involved in lipid biosynthesis are functionally nonredundant and serve to link fatty acid and polyketide synthesis to produce some of the most architecturally complex natural lipids including the essential mycolic acids as well as the virulence-conferring phthiocerol dimycocerosates, phenolic glycolipids, and mycobactins.”

The news reporters obtained a quote from the research from the University of Minnesota, “Here we describe the systematic development and optimization of a fluorescence polarization assay to identify small molecule inhibitors as potential antitubercular agents. We fluorescently labeled a bisubstrate inhibitor to generate a fluorescent probe/tracer, which bound with a K(D) of 245 nM to FadD28. Next, we evaluated assay performance by competitive binding experiments with a series of known ligands and assessed the impact of control parameters including incubation time, stability of the signal, temperature, and DMSO concentration.”

According to the news reporters, the research concluded: “As a final level of validation the LOPAC1280 library was screened in a 384-well plate format and the assay performed with a Z-factor of 0.75, demonstrating its readiness for high-throughput screening.”


Our news correspondents report that additional information may be obtained by contacting K.D. Grimes, Center for Drug Design, University of Minnesota, Minneapolis, MN, United States. (2012 Oct 29)
Chongqing Medical University: Screening and comparison of differentially expressed genes between one MDR-TB strain and the virulent M. tuberculosis H37Rv

By a News Reporter-Staff News Editor at Health & Medicine Week – Current study results on Genetic Research have been published. According to news originating from Chongqing, People’s Republic of China, by NewsRx correspondents, research stated, “To screen and compare the differentially expressed genes between one MDR-TB strain separated from one child patient and the virulent Mycobacterium tuberculosis H37Rv, suppression subtractive hybridization (SSH) technology was used to build a library of cDNAs that were differentially expressed in the MDR and H37Rv. From this cDNA library, genes that were expressed in the MDR-TB but not in the H37Rv were selected for gene sequencing and homology analysis; 113 positive clones were obtained, their cDNA fragments were sequenced, and homology analysis was performed.”

Our news journalists obtained a quote from the research from Chongqing Medical University, “Four novel sequences were identified. The results provide a partial list of genes differentially expressed in MDR-TB and four novel genes were found.”

According to the news editors, the researchers concluded: “Identification of these genes may contribute to our understanding of MDR-TB development.”

For more information on this research see: Screening and comparison of differentially expressed genes between one MDR-TB strain and the virulent M. tuberculosis H37Rv. Gene, 2012;506(1):223-229. Gene can be contacted at: Elsevier Science Bv, PO Box 211, 1000 Ae Amsterdam, Netherlands. (Elsevier - www.elsevier.com; Gene - http://www.elsevier.com/wps/product/cws_home/506033)

The news correspondents report that additional information may be obtained from Y.L. Zhang, Chongqing Med Univ, Chongqing Int Sci & Technol Cooperat Center Child De, Infect & Digestol DepAffiliated Childrens Hosp, Pediat InstMinist EducKey Lab Pediat Chongqing, Chongqing 0086400014, People’s Republic of China. (2012 Oct 19)

World Health Organization, Geneva: Evaluation of Immigrant Tuberculosis Screening in Industrialized Countries

By a News Reporter-Staff News Editor at Tuberculosis Week – Research findings on Mycobacterium Infections are discussed in a new report. According to news reporting out of Geneva, Switzerland, by NewsRx editors, research stated, “In industrialized countries, tuberculosis (TB) cases are concentrated among immigrants and driven by reactivation of
imported latent TB infection (LTBI). We examined mechanisms used to screen immigrants for TB and LTBI by sending an anonymous, 18-point questionnaire to 31 member countries of the Organisation for Economic Cooperation and Development.”

Our news journalists obtained a quote from the research from World Health Organization, “Twenty-nine (93.5%) of 31 responded; 25 (86.2%) screened immigrants for active TB. Fewer countries (16/29, 55.2%) screened for LTBI. Marked variations were observed in targeted populations for age (range <5 years of age to all age groups) and TB incidence in countries of origin of immigrants (>20 cases/100,000 population to >500 cases/100,000). LTBI screening was conducted in 11/16 countries by using the tuberculin skin test. Six countries used interferon-gamma release assays, primarily to confirm positive tuberculin skin test results. Industrialized countries performed LTBI screening infrequently and policies varied widely.”

According to the news editors, the researchers concluded: “There is an urgent need to define the cost-effectiveness of LTBI screening strategies for immigrants.”

For more information on this research see: Evaluation of Immigrant Tuberculosis Screening in Industrialized Countries. Emerging Infectious Diseases, 2012;18(9):1422-1429. Emerging Infectious Diseases can be contacted at: Centers Disease Control, 1600 Clifton Rd, Atlanta, GA 30333, USA.

Our news journalists report that additional information may be obtained by contacting M. Pareek, WHO, CH-1211 Geneva, Switzerland. (2012 Oct 15)

Misericordia Hospital, Udine: Clinical validation of Xpert MTB/RIF for the diagnosis of extrapulmonary tuberculosis

By a News Reporter-Staff News Editor at Pediatrics Week – Research findings on Respiratory Research are discussed in a new report. According to news originating from Udine, Italy, by VerticalNews correspondents, research stated, “Extrapulmonary tuberculosis (EPTB) accounts for more than 20% of tuberculosis (TB) cases. Xpert MTB/RIF (Xpert) (Cepheid, Sunnyvale, CA, USA) is a fully automated amplification system, for which excellent results in the diagnosis of pulmonary TB in highly endemic countries have been recently reported.”

Our news journalists obtained a quote from the research from Misericordia Hospital, “We aimed to assess the performance of the Xpert system in diagnosing EPTB in a low incidence setting. We investigated with Xpert a large number of consecutive extrapulmonary clinical specimens (1,476, corresponding to 1,068 patients) including both paediatric (494) and adult samples. We found, in comparison with a
reference standard consisting of combination of culture and clinical diagnosis of TB, an overall sensitivity and specificity of 81.3% and 99.8% for Xpert, while the sensitivity of microscopy was 48%. For biopsies, urines, pus and cerebrospinal fluids the sensitivity exceeded 85%, while it was slightly under 80% for gastric aspirates. It was, in contrast, lower than 50% for cavitary fluids. High sensitivity and specificity (86.9% and 99.7%, respectively) were also obtained for paediatric specimens. Although the role of culture remains central in the microbiological diagnosis of EPTB, the sensitivity of Xpert in rapidly diagnosing the disease makes it a much better choice compared to smear microscopy.”

According to the news editors, the researchers concluded: “The ability to rule out the disease still remains suboptimal.”


The news correspondents report that additional information may be obtained from E. Tortoli, Misericordia Hosp, Microbiol Lab, Udine, Italy. (2012 Oct 13)

**National Institutes of Health, Bethesda: Pathway-Selective Sensitization of Mycobacterium tuberculosis for Target-Based Whole-Cell Screening**

By a News Reporter-Staff News Editor at Health & Medicine Week – Investigators publish new report on General Chemistry. According to news reporting originating in Bethesda, Maryland, by NewsRx journalists, research stated, “Whole-cell screening of Mycobacterium tuberculosis (Mtb) remains a mainstay of drug discovery, but subsequent target elucidation often proves difficult. Conditional mutants that underexpress essential genes have been used to identify compounds with known mechanism of action by target-based whole-cell screening (TB-WCS).”

The news reporters obtained a quote from the research from the National Institutes of Health, “Here, the feasibility of TB-WCS in Mtb was assessed by generating mutants that conditionally express pantothenate synthetase (panC), diaminopimelate decarboxylase (lysA), and isocitrate lyase (icl1). The essentiality of panC and lysA, and conditional essentiality of icl1 for growth on fatty acids, was confirmed. Depletion of PanC and Icl1 rendered mutants hypersensitive to target-specific
inhibitors. Stable reporter strains were generated for use in high-throughput screening, and their utility was demonstrated by identifying compounds that display greater potency against a PanC-depleted strain.”

According to the news reporters, the researchers concluded: “These findings illustrate the power of TB-WCS as a tool for tuberculosis drug discovery.”


Our news correspondents report that additional information may be obtained by contacting G.L. Abrahams, NIAID, TB Res Sect, Lab Clin Infect Dis, National Institutes of Health, Bethesda, MD 20892, United States. (2012 Oct 05)

Liverpool School of Tropical Medicine: Modelling the impacts of new diagnostic tools for tuberculosis in developing countries to enhance policy decisions

By a News Reporter-Staff News Editor at Life Science Weekly – Current study results on Health Care Management have been published. According to news reporting originating in Liverpool, United Kingdom, by NewsRx journalists, research stated, “The introduction and scale-up of new tools for the diagnosis of Tuberculosis (TB) in developing countries has the potential to make a huge difference to the lives of millions of people living in poverty. To achieve this, policy makers need the information to make the right decisions about which new tools to implement and where in the diagnostic algorithm to apply them most effectively.”

The news reporters obtained a quote from the research from the Liverpool School of Tropical Medicine, “These decisions are difficult as the new tools are often expensive to implement and use, and the health system and patient impacts uncertain, particularly in developing countries where there is a high burden of TB. The authors demonstrate that a discrete event simulation model could play a significant part in improving and informing these decisions. The feasibility of linking the discrete event simulation to a dynamic epidemiology model is also explored in order to take account of longer term impacts on the incidence of TB.”

According to the news reporters, the researchers concluded: “Results from two diagnostic districts in Tanzania are used to illustrate how the approach could be used to improve decisions.”

Our news correspondents report that additional information may be obtained by contacting I. Langley, Clinical Group, Liverpool School of Tropical Medicine, Liverpool, UK.

The publisher of the journal *Health Care Management Science* can be contacted at: Springer, 233 Spring Street, New York, NY 10013, USA. (2012 Oct 02)

**Johns Hopkins University, Baltimore: Rapid Implementation of New TB Diagnostic Tests: Is It Too Soon for a Global Roll-Out of Xpert MTB/RIF?**

By a News Reporter-Staff News Editor at Malaria Weekly – Investigators publish new report on Tropical Medicine and Public Health. According to news reporting out of Baltimore, Maryland, by NewsRx editors, research stated, “In 2011 the World Health Organization approved Xpert MTB/RIF for tuberculosis diagnosis and recommended its rapid implementation. Xpert MTB/RIF is accurate: sensitivity is 72.5-98.2% (smear-negative and -positive cases, respectively) and specificity 99.2%.”

Our news journalists obtained a quote from the research from Johns Hopkins University, “Benefits include same-day diagnosis and simultaneous detection of rifampicin resistance. However, the test has some shortcomings and has not had time for thorough evaluation. Cost-effectiveness studies are difficult to perform and few have been completed. Existing data suggest cost-effectiveness in some, but not all, settings. The urgent need for better diagnostics is evident. Yet, serial implementation of new technologies causes ineffective spending and fragmentation of services. How new tests are incorporated into existing diagnostic algorithms affects both outcomes and costs. More detailed data on performance, effect on patient-important outcomes, and costs when used with adjunct tests are needed for each setting before implementation.”

According to the news editors, the researchers concluded: “While awaiting further clarification it seems prudent to slow its implementation among resource-constrained tuberculosis control programs.”

For more information on this research see: Rapid Implementation of New TB Diagnostic Tests: Is It Too Soon for a Global Roll-Out of Xpert MTB/RIF? *American Journal of Tropical Medicine and Hygiene,*
CHAPTER 2  DIAGNOSIS AND SCREENING

2012;87(2):197-201. *American Journal of Tropical Medicine and Hygiene* can be contacted at: Amer Soc Trop Med & Hygiene, 8000 Westpark Dr, Ste 130, Mclean, VA 22101, USA.

Our news journalists report that additional information may be obtained by contacting D.E. Kirwan, Johns Hopkins University, Sch Public Hlth, Dept. of Int Hlth, Baltimore, MD, United States. (*2012 Oct 01*)

**School of Medicine, London: Diagnostic accuracy of induced sputum LAM ELISA for tuberculosis diagnosis in sputum-scarce patients**

By a News Reporter-Staff News Editor at AIDS Weekly – Investigators discuss new findings in Tuberculosis and Lung Disease. According to news reporting out of London, United Kingdom, by NewsRx editors, research stated, “To examine whether a lipoarabinomannan (LAM) enzyme-linked immunosorbent assay (ELISA) that offers diagnostic utility using urine in patients with tuberculosis (TB) and human immunodeficiency virus (HIV) co-infection can be used in induced sputum to diagnose sputum-scarce patients with suspected TB. LAM was measured in induced sputum samples obtained from 61 consecutively recruited sputum-scarce TB suspects in a tertiary hospital respiratory clinic in South Africa.”

Our news journalists obtained a quote from the research from the School of Medicine, “Liquid culture positivity for Mycobacterium tuberculosis was used as the reference standard. Receiver operating characteristic analysis was used to assess alternative LAM concentration cut-offs. A total of 87% (53/61) of study patients had a valid M. tuberculosis culture result; 49% (23/53) were HIV-infected and 17% (9/53) were culture-positive for M. tuberculosis. Induced sputum smear microscopy and LAM ELISA had an overall sensitivity of 56% (95%CI 27-81); however, the specificity of LAM ELISA was 48% (95%CI 34-62), while the positive and negative predictive values were respectively 18% (95%CI 8-36) and 84% (95%CI 65-94). An optimal rule-in cut-off selected by receiver operating characteristic (LAM concentration $>5.73$ ng/ml) increased test specificity to 98% and reduced sensitivity to 22%. Normalisation of the assay for sample total protein or cell count did not improve diagnostic accuracy.”

According to the news editors, the researchers concluded: “In this proof-of-concept study, the ELISA was not clinically useful for TB diagnosis using induced sputum.”

For more information on this research see: Diagnostic accuracy of induced sputum LAM ELISA for tuberculosis diagnosis in sputum-scarce patients. *International Journal of Tuberculosis and Lung Disease*, 2012;16(8):1108-1112. *International Journal of Tuberculosis and
University of Cape Town, Western Cape: Promising directions in the diagnosis of childhood tuberculosis

By a News Reporter-Staff News Editor at AIDS Weekly – Researchers detail new data in Immune System Diseases and Conditions. According to news reporting from Western Cape, South Africa, by NewsRx journalists, research stated, “Estimates of the burden of childhood tuberculosis have been hampered by the lack of a reliable diagnostic test. Clinical scoring systems, radiological findings and tuberculin skin testing (the traditional methods used for diagnosis) are unreliable, particularly in the era of HIV.”

The news correspondents obtained a quote from the research from the University of Cape Town, “Microbiologic confirmation using induced sputum is feasible and has become increasingly important to define the burden of disease and to enable appropriate treatment. The availability of a rapid molecular diagnostic test (Xpert® MTB/RIF; Cepheid) is an important advance that can improve case detection in children and enable rapid detection of mycobacterial drug resistance. Xpert testing of two induced sputum specimens detected approximately 75% of children with culture-confirmed disease. Urine lipoarabinomannan has shown promise as a rapid diagnostic in a subgroup of HIV-infected severely immunocompromised adults, but there have been no data in children so far.”

According to the news reporters, the researchers concluded: “Further research is needed to develop a rapid point-of-care, reliable and affordable diagnostic test for childhood tuberculosis that can be widely used.”

For more information on this research see: Promising directions in the diagnosis of childhood tuberculosis. Expert Review of Respiratory Medicine, 2012;6(4):385-95.

Our news journalists report that additional information may be obtained by contacting E. Whittaker, Dept. of Paediatrics and Child Health, Red Cross War Memorial Children’s Hospital, University of Cape Town, Cape Town, Western Cape, South Africa. (2012 Oct 01)
Maharshi Dayanand University, Haryana: Diagnosis of extrapulmonary tuberculosis by PCR

By a News Reporter-Staff News Editor at Tuberculosis Week – Current study results on Immunology and Medical Microbiology have been published. According to news reporting originating in Haryana, India, by NewsRx journalists, research stated, “During the last two decades, the resurgence of tuberculosis (TB) has been documented in both developed and developing nations, and much of this increase in TB burden coincided with human immunodeficiency virus (HIV) epidemics. Since then, the disease pattern has changed with a higher incidence of extrapulmonary tuberculosis (EPTB) as well as disseminated TB.”

The news reporters obtained a quote from the research from Maharshi Dayanand University, “EPTB cases include TB lymphadenitis, pleural TB, TB meningitis, osteoarticular TB, genitourinary TB, abdominal TB, cutaneous TB, ocular TB, TB pericarditis and breast TB, although any organ can be involved. Diagnosis of EPTB can be baffling, compelling a high index of suspicion owing to paucibacillary load in the biological specimens. A negative smear for acid-fast bacilli, lack of granulomas on histopathology and failure to culture *Mycobacterium tuberculosis* do not exclude the diagnosis of EPTB. Novel diagnostic modalities such as nucleic acid amplification (NAA) can be useful in varied forms of EPTB.”

According to the news reporters, the researchers concluded: “This review is primarily focused on the diagnosis of several clinical forms of EPTB by polymerase chain reaction (PCR) using different gene targets.”


Our news correspondents report that additional information may be obtained by contacting P.K. Mehta, Centre for Biotechnology, Maharshi Dayanand University, Rohtak, Haryana, India. (2012 Sep 24)

Hebrew University, Jerusalem: Chest Radiography Validity in Screening Pulmonary Tuberculosis in Immigrants From a High-Burden Country

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – Current study results on *Mycobacterium* Infections have been published. According to news originating from Jerusalem, Israel, by NewsRx correspondents, research stated, “Chest x-ray (CXR) is widely used for diagnosing and screening pulmonary tuberculosis (PTB), yet
its validity is debatable and its costs are relatively high. This study aimed to determine the validity of CXR screening in detecting radiological findings compatible with active PTB or with old healed tuberculosis (OHTB).”

Our news journalists obtained a quote from the research from Hebrew University, “All Ethiopian immigrants to Israel between 2001 and 2005 were radiographed before emigration. Immigrants whose CXR demonstrated PTB or OHTB were evaluated, treated, and followed for one year after arrival. The end point of this historical cohort study was a diagnosis of active pulmonary disease within the study period. CXR was performed on 13,379 immigrants. Changes suggesting PTB were identified in 150 (1.1%) of those, and 46 were diagnosed with active PTB. Sensitivity, specificity, and positive predictive value of a CXR suggesting PTB were 80.1%, 99.2%, and 31%, respectively. As PTB prevalence in this cohort is 0.4%, post-test odds for CXR suggestive of PTB were 75.5. Changes suggesting OHTB were identified in 257 (1.9%) immigrants. Of those, 15 (5.8%) developed active PTB within one year following arrival. Sensitivity, specificity, and positive predictive value of CXR suggestive of OHTB were 17.2%, 98.2%, and 5.8%, respectively, when active PTB during the first year was the end point. In this study, 291 CXR were required to detect one active PTB patient, costing $5,802.”

According to the news editors, the researchers concluded: “CXR is a valid and cost-saving tool for screening active PTB in immigrants originating in high-burden countries, and is beneficial in detecting OHTB in immigrants who are at a higher risk for developing active PTB.”

For more information on this research see: Chest Radiography Validity in Screening Pulmonary Tuberculosis in Immigrants From a High-Burden Country. Respiratory Care, 2012;57(7):1137-1144. Respiratory Care can be contacted at: Daedalus Enterprises Inc, 9425 N Mac Arthur Blvd, Ste 100, Irving, TX 75063-4706, USA.

The news correspondents report that additional information may be obtained from Z. Mor, Hebrew University of Jerusalem, Braun Sch Public Hlth, Jerusalem, Israel. (2012 Aug 27)

Srinakharinwirot University, Bangkok: Evaluation of Real-time Polymerase Chain Reaction for Detection of the 16S Ribosomal RNA Gene of Mycobacterium tuberculosis and the Diagnosis of Cervical Tuberculous Lymphadenitis in a Country With a High Tuberculosis Incidence

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators publish new report on Mycobacteria. According to news originating from Bangkok, Thailand, by NewsRx correspondents, research stated, “Tuberculous lymphadenitis (TBL) is the most common form of
extrapulmonary tuberculosis. Currently, the standard diagnostic test for TBL is culture, which takes more than several weeks to yield results.”

Our news journalists obtained a quote from the research from Srinakharinwirot University, “We studied a real-time polymerase chain reaction (PCR) for rapid detection of Mycobacterium tuberculosis in cervical lymph node specimens obtained from patients in a country where the tuberculosis incidence is high. Patients with cervical lymphadenopathy were prospectively enrolled between April 2009 and March 2010. Clinical specimens obtained through fine-needle aspiration (FNA) and excisional biopsy were tested for M. tuberculosis by the COBAS TaqMan MTB Test, a real-time PCR assay for detecting the 16S ribosomal RNA gene of M. tuberculosis. Mycobacterial culture and histopathological findings from tissue biopsy specimens were used as a reference standard for sensitivity and specificity calculations. Of 73 patients, 41 received a diagnosis of TBL. For biopsy specimens, the sensitivity of real-time PCR was 63.4%, and the specificity was 96.9%. For FNA specimens, the sensitivity was 17.1%, and the specificity was 100%. The sensitivity of real-time PCR of biopsy specimens was comparable to that of tissue culture but significant lower than that of histopathological examination (P < .01).”

According to the news editors, the researchers concluded: “Real-time PCR did not increase the yield for rapid diagnosis of TBL.”


The news correspondents report that additional information may be obtained from P. Linasmita, Srinakharinwirot Univ, Fac Med, Dept. of Med, Bangkok, Thailand. (2012 Aug 21)

University of Lille: Discovery of Novel N-Phenylphenoxyacetamide Derivatives as EthR Inhibitors and Ethionamide Boosters by Combining High-Throughput Screening and Synthesis

By a News Reporter-Staff News Editor at Tuberculosis Week – Data detailed on Mycobacterium Infections have been presented. According to news reporting originating from Lille, France, by NewsRx cor-
respondents, research stated, “In this paper, we describe the screening of a 14640-compound library using a novel whole mycobacteria phenotypic assay to discover inhibitors of EthR, a transcriptional repressor implicated in the innate resistance of *Mycobacterium tuberculosis* to the second-line antituberculosis drug ethionamide. From this screening a new chemical family of EthR inhibitors bearing an N-phenylphenoxyacetamide motif was identified.”

Our news editors obtained a quote from the research from the University of Lille, “The X-ray structure of the most potent compound crystallized with EthR inspired the synthesis of a 960-member focused library. These compounds were tested in vitro using a rapid thermal shift assay on EthR to accelerate the optimization. The best compounds were synthesized on a larger scale and confirmed as potent ethionamide boosters on *M. tuberculosis* -infected macrophages.”

According to the news editors, the researchers concluded: “Finally, the cocrystallization of the best optimized analogue with EthR revealed an unexpected reorientation of the ligand in the binding pocket.”


The news editors report that additional information may be obtained by contacting M. Flipo, Universite Lille Nord de France, F-59000 Lille, France. (2012 Aug 20)

**Tongji University School of Medicine, Shanghai: Clinical Value of ELISA-MPT64 for the Diagnosis of Tuberculous Pleurisy**

By a News Reporter-Staff News Editor at Life Science Weekly – Current study results on Mycobacterium Infections have been published. According to news reporting out of Shanghai, People’s Republic of China, by NewsRx editors, research stated, “Tuberculous pleurisy is one of the common extrapulmonary tuberculosis diseases. However, the diagnosis of tuberculous pleurisy still lacks a useful and effective tool, mainly due to paucity of *Mycobacterium tuberculosis* organisms in pleural effusion.”

Our news journalists obtained a quote from the research from the Tongji University School of Medicine, “Previous studies have confirmed that the MPT64 protein is highly specific and is secreted only by *M. tuberculosis* (MTB) complex. Therefore, in this study, we developed ELISA based on recombinantly expressed MPT64 in combination with rabbit polyclonal antibodies. The ELISA-MPT64 method was validated
using MTB strains and tested against clinical samples. Nested PCR, Lowenstein-Jensen (L-J) culture and smear microscopy were employed as the comparative tools for assessing the performance of the assay.”

According to the news editors, the researchers concluded: “Our results demonstrate that the newly established ELISA-MPT64 technique is a rapid and useful tool for the diagnosis of tuberculous pleurisy.”

For more information on this research see: Clinical Value of ELISA-MPT64 for the Diagnosis of Tuberculous Pleurisy. Current Microbiology, 2012;65(3):313-8. Current Microbiology can be contacted at: Springer, 233 Spring Street, New York, NY 10013, USA. (Springer - www.springer.com; Current Microbiology - http://www.springerlink.com/content/0343-8651/)

Our news journalists report that additional information may be obtained by contacting Z. Liu, Shanghai Key Laboratory of Tuberculosis, Shanghai Pulmonary Hospital, Tongji University School of Medicine, No 507 Zhengmin Rd, Shanghai, 200433, People’s Taiwan.

Publisher contact information for the journal Current Microbiology is: Springer, 233 Spring Street, New York, NY 10013, USA. (2012 Aug 14)

Nonclinical selection criteria for maximizing yield of nucleic Acid amplification tests in tuberculosis diagnosis

By a News Reporter-Staff News Editor at Tuberculosis Week – Current study results on Clinical Microbiology have been published. According to news reporting originating from Jamaica Plain, Massachusetts, by NewsRx correspondents, research stated, “In spite of the excellent performance of rapid tuberculosis (TB) nucleic acid amplification (NAA) tests and the clear benefits of immediate diagnosis of TB disease, NAA tests frequently are not used in the diagnosis of pulmonary TB cases, particularly TB cases with smear-negative sputa. Public health laboratories primarily perform TB NAA tests only on a targeted subset of specimens, usually including those that are smear positive and those for which a clinician has specifically requested NAA testing.”

Our news editors obtained a quote from the research, “As an alternative to targeted testing, some laboratories use TB NAA tests universally for all respiratory specimens, though this practice can be prohibitively costly and can be associated with an increased frequency of false-positive results due to testing of lower-risk patients. We propose a strategy for identifying individuals for NAA testing on the basis of non-clinical risk criteria that are routinely provided on the test requisition form, such as type of health care facility from which the specimen is received and patient age group. Use of this strategy at the Massachusetts Department of Public Health Laboratory would allow for NAA test identification of approximately 54 (74%) of 72 culture-positive pulmonary
TB cases over a 1-year period while requiring NAA testing for only 933 (17%) of 5,469 individuals submitting respiratory specimens.”

According to the news editors, the researchers concluded: “We demonstrate that use of nonclinical NAA test selection criteria is an effective strategy for maximizing the number of TB cases that can be rapidly identified while minimizing the number of specimens that must be tested.”


The news editors report that additional information may be obtained by contacting L.L. Han, Massachusetts Dept. of Public Health Bureau of Laboratory Sciences, Jamaica Plain, Massachusetts, United States. *(2012 Aug 13)*

**University of Washington, Seattle: Serological tests for the diagnosis of active tuberculosis: Relevance for India**

By a News Reporter-Staff News Editor at Journal of India – Current study results on Mycobacterium Infections have been published. According to news reporting from Seattle, Washington, by VerticalNews journalists, researchers stated “Diagnostic tests for active tuberculosis (TB) based on the detection of antibodies (serological tests) have been commercially available for decades, although no international guidelines have recommended their use. An estimated 1.5 million serological TB tests, mainly enzyme-linked immunosorbent assays, are performed in India alone every year, mostly in the private sector.”

The news correspondents obtained a quote from the research from the University of Washington, “The cost of serological tests in India is conservatively estimated at US $15 million (‘ 825 million) per year. Findings from systematic reviews on the diagnostic accuracy of serological tests for both pulmonary and extra-pulmonary TB suggest that these tests are inaccurate and imprecise. A cost-effectiveness modelling study suggests that, if used as a replacement test for sputum microscopy, serology would increase costs to the Indian TB control sector approximately 4-fold and result in fewer disability-adjusted life years averted and more false-positive diagnoses. After considering all available evidence, the World Health Organization issued a strong recommendation against the use of currently available commercial serological tests for the diagnosis of TB disease. The expanding evidence base continues to demonstrate that the harms/risks of serological tests far outweigh the benefits. Greater engagement of the private sector is needed to discontinue the use of serological tests and to replace these tests with WHO-endorsed new diagnostics in India.”

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According to the news reporters, the researchers concluded: “The recent ban on import or sale of TB serological tests by the Indian health ministry is a welcome step in the right direction.”

For more information on this research see: Serological tests for the diagnosis of active tuberculosis: Relevance for India. The Indian Journal of Medical Research, 2012;135(5):695-702. The Indian Journal of Medical Research can be contacted at: Indian Council Medical RES, PO Box 4911 Ansari Nagar, New Delhi 110029, India.

Our news journalists report that additional information may be obtained by contacting K.R. Steingart, Dept. of Health Services, University of Washington School of Public Health, Seattle, Washington, United States.

Publisher contact information for the The Indian Journal of Medical Research is: Indian Council Medical RES, PO Box 4911 Ansari Nagar, New Delhi 110029, India. (2012 Jul 31)

World Health Organization, Geneva: The potential impact of new diagnostic tests on tuberculosis epidemics

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators publish new report on Mycobacterium Infections. According to news reporting out of Geneva, Switzerland, by NewsRx editors, the researcher stated “New diagnostic tests for tuberculosis, especially those based on nucleic acid amplification, offer the possibility of early and accurate diagnosis of active TB. In this study we use mathematical modelling to explore the potential epidemiological impact of these new tests, with particular reference to India.”

Our news journalists obtained a quote from the research from World Health Organization, “A behavioural model of patient-doctor interactions embedded in an epidemiological model of Mycobacterium tuberculosis transmission, linked to field data, was used to investigate the effects of early diagnosis in preventing future TB cases. New diagnostic tests for active TB will have a bigger impact sooner where: disease incidence is high and most cases are due to recent infection; advances in test technology (test sensitivity, specificity, etc.) are combined with early diagnosis; new tests have not only better technical specifications than current tests, but also compensate for the misuse of existing tests; health system delays are long compared with patient delays, assuming the former are more amenable to change. New diagnostic tests will certainly improve TB control, but the highest impact will be obtained by applying tests with higher sensitivity and specificity early in the infectious period.”

According to the news editors, the researchers concluded: “Refined behavioural and epidemiological models should be able to investigate
the mechanisms by which early diagnosis could be achieved, in addition to the consequent epidemiological effects.”

For more information on this research see: The potential impact of new diagnostic tests on tuberculosis epidemics. The Indian Journal of Medical Research, 2012;135(5):737-44. The Indian Journal of Medical Research can be contacted at: Indian Council Medical RES, PO Box 4911 Ansari Nagar, New Delhi 110029, India.

Our news journalists report that additional information may be obtained by contacting C. Dye, HIV, AIDS, Tuberculosis, Malaria & Neglected Tropical Diseases Cluster, World Health Organization, Geneva, Switzerland.

Publisher contact information for the The Indian Journal of Medical Research is: Indian Council Medical RES, PO Box 4911 Ansari Nagar, New Delhi 110029, India. (2012 Jul 31)

All India Institute of Medical Sciences, New Delhi: Diagnostic potential of 16 kDa (HspX, a-crystalline) antigen for serodiagnosis of tuberculosis

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – Fresh data on Meningitis are presented in a new report. According to news reporting out of New Delhi, India, by NewsRx editors, researchers stated “Tuberculosis (TB) is a public health problem worldwide. Rapid and accurate diagnosis of tuberculosis is crucial to facilitate early treatment of infectious cases and to reduce its spread.”

Our news journalists obtained a quote from the research from the All India Institute of Medical Sciences, “The present study was aimed to evaluation of 16 kDa antigen as a serodiagnostic tool in pulmonary and extra-pulmonary tuberculosis patients in an effort to improve diagnostic algorithm for tuberculosis. In this study, 200 serum samples were collected from smear positive and culture confirmed pulmonary tuberculosis patients, 30 tubercular pleural effusions and 21 tubercular meningitis (TBM) patients. Serum samples from 36 healthy, age matched controls (hospital staff), along with 60 patients with non-tubercular respiratory diseases were also collected and evaluated. Humoral response (both IgG and IgA) was looked for 16 kDa antigen using indirect ELISA. Sensitivity of detection in various categories of pulmonary TB patients ranged between 73.8 and 81.2 per cent. While in the extra-pulmonary TB samples the sensitivity was 42.8 per cent (TBM) and 63.3 per cent (tubercular pleural effusion). The test specificity in both the groups was high (94.7%). All of the non-disease controls were negative. Among non-tubercular disease controls, five patients gave a positive humoral response against 16 kDa. Serodiagnostic tests for TB have always had drawbacks of suboptimal sensitivity and specificity. The antigen used in this study gave encouraging results in
pulmonary TB only, while in extra-pulmonary TB (tubercular meningitis and tubercular pleural effusion), this has shown a limited role in terms of sensitivity.

According to the news editors, the researchers concluded: “Further work is required to validate its role in serodiagnosis of TB especially extra-pulmonary TB.”

For more information on this research see: Diagnostic potential of 16 kDa (HspX, α-crystalline) antigen for serodiagnosis of tuberculosis. *The Indian Journal of Medical Research*, 2012;135(5):771-7. *The Indian Journal of Medical Research* can be contacted at: Indian Council Medical RES, PO Box 4911 Ansari Nagar, New Delhi 110029, India.

Our news journalists report that additional information may be obtained by contacting A. Kaushik, Dept. of Microbiology, All India Institute of Medical Sciences, New Delhi, India.

Publisher contact information for the *The Indian Journal of Medical Research* is: Indian Council Medical RES, PO Box 4911 Ansari Nagar, New Delhi 110029, India. *(2012 Jul 30)*

**Centers for Disease Control and Prevention, Atlanta: Lessons learned during tuberculosis screening in public medical clinics in Francistown, Botswana**

By a News Reporter-Staff News Editor at Tuberculosis Week – Investigators publish new report on Mycobacterium Infections. According to news originating from Atlanta, Georgia, by NewsRx correspondents, researchers stated “In Botswana, where one quarter of the adult population is infected with the human immunodeficiency virus and the annual tuberculosis (TB) incidence is among the highest globally, intensified TB case finding is needed in health care facilities to detect and treat TB cases early and prevent transmission. During August-December 2009, TB screening was implemented among adults at patient intake in five clinics in Francistown.”

Our news journalists obtained a quote from the research from Centers for Disease Control and Prevention, “Among 11?779 TB screenings at intake, 926 were positive. Nineteen patients were diagnosed with TB. Routine TB screening at intake was operationally feasible, but had low yield.”

According to the news editors, the researchers concluded: “Innovative case-finding strategies are needed in Botswana.”

The news correspondents report that additional information may be obtained from E. Bloss, US Centers for Disease Control and Prevention, Atlanta, Georgia, United States. (2012 Jul 30)

University of Cape Town, Observatory: Diagnosis of extrapulmonary tuberculosis using the Xpert® MTB/RIF assay


The news reporters obtained a quote from the research by the authors from the University of Cape Town, “The Xpert® MTB/RIF assay has been CE-marked for rapid molecular diagnosis of TB in Europe and has been endorsed by the WHO as a replacement for sputum smear microscopy for diagnosis of pulmonary TB in low-and middle-income countries. However, few data are available to inform recommendations for use of the assay for testing nonsputum clinical samples when investigating suspected extrapulmonary TB (EPTB). We review and discuss the findings of Tortoli and colleagues, who evaluated the assay used for this purpose in a large study of adults and children in Italy. They provide a per-sample analysis of 268 diagnoses of EPTB at a range of anatomic sites (sensitivity: 81.3%; 95% CI: 76.2-85.8) and data for 1206 samples in which EPTB was excluded (specificity: 99.8%; 95% CI: 99.4-100).”

According to the news reporters, the researchers concluded: “We discuss how this paper forms an important addition to the growing body of literature demonstrating the utility of Xpert MTB/RIF for EPTB diagnosis when applied to diverse types of clinical samples.”


Our news correspondents report that additional information may be obtained by contacting S.D. Lawn, The Desmond Tutu HIV Centre, Institute of Infectious Disease & Molecular Medicine, University of Cape Town, Anzio Road, Observatory 7925, Cape Town, South Africa. (2012 Jul 24)
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Ningxia Medical University, Yinchuan: Diagnostic Performance of the Urinary Deoxypyridinoline in Spinal Tuberculosis

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – Research findings on Mycobacterium Infections are discussed in a new report. According to news reporting from Yinchuan, People’s Republic of China, by NewsRx journalists, researchers stated “This study investigated the diagnostic significance of urinary deoxypyridinoline measurement as a screening tool for spinal tuberculosis in patients with pulmonary tuberculosis. Urinary deoxypyridinoline levels were measured by automated chemiluminescence immunoassay and automated chemistry methods in patients with spinal (n=33) and pulmonary tuberculosis (n=33) and in healthy controls (n=30).”

The news correspondents obtained a quote from the research by the authors from Ningxia Medical University, “Urinary deoxypyridinoline was divided by urinary creatine to exclude the factors of body mass index and urine dilution. The results underwent validity analysis. The measurements of urinary deoxypyridinoline in the spinal tuberculosis, pulmonary tuberculosis, and control groups were 14.9 +/- 9.8, 6.4 +/- 2.6, and 6.3 +/- 2.0 mu mol/molCr, respectively. Compared with the other 2 groups, the urinary deoxypyridinoline level in the spinal tuberculosis group was significantly increased (P=.001 and P=.000, respectively). However, urinary deoxypyridinoline levels were not significantly different between the pulmonary tuberculosis and control groups (P=.751). The receiver operating characteristic curve in the spinal tuberculosis group was 0.83. For deoxypyridinoline, the sensitivity (88%) and specificity (95%) were seen at the cutoff level of 8.0 mu mol/molCr. The false positive and false negative were 12% and 5%, respectively. Diagnostic validity of the method was 93%. Bone metabolism alteration occurs during the progression of spinal tuberculosis, which can be reflected by the sensitivity and specificity of urinary deoxypyridinoline.”

According to the news reporters, the researchers concluded: “The detection of urinary deoxypyridinoline is a benefit of screening patients with pulmonary tuberculosis for spinal tuberculosis.”


Our news journalists report that additional information may be obtained by contacting J.D. Shi, Ningxia Med Univ, General Hospital, Dept. of Spinal Surg, Xingqing Dist 750004, Yinchuan, People’s Republic of China. (2012 Jul 23)
Eulji University, Taejon: Diagnostic sensitivity of culture and drug resistance patterns in Korean patients with intestinal tuberculosis

By a News Reporter-Staff News Editor at Asia Business Newsweekly – Investigators publish new report on Tuberculosis. According to news reporting originating from Taejon, South Korea, by VerticalNews correspondents, researchers stated “It is challenging to differentiate between intestinal tuberculosis (ITB) and Crohn’s disease in areas where TB is still prevalent. The use of diagnostic tools and verifying the drug resistance patterns of ITB can be helpful for its correct diagnosis.”

Our news editors obtained a quote from the research by the authors from Eulji University, “To determine the diagnostic sensitivity of a culture assay using colonoscopic biopsy specimens and the drug resistance patterns of Mycobacterium tuberculosis isolated from ITB. Data from 400 patients diagnosed with ITB were retrospectively analysed. Of the 400 patients, 170 (42.5%) were males; the median age at diagnosis was 40 years. The sensitivity of culture was 44.1% (145/329). Resistance to at least one anti-tuberculosis drug was identified in 13 (17.6%) and multidrug-resistant TB (MDR-TB) was diagnosed in two (2.7%) of the 74 patients for whom drug susceptibility testing was performed. Including M. tuberculosis isolated from respiratory specimens, the proportion of MDR-TB was 4.4% (5/113); previous anti-tuberculosis treatment was an independent risk factor for MDR-TB (26.7% vs. 1.0%, P< 0.01).”

According to the news editors, the researchers concluded: “Culture of colonoscopic biopsy specimens shows substantial diagnostic sensitivity; the frequency of MDR-TB is higher in previously treated cases than in new cases.”


The news editors report that additional information may be obtained by contacting B.D. Ye, Eulji Univ, Coll Med, Dept. of Internal Med, Div Gastroenterol, Taejon, South Korea. (2012 Jul 03)
Sanjay Gandhi Postgraduate Institute of Medical Sciences, Uttar Pradesh: Detection of 123 bp fragment of insertion element IS6110 Mycobacterium tuberculosis for diagnosis of extrapulmonary tuberculosis

By a News Reporter-Staff News Editor at Journal of India – Fresh data on Tuberculosis are presented in a new report. According to news reporting out of Uttar Pradesh, India, by VerticalNews editors, researchers stated “Extrapulmonary tuberculosis (EPTB) is emerging problem in developing and developed countries. The diagnosis of EPTB in its different clinical presentations remains a true challenge.”

Our news journalists obtained a quote from the research by the authors from the Sanjay Gandhi Postgraduate Institute of Medical Sciences, “IS6110-based polymerase chain reaction (PCR) is used for rapid identification and positivity rate of the Mycobacterium tuberculosis complex in clinical isolates of different sites of EPTB. The present study was carried out to study the prevalence of M. tuberculosis complex in clinical isolates of EPTB at tertiary care centres in Lucknow. Seven hundred fifty-six specimens were collected from the suspected cases of EPTB which were processed for Mycobacteria by Ziehl-Neelson (ZN) staining and BACTEC culture. All the specimens were also processed for IS6110-based PCR amplification with primers targeting 123 bp fragment of insertion element IS6110 of the M. tuberculosis complex. Of these 756 specimens, 71(9.3%) were positive for acid fast bacilli (AFB) by ZN staining, 227(30.1%) were positive for mycobacteria by BACTEC culture and IS6110 PCR were positive for M. tuberculosis complex in 165 (20.7%) isolates. We found a significant difference in sensitivities of different tests (p <0.05). This study reveals the positivity of M. tuberculosis complex in clinical isolates of EPTB case in tertiary care hospitals in Northern India. 72.7% of M. tuberculosis complex was confirmed by IS6110-PCR in culture isolates from different sites of EPTB. The high prevalence of the M. tuberculosis complex was seen in lymph node aspirate and synovial fluid.”

According to the news editors, the researchers concluded: “However, utility of PCR may play a potentially significant role in strengthening the diagnosis of EPTB especially targeting IS6110.”

For more information on this research see: Detection of 123 bp fragment of insertion element IS6110 Mycobacterium tuberculosis for diagnosis of extrapulmonary tuberculosis. Indian Journal of Medical Microbiology, 2012;30(2):182-6.

Our news journalists report that additional information may be obtained by contacting A.K. Maurya, Dept. of Microbiology, Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow 226 014, Uttar Pradesh, India. (2012 Jul 03)
Department of Neurology, Niigata: The PCR-Based Diagnosis of Central Nervous System Tuberculosis: Up to Date

By a News Reporter-Staff News Editor at Pain & Central Nervous System Week – Investigators publish new report on Central Nervous System Tuberculosis. According to news originating from Niigata, Japan, by NewsRx correspondents, researchers stated “Central nervous system (CNS) tuberculosis, particularly tuberculous meningitis (TBM), is the severest form of Mycobacterium tuberculosis (M.Tb) infection, causing death or severe neurological defects in more than half of those affected, in spite of recent advancements in available anti-tuberculosis treatment. The definitive diagnosis of CNS tuberculosis depends upon the detection of M.Tb bacilli in the cerebrospinal fluid (CSF).”

Our news journalists obtained a quote from the research by the authors from the Department of Neurology, “At present, the diagnosis of CNS tuberculosis remains a complex issue because the most widely used conventional ‘gold standard’ based on bacteriological detection methods, such as direct smear and culture identification, cannot rapidly detect M.Tb in CSF specimens with sufficient sensitivity in the acute phase of TBM. Recently, instead of the conventional ‘gold standard’, the various molecular-based methods including nucleic acid amplification (NAA) assay technique, particularly polymerase chain reaction (PCR) assay, has emerged as a promising new method for the diagnosis of CNS tuberculosis because of its rapidity, sensitivity and specificity. In addition, the innovation of nested PCR assay technique is worthy of note given its contribution to improve the diagnosis of CNS tuberculosis.”

According to the news editors, the researchers concluded: “In this review, an overview of recent progress of the NAA methods, mainly highlighting the PCR assay technique, was presented.”

For more information on this research see: The PCR-Based Diagnosis of Central Nervous System Tuberculosis: Up to Date. Tuberculosis Research and Treatment, 2012;2012():831292. (Hindawi Publishing - www.hindawi.com; Tuberculosis Research and Treatment - http://www.hindawi.com/journals/trt/)

The news correspondents report that additional information may be obtained from T. Takahashi, Dept. of Neurology, Nagaoka-Nishi Hospital Mitsugohya-machi, 371-1 Nagaoka City, Niigata, Japan. (2012 Jul 02)
Research Unit, The Hague: Yield of interview screening and chest X-ray abnormalities in a tuberculosis prevalence survey

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – Researchers detail new data in Tuberculosis. According to news reporting from The Hague, Netherlands, by NewsRx journalists, researchers stated “Tuberculosis (TB) prevalence surveys generally rely on a combination of screening methods to identify suspects eligible for sputum culture. To assess the yield of screening methods applied in a recent prevalence survey in Viet Nam and estimate the proportion of TB cases missed due to incomplete participation.”

The news correspondents obtained a quote from the research by the authors from Research Unit, “TB suspects were identified based on self-reported TB history or productive cough by interview and chest X-ray (CXR). We calculated the case yield of these two screening methods by dividing the number of cases detected per method by the total number of cases detected. As not all participants underwent the full screening procedure, we recalculated the maximum yield of the screening methods using multiple imputation methods. The yield from screening by interview and CXR were respectively 38% and 91%. Adjusting for missing data by multiple imputation, we estimated that we missed 9.9% (95% CI 6.8-14.2) of expected TB cases. In prevalence surveys, screening by pre-structured interview is insufficient, and should be supplemented with CXR to achieve sufficient identification of TB cases.”

According to the news reporters, the researchers concluded: “The effect of incomplete participation in the full screening procedure may be substantial and should be adjusted for in the analysis.”


Our news journalists report that additional information may be obtained by contacting N.B. Hoa, KNCV TB Fdn, Res Unit, The Hague, Netherlands. (2012 Jul 02)
University of Stellenbosch, Cape Town: Breath analysis as a potential diagnostic tool for tuberculosis

By a News Reporter-Staff News Editor at Journal of Robotics & Machine Learning – Data detailed on Tuberculosis have been presented. According to news reporting out of Cape Town, South Africa, by VerticalNews editors, researchers stated “Cape Town, South Africa. We investigated the potential of breath analysis by gas chromatography-mass spectrometry (GC-MS) to discriminate between samples collected prospectively from patients with suspected tuberculosis (TB).”

Our news journalists obtained a quote from the research by the authors from the University of Stellenbosch, “Samples were obtained in a TB-endemic setting in South Africa, where 28% of culture-proven TB patients had Ziehl-Neelsen (ZN) negative sputum smear. A training set of breath samples from 50 sputum culture-proven TB patients and 50 culture-negative non-TB patients was analysed using GC-MS. We used support vector machine analysis for classification of the patient samples into TB and non-TB. A classification model with seven compounds had a sensitivity of 72%, a specificity of 86% and an accuracy of 79% compared with culture. The classification model was validated with breath samples from a different set of 21 TB and 50 non-TB patients from the same area, giving a sensitivity of 62%, a specificity of 84% and an accuracy of 77%. This study shows that GC-MS breath analysis is able to differentiate between TB and non-TB breath samples even among patients with a negative ZN sputum smear but a positive culture for Mycobacterium tuberculosis.”

According to the news editors, the researchers concluded: “We conclude that breath analysis by GC-MS merits further research.”


Our news journalists report that additional information may be obtained by contacting A.H.J. Kolk, University of Stellenbosch, Dept. of Paediat & Child Hlth, Desmond Tutu TB Center, Cape Town, South Africa. (2012 Jul 02)
TB Research Group, Surrey: Evaluation of two cocktails containing ESAT-6, CFP-10 and Rv-3615c in the intradermal test and the interferon-gamma assay for diagnosis of bovine tuberculosis

By a News Reporter-Staff News Editor at Veterinary Week – Current study results on Intercellular Signaling Peptides and Proteins have been published. According to news reporting originating in Surrey, United Kingdom, by VerticalNews journalists, researchers stated “The intradermal tuberculin tests and the interferon-gamma (IFN-gamma) assay are the principal tests used worldwide for the ante-mortem diagnosis of bovine tuberculosis. The conventional reagent currently in use in these tests is purified protein derivative (PPD) tuberculin obtained from Mycobacterium bovis culture.”

The news reporters obtained a quote from the research by the authors from TB Research Group, “The components of PPD are poorly characterized and difficult to standardize. To overcome this issue, antigens specific to the Mycobacterium tuberculosis complex are being studied. Here we have assessed the biological potency of ESAT-6, CFP-10 and Rv-3615c presented as peptide or recombinant protein cocktails in comparison with the standard bovine PPD used routinely in Spanish eradication campaigns. The study was performed in cattle (n = 23) from a herd with natural M. bovis infection. Animals were simultaneously injected with PPD and the peptide and protein cocktails. The percentages of cattle reacting positively to single intradermal test were 60.9% (bovine PPD), 47.8% (peptide cocktail) and 60.9% (protein cocktail), with no significant difference between the actual skin fold thickness increases (p > 0.05). The IFN-gamma assay detected 60.9% of animals when stimulation was performed with bovine PPD, but decreased to 52.2% when stimulation was performed with the peptide cocktail and to 47.8% when stimulation was performed with the protein cocktail. However, no significant differences were found between IFN-gamma responder frequencies (p > 0.05).”

According to the news reporters, the researchers concluded: “These results show a potential use of these defined reagents for in vivo tuberculosis diagnosis.”

For more information on this research see: Evaluation of two cocktails containing ESAT-6, CFP-10 and Rv-3615c in the intradermal test and the interferon-gamma assay for diagnosis of bovine tuberculosis. Preventive Veterinary Medicine, 2012;105(1-2):149-154. Preventive Veterinary Medicine can be contacted at: Elsevier Science Bv, PO Box 211, 1000 Ae Amsterdam, Netherlands. (Elsevier - www.elsevier.com; Preventive Veterinary Medicine - http://www.elsevier.com/wps/product/cws_home/503315)
Our news correspondents report that additional information may be obtained by contacting C. Casal, AHVLA, TB Res Grp, Addlestone, Surrey, United Kingdom. (2012 Jun 25)

National Cheng Kung University Hospital, Tainan: Factors Associated With Misdiagnosis of Smear-Negative Tuberculosis: An Experience in Taiwan

By a News Reporter-Staff News Editor at Asia Business Newsweekly – Current study results on Tuberculosis have been published. According to news reporting from Tainan, Taiwan, by VerticalNews journalists, researchers stated “A negative sputum smear from a patient with history, physical examination, and chest x-ray findings suggestive of tuberculosis (TB) presents a diagnostic dilemma. We investigated the possible factors associated with a misdiagnosis and inappropriate treatment of TB among such patients.”

The news correspondents obtained a quote from the research by the authors from National Cheng Kung University Hospital, “We reviewed the records of 193 patients whose diagnoses with TB included conflicting test results and were reported to the Taiwan Centers for Disease Control in 2004. When other conditions were found to underlie the initial abnormal chest x-ray finding, the diagnosis was revised. Mycobacterium tuberculosis was isolated from sputum samples in 72 of 193 patients (37%), nontuberculous mycobacteria from 4 (2%), and no bacteriologic evidence of M. tuberculosis from 117 (61%). The initial diagnosis of TB was revised for 26 (13.5%) patients. Patients with positive M. tuberculosis culture had a lower incidence of revised diagnoses (4.2%, P< .001) than those negative for mycobacterial culture (17.1%) and those with nontuberculous mycobacteria (75%). Chest cavitations in this study were not a significant predictor of revised diagnosis (odds ratio 0.30, P = .08).”

According to the news reporters, the researchers concluded: “An incorrect diagnosis of TB despite a negative sputum smear result is more likely to be made for patients positive for nontuberculous mycobacteria culture and less likely for patients with positive M. tuberculosis culture.”

For more information on this research see: Factors Associated With Misdiagnosis of Smear-Negative Tuberculosis: An Experience in Taiwan. Respiratory Care, 2012;57(5):753-757. Respiratory Care can be contacted at: Daedalus Enterprises Inc, 9425 N Mac Arthur Blvd, Ste 100, Irving, TX 75063-4706, USA.

Our news journalists report that additional information may be obtained by contacting C.Y. Yang, Natl Cheng Kung Univ Hosp, Dept. of Occupat & Environm Med, Tainan 70428, Taiwan. (2012 Jun 19)
CHAPTER 2  DIAGNOSIS AND SCREENING

University of London: An integrated surrogate model for screening of drugs against Mycobacterium tuberculosis

By a News Reporter-Staff News Editor at Life Science Weekly – Current study results on Tuberculosis have been published. According to news reporting out of London, United Kingdom, by NewsRx editors, researchers stated “The intracellularly surviving and slow-growing pathogen, Mycobacterium tuberculosis, adapts the host cell environment for its active and dormant life cycle. It is evident that the lack of appropriate high-throughput screening of inhibitors within host cells is an impediment for the early stages of anti-tubercular drug discovery.”

Our news journalists obtained a quote from the research by the authors from the University of London, “We aimed to develop an integrated surrogate model that enhances the screening of large inhibitor libraries. Different mycobacterial species were compared for their growth, drug susceptibility and intracellular uptake. A 6-well plate solid agar-based spot culture growth inhibition (SPOTi) assay was developed into a higher throughput format. The uptake and intracellular survival of Mycobacterium aurum within mouse macrophage cells (RAW 264.7) were optimized using 24/96-well plate formats. Fast-growing, non-pathogenic M. aurum was found to have an antibiotic-susceptibility profile similar to that of M. tuberculosis. The sensitivity to an acidic pH environment and the ability to multiply inside RAW 264.7 macrophages provided additional advantages for employing M. aurum in intracellular drug screening methods. A selection of anti-tubercular drugs inhibited the growth and viability of M. aurum inside the macrophages at different levels. We present a rapid, convenient, high-throughput surrogate model, which provides a comprehensive evaluation platform for new chemical scaffolds against different physiological stages of mycobacteria within the primary cell environment of the host.”

According to the news editors, the researchers concluded: “The results using anti-tubercular drugs validate this model for screening libraries of existing and novel chemical entities.”


Our news journalists report that additional information may be obtained by contacting A. Gupta, University of London, Inst Struct & Mol Biol, Dept. of Biol Sci, Mycobacteria Res Lab, London WC1E 7HX, United Kingdom. (2012 Jun 19)
Georgetown University, Washington: Rapid diagnosis of Mycobacterium tuberculosis infection in children using interferon-gamma release assays (IGRAs)

By a News Reporter-Staff News Editor at Pediatrics Week – Investigators publish new report on Asthma. According to news reporting originating from Washington, District of Columbia, by VerticalNews correspondents, researchers stated “Diagnosis of tuberculosis (TB) in children by the tuberculin skin test (TST) poses a diagnostic challenge for physicians due to its low specificity and cross-reactivity with nontuberculous mycobacteria and bacille Calmette-Guerin (BCG). Although interferon-gamma release assays (IGRAs) have been shown as novel TST alternatives for diagnosis of latent TB infection (LTBI) in adults, their effectiveness is less clear in children.”

Our news editors obtained a quote from the research by the authors from Georgetown University, “The present study examined QuantiFERON-TB Gold (QFT-G) responses and IFN-gamma production capacity of TST-positive children, younger children=5 years. A total of 517 children of whom 434 were TST positive ranging in age from 1 month to 18 years were evaluated by the QFT-G. Of the 517 children, 434 (84%) were TST positive, 25 (5.8%) of whom were found to be QFT-G positive and 25 (5.4%) with an indeterminate response. Of the 517 children, 355 (68.7%) were previously BCG immunized and 310/355 (87.3%) were TST positive including 18/27 (66.7%) QFT-positive children. Adequate IFN-gamma production by purified TB peptides or mitogen was observed in 92.8% of children, 29.6% of whom were <5 years. This study shows that the QFT-G assay is useful for diagnosis of LTBI. The finding of 5.8% positive QFT-G in 434 TST-positive children underscores the superior specificity of the QFT-G than the TST and its greater cost effectiveness in preventing unnecessary and potentially toxic treatment in children.”

According to the news editors, the researchers concluded: “The study suggests that the majority of positive TST in children represent false-positive reactions and supports the use of IGRAs for diagnosis of LTBI in children, including those <5 years of age.”


The news editors report that additional information may be obtained by contacting S. Riazi, International Center for Interdisciplinary Studies of Immunology, Georgetown University Medical Center, Washington, DC, United States. (2012 Jun 16)
Harvard University, Belmont: Super-paramagnetic iron oxide nanoparticles for use in extrapulmonary tuberculosis diagnosis

By a News Reporter-Staff News Editor at Tuberculosis Week – Fresh data on Tuberculosis are presented in a new report. According to news reporting originating from Belmont, Massachusetts, by NewsRx correspondents, researchers stated “Clin Microbiol Infect 2012; 18: E149E157 Abstract The limited sensitivity of serological tests for mycobacterial antigens has encouraged the development of a nanoparticle probe specific for the extrapulmonary form of Mycobacterium tuberculosis (Mtb). We developed an innovative probe comprised of superparamagnetic iron oxide (SPIO) nanoparticles conjugated with Mtb surface antibody (MtbsAb-nanoparticles) to provide ultrasensitive imaging of biomarkers involved in extrapulmonary Mtb infection.”

Our news editors obtained a quote from the research by the authors from Harvard University, “MtbsAb-nanoparticles were significantly conjugated with Mtb bacilli. The extent of contrast enhancement reduction on magnetic resonance imaging (MRI) for Mtb and human monocytic THP1 cells was proportional to the concentration of MtbsAb-nanoparticles. When MtbsAb-nanoparticles were intravenously injected into mice bearing Mtb granulomas, the granulomatous site showed a 14-fold greater reduction in signal intensity enhancement on T2-weighted MR images compared with an opposing site that received PBS injection.”

According to the news editors, the researchers concluded: “Mtb sAb-nanoparticles represent a new non-invasive technology for the diagnosis of extrapulmonary Mtb.”


The news editors report that additional information may be obtained by contacting C.N. Lee, Harvard University, McLean Hospital, Sch Med, Brain Imaging Center, Belmont, MA 02478, United States. (2012 Jun 11)
Ottawa Hospital: Effective screening tool to triage recovery rooms for possible tuberculosis patients undergoing bronchoscopy

By a News Reporter-Staff News Editor at Tuberculosis Week—Fresh data on Tuberculosis are presented in a new report. According to news originating from Ottawa, Canada, by NewsRx correspondents, researchers stated “In 2005, tuberculin skin test conversions were observed following exposure to a patient with active pulmonary tuberculosis (TB) who recovered post-bronchoscopy in an open area at The Ottawa Hospital, Canada. In response, we implemented a screening tool to triage patients to an airborne infection isolation (AII) room pre- and post-bronchoscopy.”

Our news journalists obtained a quote from the research by the authors from Ottawa Hospital, “To evaluate the performance of the screening tool in detecting patients with culture-confirmed TB. All bronchoscopies performed between 1 March 2006 and 31 March 2010 were retrospectively reviewed. Of 1839 patients included (55.3% of bronchoscopies), 210 screened positive, capturing 28 culture-confirmed TB cases. Three patients with positive TB cultures screened negative. The sensitivity of the screening tool was 90.3%; the negative predictive value was 99.8%. A positive screening result was strongly predictive of a positive TB culture. The screening tool is effective for identifying high-risk patients and triaging them to AII rooms.”

According to the news editors, the researchers concluded: “The pre-bronchoscopy screening tool is simple and inexpensive to implement and has the potential to reduce intra-institutional spread of TB.”


The news correspondents report that additional information may be obtained from M. Di Quinzio, Ottawa Hospital, Dept. of Infect Control, Ottawa, ON, Canada. (2012 Jun 11)
Pugliese-Ciaccio Hospital, Catanzaro: Tuberculosis of superficial lymph nodes, a not so rare event to consider in diagnosis. A case in an elderly male

By a News Reporter-Staff News Editor at Biotech Week – New research on Tuberculosis is the subject of a report. According to news reporting originating in Catanzaro, Italy, by NewsRx journalists, researchers stated “Tuberculosis (TB) is still one of the most frequent infectious diseases worldwide. Until the 1990s, Western European countries showed a low frequency of TB infection, but the rise of immigration has led to a rapid increase in its occurrence.”

The news reporters obtained a quote from the research by the authors from Pugliese-Ciaccio Hospital, “In the elderly, TB is emerging as a significant health problem (age-related decline of the cell-mediated immunity, associated illnesses, use of immunosuppressive drugs, malnutrition, poor life conditions), although its detection and diagnosis is not easy also considering its subclinical presentation. Almost 70% of all TB infections in Italy are found in the lungs; 50% of the extrapulmonary infections affect lymph nodes. Due to the low incidence of superficial tuberculous lymphadenitis without pulmonary manifestations, the possibility of a TB aetiology is often not taken into consideration in the differential diagnosis of lymphadenopathy, resulting in significant delay of appropriate treatment. Herein, we describe the case of a 78-year-old male with nocturnal fever, weakness, night sweats, loss of weight and decay in general condition. The patient had a past medical history of prostate adenocarcinoma treated with hormone therapy. The past medical history in association with clinical findings and laboratory data (anaemia, high titers of fibrinogen and reactive C-protein) led to the suspect of metastatic adenocarcinoma.”

According to the news reporters, the researchers concluded: “Only histological and molecular biology findings allowed us to make a correct diagnosis of TB.”

For more information on this research see: Tuberculosis of superficial lymph nodes, a not so rare event to consider in diagnosis. A case in an elderly male. Pathologica, 2011;103(6):340-2. (Springer - www.springer.com; Pathologica - http://www.springerlink.com/content/0031-2983/)

Our news correspondents report that additional information may be obtained by contacting A. Merante, Geriatric Unit, Pugliese-Ciaccio Hospital, Catanzaro, Italy. (2012 Jun 06)
National Medical Center, Seoul: Diagnostic accuracy of notified cases as pulmonary tuberculosis in private sectors of Korea

By a News Reporter-Staff News Editor at China Weekly News – Current study results on Tuberculosis have been published. According to news reporting originating in Seoul, South Korea, by VerticalNews journalists, researchers stated “The diagnostic accuracy of the data reported in the Korean tuberculosis surveillance system (KTBS) has not been adequately investigated. We reviewed the clinical data of pulmonary tuberculosis (PTB) cases notified from private medical facilities through KTBS between January and June, 2004.”

The news reporters obtained a quote from the research by the authors from National Medical Center, “PTB cases were classified into definite (culture-proven), probable (based on smear, polymerase chain reaction, histology, bronchoscopic finding, computed tomography, or both chest radiograph and symptoms) or possible (based only on chest radiograph) tuberculosis. Of the 1126 PTB cases, sputum AFB smear and culture were requested in 79% and 51% of the cases, respectively. Positive results of sputum smear and culture were obtained in 43% and 29% of all the patients, respectively. A total of 73.2% of the notified PTB cases could be classified as definite or probable and 81.7% as definite, probable, or possible. However, where infection was not confirmed bacteriologically or histologically, only 60.1% of the patients were definite, probable, or possible cases. More than 70% of PTB notified from private sectors in Korea can be regarded as real TB.”

According to the news reporters, the researchers concluded: “The results may also suggest the possibility of over-estimation of TB burden in the use of the notification-based TB data.”

For more information on this research see: Diagnostic accuracy of notified cases as pulmonary tuberculosis in private sectors of Korea. Journal of Korean Medical Science, 2012;27(5):525-31.

Our news correspondents report that additional information may be obtained by contacting I. Jeong, Dept. of Internal Medicine, National Medical Center, Seoul, South Korea. (2012 Jun 05)

Freeman Hospital, Newcastle-upon-Tyne: Tuberculosis and the pancreas: a diagnostic challenge solved by endoscopic ultrasound. A case series

By a News Reporter-Staff News Editor at Gastroenterology Week – Current study results on Tuberculosis have been published. According to news reporting out of Newcastle-upon-Tyne, United Kingdom, by NewsRx editors, researchers stated “Pancreatic tuberculosis is a rare
disease. It can be easily confused with malignancy or pancreatitis on imaging.”

Our news journalists obtained a quote from the research by the authors from Freeman Hospital, “This could result in unnecessary surgery. As this is a treatable disease it is imperative to diagnose this condition pre-operatively. We report three cases of pancreatic tuberculosis that were diagnosed by endoscopic ultrasound.”

According to the news editors, the researchers concluded: “Endoscopic ultrasound is the diagnostic modality of choice for pancreatic tuberculosis facilitating high resolution imaging, as well as sampling of tissue for staining, cytology, culture and polymerase chain reaction assay.”


Our news journalists report that additional information may be obtained by contacting S. Chatterjee, HPB Unit, Freeman Hospital, Newcastle upon Tyne, UK. (2012 Jun 04)


By a News Reporter-Staff News Editor at Pediatrics Week – Investigators discuss new findings in Tuberculosis. According to news reporting out of Rockville, Maryland, by VerticalNews editors, researchers stated “Confirming the diagnosis of childhood tuberculosis is a major challenge. However, research on childhood tuberculosis as it relates to better diagnostics is often neglected because of technical difficulties, such as the slow growth in culture, the difficulty of obtaining specimens, and the diverse and relatively nonspecific clinical presentation of tuberculosis in this age group.”

Our news journalists obtained a quote from the research by the authors from the Eunice Kennedy Shriver National Institute of Child Health and Human Development, “Researchers often use individually designed criteria for enrollment, diagnostic classifications, and reference standards, thereby hindering the interpretation and comparability of their findings. The development of standardized research approaches and definitions is therefore needed to strengthen the evaluation of new diagnostics for detection and confirmation of tuberculosis in children.
In this article we present consensus statements on methodological issues for conducting research of Tuberculosis diagnostics among children, with a focus on intrathoracic tuberculosis. The statements are complementary to a clinical research case definition presented in an accompanying publication and suggest a phased approach to diagnostics evaluation; entry criteria for enrollment; methods for classification of disease certainty, including the rational use of culture within the case definition; age categories and comorbidities for reporting results; and the need to use standard operating procedures. Special consideration is given to the performance of microbiological culture in children and we also recommend for alternative methodological approaches to report findings in a standardized manner to overcome these limitations are made.”

According to the news editors, the researchers concluded: “This consensus statement is an important step toward ensuring greater rigor and comparability of pediatric tuberculosis diagnostic research, with the aim of realizing the full potential of better tests for children.”


Our news journalists report that additional information may be obtained by contacting L.E. Cuevas, Eunice Kennedy Shriver Natl Inst Child Hlth & Hum, Pediat Adolescent & Maternal AIDS Branch, National Institutes of Health, Rockville, MD, United States. (2012 Jun 02)

**Evaluation of Tuberculosis Diagnostics in Children: 1. Proposed Clinical Case Definitions for Classification of Intrathoracic Tuberculosis Disease. Consensus From an Expert Panel**

By a News Reporter-Staff News Editor at Pediatrics Week – Researchers detail new data in Tuberculosis. According to news originating from New York City, New York, by VerticalNews correspondents, researchers stated “There is a critical need for improved diagnosis of tuberculosis in children, particularly in young children with intrathoracic disease as this represents the most common type of tuberculosis in children and the greatest diagnostic challenge. There is also a need for standardized
clinical case definitions for the evaluation of diagnostics in prospective clinical research studies that include children in whom tuberculosis is suspected but not confirmed by culture of Mycobacterium tuberculosis.”

Our news journalists obtained a quote from the research by the authors, “A panel representing a wide range of expertise and child tuberculosis research experience aimed to develop standardized clinical research case definitions for intrathoracic tuberculosis in children to enable harmonized evaluation of new tuberculosis diagnostic technologies in pediatric populations. Draft definitions and statements were proposed and circulated widely for feedback. An expert panel then considered each of the proposed definitions and statements relating to clinical definitions. Formal group consensus rules were established and consensus was reached for each statement. The definitions presented in this article are intended for use in clinical research to evaluate diagnostic assays and not for individual patient diagnosis or treatment decisions.”

According to the news editors, the researchers concluded: “A complementary article addresses methodological issues to consider for research of diagnostics in children with suspected tuberculosis.”


The news correspondents report that additional information may be obtained from S.M. Graham, Treatment Act Grp, New York, NY, United States. (2012 Jun 02)
Chapter 3

Genetics

Necker Hospital for Sick Children, Paris: Age-Dependent Association between Pulmonary Tuberculosis and Common TOX Variants in the 8q12-13 Linkage Region

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators discuss new findings in Human Genetics. According to news originating from Paris, France, by NewsRx correspondents, research stated, “Only a small fraction of individuals infected with Mycobacterium tuberculosis develop clinical tuberculosis (TB) in their lifetime. Genetic epidemiological evidence suggests a genetic determinism of pulmonary TB (PTB), but the molecular basis of genetic predisposition to PTB remains largely unknown.”

Our news journalists obtained a quote from the research from Necker Hospital for Sick Children, “We used a positional-cloning approach to carry out ultrafine linkage-disequilibrium mapping of a previously identified susceptibility locus in chromosomal region 8q12-13 by genotyping 3,216 SNPs in a family-based Moroccan sample including 286 offspring with PTB. We observed 44 PTB-associated SNPs (p < 0.01), which were genotyped in an independent set of 317 cases and 650 controls from Morocco. A single signal, consisting of two correlated SNPs close to TOX, rs1568952 and rs2726600 (combined p = 1.1 x 10(-5) and 9.2 x 10(-5), respectively), was replicated. Stronger evidence of association was found in individuals who developed PTB before the age of 25 years (combined p for rs1568952 = 4.4 x 10(-8); odds ratio of PTB for AA versus AG/GG = 3.09 [1.99-4.78]). The association with rs2726600 (p = 0.04) was subsequently replicated in PTB-affected subjects under 25 years in a study of 243 nuclear families from Madagascar. Stronger evidence of replication in Madagascar was obtained for additional SNPs in strong linkage disequilibrium with the two initial SNPs (p = 0.003 for rs2726597), further confirming the signal. We thus identified around
rs1568952 and rs2726600 a cluster of SNPs strongly associated with early-onset PTB in Morocco and Madagascar.”

According to the news editors, the research concluded: “SNP rs2726600 is located in a transcription-factor binding site in the 3’ region of TOX, and further functional explorations will focus on CD4 T lymphocytes.”


The news correspondents report that additional information may be obtained from A.V. Grant, Hopital Necker Enfants Malad, AP HP, Pediat Hematol Immunol Unit, F-75015 Paris, France. (2013 Apr 23)

**Stellenbosch University: The Rationale for Using Rifabutin in the Treatment of MDR and XDR Tuberculosis Outbreaks**

By a News Reporter-Staff News Editor at Biotech Week – Investigators publish new report on Mycobacterium Infections. According to news reporting from Stellenbosch, South Africa, by NewsRx journalists, research stated, “Genetically related *Mycobacterium tuberculosis* strains with alterations at codon 516 in the rpoB gene were observed amongst a substantial number of patients with drug resistant tuberculosis in the Eastern Cape Province (ECP) of South Africa. Mutations at codon 516 are usually associated with lower level rifampicin (RIF) resistance, while susceptibility to rifabutin (RFB) remains intact.”

The news correspondents obtained a quote from the research from Stellenbosch University, “This study was conducted to assess the rationale for using RFB as a substitution for RIF in the treatment of MDR and XDR tuberculosis outbreaks. Minimum inhibitory concentrations (MICs) of 34 drug resistant clinical isolates of *M tuberculosis* were determined by MGIT 960 and correlated with rpoB mutations. RFB MICs ranged from 0.125 to 0.25 g/ml in the 34 test isolates thereby confirming phenotypic susceptibility as per critical concentration (CC) of 0.5 g/ml. The corresponding RIF MICs ranged between 5 and 15 g/ml, which is well above the CC of 1.0 g/ml. Molecular-based drug susceptibility testing provides important pharmacogenetic insight by demonstrating a direct correlation between defined rpoB mutation and the
level of RFB susceptibility. We suggest that isolates with marginally reduced susceptibility as compared to the epidemiological cut-off for wild-type strains (0.064 g/ml), but lower than the current CC (=0.5 g/ml), are categorised as intermediate. Two breakpoints (0.064 g/ml and 0.5 g/ml) are recommended to distinguish between susceptible, intermediate and RFB resistant strains. This concept may assist clinicians and policy makers to make objective therapeutic decisions, especially in situations where therapeutic options are limited.”

According to the news reporters, the research concluded: “The use of RFB in the ECP may improve therapeutic success and consequently minimise the risk of ongoing transmission of drug resistant M.”

For more information on this research see: The Rationale for Using Rifabutin in the Treatment of MDR and XDR Tuberculosis Outbreaks. Plos One, 2013;8(3):e59414. (Public Library of Science - www.plos.org; Plos One - www.plosone.org)

Our news journalists report that additional information may be obtained by contacting F.A. Sirgel, DST, NRF Centre of Excellence for Biomedical TB Research, MRC Centre for Molecular and Cellular Biology, Division of Molecular Biology and Human Genetics, Faculty of Health Science, Stellenbosch University, Stellenbosch, South Africa. (2013 Apr 17)

NAT2 and CYP2E1 polymorphisms associated with antituberculosis drug-induced hepatotoxicity in Chinese patients

By a News Reporter-Staff News Editor at Gastroenterology Week – Current study results on Pharmacology and Physiology have been published. According to news reporting originating from Beijing, People’s Republic of China, by NewsRx correspondents, research stated, “1. The present study investigated the relationship between antituberculosis (anti-TB) drug-induced hepatotoxicity and genetic polymorphisms of two important drug-metabolizing enzymes involved in the metabolism of isoniazid, namely N-acetyltransferase 2 (NAT2) and cytochrome P450 2E1 (CYP2E1). 2.”

Our news editors obtained a quote from the research, “A polymerase chain reaction direct sequencing approach was used to detect genetic polymorphisms of the NAT2 and CYP2E1 genes in tuberculosis (TB) patients with (n=101) or without (n=107) anti-TB drug-induced hepatotoxicity. Associations between various genetic polymorphisms and anti-TB drug-induced hepatotoxicity were then determined. 3. Patients with NAT2 (282TT , 590AA and 857GA) alleles had an increased susceptibility to anti-TB drug-induced hepatotoxicity. The slow acetylator NAT2 genotypes (especially NAT2*6A/7B and NAT2*6A/6A) were risk factors for hepatotoxicity (odds ratio (OR) 9.57 (p &lt;0.001) for
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NAT2*6A/7B; OR 5.24 (p=0.02) for NAT2*6A/6A). 4. The CYP2E1 genotype per se was not significantly associated with the development of anti-TB drug-induced hepatotoxicity. However, the combination of the CYP2E1 C1/C1 genotype with a slow acetylator NAT2 genotype increased the risk of anti-TB drug-induced hepatotoxicity (OR 5.33; p=0.003) compared with the combination of a rapid acetylator NAT2 genotype with either a C1/C2 or C2/C2 genotype. 5. Thus, slow acetylators with the NAT2*6A/7B and NAT2*6A/6A genotypes combined with the C1/C1 CYP2E1 genotype may be involved in the pathogenesis of anti-TB drug-induced hepatotoxicity. 6.”

According to the news editors, the research concluded: “The present findings may be explained, in part, by changes in the metabolism of the anti-TB drug isoniazid induced via NAT2 and CYP2E1, a metabolic process known to produce hepatotoxic intermediates.”


The news editors report that additional information may be obtained by contacting H.R. An, Institute of Tuberculosis Research, 309th Hospital of Chinese People’s Liberation Army, Beijing, People’s Taiwan. (2013 Apr 15)

Swiss Federal Institute of Technology, Lausanne: Database resources for the tuberculosis community

By a News Reporter-Staff News Editor at Life Science Weekly – Researchers detail new data in Tuberculosis and Lung Disease. According to news reporting originating in Lausanne, Switzerland, by NewsRx journalists, research stated, “Access to online repositories for genomic and associated ‘-omics’ datasets is now an essential part of everyday research activity.”

The news reporters obtained a quote from the research from the Swiss Federal Institute of Technology, “It is important therefore that the Tuberculosis community is aware of the databases and tools available to them online, as well as for the database hosts to know what the needs of the research community are. One of the goals of the Tuberculosis Annotation Jamboree, held in Washington DC on March 7th-8th 2012, was therefore to provide an overview of the current status of three key Tuberculosis resources, TubercuList (tuberculist.epfl.ch), TB Database (www.tbdb.org), and Pathosystems Resource Integration Center (PATRIC, www.patricbrc.org).”
According to the news reporters, the research concluded: “Here we summarize some key updates and upcoming features in TubercuList, and provide an overview of the PATRIC site and its online tools for pathogen RNA-Seq analysis.”


Our news correspondents report that additional information may be obtained by contacting J.M. Lew, Ecole Polytechnic Fed Lausanne, Nestle Inst Hlth Sci, CH-1015 Lausanne, Switzerland. (2013 Apr 02)

Fudan University, Shanghai: Identification of genetic associations of SP110/MYBBP1A/RELA with pulmonary tuberculosis in the Chinese Han population

By a News Reporter-Staff News Editor at Health & Medicine Week – Researchers detail new data in Human Genetics. According to news reporting originating from Shanghai, People’s Republic of China, by NewsRx correspondents, research stated, “Genetic factors play important roles in the development of tuberculosis (TB). SP110 is a promising candidate target for controlling TB infections.”

Our news editors obtained a quote from the research from Fudan University, “However, several studies associating SP110 single nucleotide polymorphisms (SNPs) with TB have yielded conflicting results. This may be partly resolved by studying other genes associated with SP110, such as MYBBP1A and RELA. Here, we genotyped 6 SP110 SNPs, 8 MYBBP1A SNPs and 5 RELA SNPs in 702 Chinese pulmonary TB patients and 425 healthy subjects using MassARRAY and SNaPshot methods. Using SNP-based analysis with Bonferroni correction, rs3809849 in MYBBP1A \( P_{\text{corrected}} = 0.0038 \) and rs9061 in SP110 \( P_{\text{cor}} = 0.019 \) were found to be significantly associated with TB. Furthermore, meta-analysis of rs9061 in East Asian populations showed that the rs9061 T allele conferred significant risk for TB \( P = 0.002 \), pooled odds ratio (OR), 1.24, 95% confidence interval (CI) = 1.08-1.43. The MYBBP1A GTCTTGGG haplotype and haplotypes CGACCG/TGATTG within SP110 were found to be markedly and significantly associated with TB \( P = 2.00E-06, 5.00E-6 \) and 2.59E-4, respectively. Gene-based analysis also demonstrated that SP110 and MYBBP1A were each associated with TB \( P_{\text{cor}} = 0.011 \) and 0.035, respectively. The logistic regression analysis results supported interactions between SP110 and MYBBP1A, indicating that subjects carrying...
a GC/CC genotype in MYBBP1A and CC genotype in SP110 possessed the high risk of developing TB (P = 1.74E-12).

According to the news editors, the research concluded: “Our study suggests that a combination of SP110 and MYBBP1A gene polymorphisms may serve as a novel marker for identifying the risk of developing TB in the Chinese Han population.”


The news editors report that additional information may be obtained by contacting L. Cai, Fudan University, Sch Life Sci & Technol, Adv Inst Translat Med, Shanghai 200433, People’s Republic of China. (2013 Mar 29)

Virginia Bioinformatics Institute, Blacksburg: Functional assignment of Mycobacterium tuberculosis proteome revealed by genome-scale fold-recognition

By a News Reporter-Staff News Editor at Health & Medicine Week – Researchers detail new data in Mycobacterium Infections. According to news reporting out of Blacksburg, Virginia, by NewsRx editors, research stated, “Hundreds of putative enzymes from Mycobacterium tuberculosis as well as other mycobacteria remain categorized as ‘conserved hypothetical proteins’ or ‘hypothetical proteins’, offering little or no information on their functional role in pathogenic and non-pathogenic processes. In this study we have predicted the fold and 3-D structure of more than 99% of all proteins encoded in the genome of M. tuberculosis H37Rv.”

Our news journalists obtained a quote from the research from Virginia Bioinformatics Institute, “Fold-recognition, database search, 3-D modelling was performed using Protein Homology/analogy Recognition Engine V 2.0 (Phyre(2)). These results are used to tentatively assign potential function for unannotated enzymes and proteins.”

According to the news editors, the research concluded: “In summary, fold-recognition and structural homology might be used as a complementary tool in genome annotation efforts and furthermore, it can deliver primary sequence-independent information regarding structure, ligands and even substrate specificity for enzymes that display low primary sequence identity with potential homologues in other species.”

For more information on this research see: Functional assignment of Mycobacterium tuberculosis proteome revealed by genome-scale fold-recognition. Tuberculosis, 2013;93(1):40-6. (Elsevier -
Chinese Center for Disease Control and Prevention, Beijing: The IL-17F sequence variant is associated with susceptibility to tuberculosis

By a News Reporter-Staff News Editor at Life Science Weekly – Current study results on Genetic Research have been published. According to news reporting out of Beijing, People’s Republic of China, by NewsRx editors, research stated, “The interleukin (IL)-17 gene plays a key role in host defence against infections from microbes, including Mycobacterium tuberculosis. Genetic factors contribute to host defence.”

Our news journalists obtained a quote from the research from Chinese Center for Disease Control and Prevention, “However, whether genetic variation in IL-17 is associated with altered susceptibility to tuberculosis is unknown. A total of 596 pulmonary tuberculosis (PTB) patients, 176 extra-pulmonary tuberculosis (EPTB) patients, and 622 control patients from a Chinese Han population were recruited. Two single-nucleotide polymorphisms (SNPs) in IL-17F (rs1889570 and rs763780) and one SNP in IL-17A (rs2275913) were genotyped using the SNaPshot technique. Of the three SNPs in the IL-17 gene tested, there was an increased frequency of the rs1889570 G allele and the rs763780 C allele in the PTB patients and an increased frequency of the rs763780 C allele in the EPTB patients compared with the control patients. There were also significant differences in the distribution of the rs763780 genotype between the PTB and EPTB patients and the controls. The patients who had the CT/TT genotype of the rs763780 SNP were more susceptible to tuberculosis, compared to the CC genotype. There was no significant difference observed between the IL-17 SNPs when the PTB and EPTB patients were compared.”

According to the news editors, the research concluded: “Genetic variation in IL-17F is associated with altered susceptibility to tuberculosis and may provide valuable information in the development of tuberculosis.”

For more information on this research see: The IL-17F sequence variant is associated with susceptibility to tuberculosis. *Gene*, 2013;515(1):229-232. *Gene* can be contacted at: Elsevier Science Bv, PO Box 211, 1000 Ae Amsterdam, Netherlands. (Elsevier - www.elsevier.com; Gene - http://www.elsevier.com/wps/product/cws_home/506033)
Sapienza-University, Rome: Improved BM212 MmpL3 Inhibitor Analogue Shows Efficacy in Acute Murine Model of Tuberculosis Infection

By a News Reporter-Staff News Editor at Life Science Weekly – Data detailed on Life Science Research have been presented. According to news reporting originating in Rome, Italy, by NewsRx journalists, research stated, “1,5-Diphenyl pyrroles were previously identified as a class of compounds endowed with high in vitro efficacy against M. tuberculosis. To improve the physical chemical properties and drug-like parameters of this class of compounds, a medicinal chemistry effort was undertaken.”

The news reporters obtained a quote from the research from Sapienza-University, “By selecting the optimal substitution patterns for the phenyl rings at N1 and C5 and by replacing the thiomorpholine moiety with a morpholine one, a new series of compounds was produced. The replacement of the sulfur with oxygen gave compounds with lower lipophilicity and improved in vitro microsomal stability. Moreover, since the parent compound of this family has been shown to target MmpL3, mycobacterial mutants resistant to two compounds have been isolated and characterized by sequencing the mmpL3 gene; all the mutants showed point mutations in this gene. The best compound identified to date was progressed to dose-response studies in an acute murine TB infection model. The resulting ED(99) of 49 mg/Kg is within the range of commonly employed tuberculosis drugs, demonstrating the potential of this chemical series.”

According to the news reporters, the research concluded: “The in vitro and in vivo target validation evidence presented here adds further weight to MmpL3 as a druggable target of interest for anti-tubercular drug discovery.”


Our news correspondents report that additional information may be obtained by contacting G. Pocce, Istituto Pasteur Fondazione Cenci-Bolognetti, Dipartimento di Chimica e Tecnologie del Farmaco, Sapienza Universita di Roma, Roma, Italy. (2013 Mar 19)
Texas A&M University, College Station: Reannotation of translational start sites in the genome of Mycobacterium tuberculosis

By a News Reporter-Staff News Editor at Life Science Weekly – A new study on Life Science is now available. According to news reporting from College Station, Texas, by NewsRx journalists, research stated, “Identification and correction of incorrect ORF start sites is important for a variety of experimental and analytical purposes, ranging from cloning to inference of operon structure. The genome of the H37Rv reference strain of Mycobacterium tuberculosis (Mtb) was originally annotated when it was first sequenced nearly 15 years ago.”

The news correspondents obtained a quote from the research from Texas A&M University, “While this annotation has served the TB research community well as a standard of reference for over a decade, it has been demonstrated experimentally that the actual start sites for an estimated 5-10% of open reading frames differ from the annotation. In this paper, we present a comprehensive bioinformatic analysis of all 3989 ORFs (open reading frames) in the M. tuberculosis H37Rv genome. Our method combines information from comparative analysis (alignment to start sites of orthologs in other Actinobacteria), sequence conservation, ‘protein likeness’, putative ribosome binding sites, and other data to identify translational start sites. The features are combined in a linear model that is trained on dataset of known start sites verified by mass spectrometry, with a cross-validated accuracy of 94%. The method can be viewed as an augmentation of Hidden Markov Model-based tools such as Glimmer and GeneMark by incorporating more information than just the raw genomic sequence to decide which position is the legitimate translational start site for each ORF. Using this analysis, we identify 269 genes that most likely need to be re-annotated, and identify the best alternative translational start site for each.”

According to the news reporters, the research concluded: “These revised ORF definitions could be used in the reannotation of the H37Rv genome, as well as to prioritize genes for experimental start-site validation.”


Our news journalists report that additional information may be obtained by contacting M.A. Dejesus, Dept. of Computer Science and Engineering, Texas A&M University, College Station, TX, United States. (2013 Mar 19)
MRC National Institute for Medical Research, London:
Long-range transcriptional control of an operon necessary for virulence-critical ESX-1 secretion in Mycobacterium tuberculosis

By a News Reporter-Staff News Editor at Health & Medicine Week – Fresh data on Bacteriology are presented in a new report. According to news originating from London, United Kingdom, by NewsRx correspondents, research stated, “The ESX-1 secretion system of Mycobacterium tuberculosis has to be precisely regulated since the secreted proteins, although required for a successful virulent infection, are highly antigenic and their continued secretion would alert the immune system to the infection. The transcription of a five-gene operon containing espACD-Rv3613c-Rv3612c, which is required for ESX-1 secretion and is essential for virulence, was shown to be positively regulated by the EspR transcription factor.”

Our news journalists obtained a quote from the research from MRC National Institute for Medical Research, “Thus, transcription from the start site, found to be located 67 bp upstream of espA, was dependent upon EspR enhancer-like sequences far upstream (between 884 and 1,004 bp), which we term the espA activating region (EAR). The EAR contains one of the known binding sites for EspR, providing the first in vivo evidence that transcriptional activation at the espA promoter occurs by EspR binding to the EAR and looping out DNA between this site and the promoter. Regulation of transcription of this operon thus takes place over long regions of the chromosome. This regulation may differ in some members of the M. tuberculosis complex, including Mycobacterium bovis, since deletions of the intergenic region have removed the upstream sequence containing the EAR, resulting in lowered espA expression. Consequent differences in expression of ESX-1 in these bacteria may contribute to their various pathologies and host ranges.”

According to the news editors, the research concluded: “The virulence-critical nature of this operon means that transcription factors controlling its expression are possible drug targets.”

For more information on this research see: Long-range transcriptional control of an operon necessary for virulence-critical ESX-1 secretion in Mycobacterium tuberculosis. Journal of Bacteriology, 2012;194(9):2307-20. (American Society for Microbiology - www.asm.org; Journal of Bacteriology - jb.asm.org)

The news correspondents report that additional information may be obtained from D.M. Hunt, Division of Mycobacterial Research, MRC National Institute for Medical Research, Mill Hill, London, UK. (2013 Mar 15)
Mixed tuberculosis infections in rural South Vietnam

By a News Reporter-Staff News Editor at AIDS Weekly – Fresh data on Clinical Microbiology are presented in a new report. According to news reporting out of Ho Chi Minh City, Vietnam, by NewsRx editors, research stated, “Tuberculosis patients may be infected with or have disease caused by more than one Mycobacterium tuberculosis strain, usually referred to as ‘mixed infections.’ These have mainly been observed in settings with a very high tuberculosis incidence and/or high HIV prevalence. We assessed the rate of mixed infections in a population-based study in rural Vietnam, where the prevalences of both HIV and tuberculosis are substantially lower than those in previous studies looking at mixed infections.”

Our news journalists obtained a quote from the research, “In total, 1,248 M. tuberculosis isolates from the same number of patients were subjected to IS6110 restriction fragment length polymorphism (RFLP) typing, spoligotyping, and variable-number-tandem-repeat (VNTR) typing. We compared mixed infections identified by the presence of (i) discrepant RFLP and spoligotype patterns in isolates from the same patient and (ii) double alleles at=2 loci by VNTR typing and assessed epidemiological characteristics of these infections. RFLP/spoligotyping and VNTR typing identified 39 (3.1%) and 60 (4.8%) mixed infections, respectively (Cohen's kappa statistic, 0.57). The number of loci with double alleles in the VNTR pattern was strongly associated with the proportion of isolates with mixed infections according to RFLP/spoligotyping (p <0.001). Mixed infections occurred more frequently in newly treated than in previously treated patients, were significantly associated with minor X-ray abnormalities, and were almost significantly associated with lower sputum smear grades.”

According to the news editors, the research concluded: “Although the infection pressure in our study area is lower than that in previously studied populations, mixed M. tuberculosis infections do occur in rural South Vietnam in at least 3.1% of cases.”


Our news journalists report that additional information may be obtained by contacting M.N. Huyen, Pham Ngoc Thach Tuberculosis and Lung Disease Hospital, Ho Chi Minh City, Vietnam. (2013 Mar 11)
Health Protection Agency, London: Insertion site mapping for repeated elements in Mycobacterium tuberculosis

By a News Reporter-Staff News Editor at Health & Medicine Week – Researchers detail new data in Mycobacterium Infections. According to news originating from London, United Kingdom, by NewsRx correspondents, research stated, “Insertion elements not only act as genetic markers for differentiation of bacteria but their movement in bacterial genomes likely plays an essential role in changing the physical and biochemical traits of the organisms when adapting to new environments. Genomic Insertion Site mapping of transposable elements could shed light on the putative altered function of adjacent genes.”

Our news journalists obtained a quote from the research from Health Protection Agency, “In the era of whole genome sequencing where repeat elements are difficult to sequence with short read technologies and in the absence of high throughput technologies especially in poorer resource settings, an alternative approach to their characterisation is needed. A rapid and simple method of insertion site mapping that uses Insertion Sequence 6110 (IS6110) fluorescent amplified fragment length polymorphism (FAFLP) PCR as a foundation and then uses additional selective bases to reduce the number of fragments generated was developed. This was applied to Mycobacterium tuberculosis H37Rv sequenced strain to compare the experimental data with the in silico results.”

According to the news editors, the research concluded: “This was successfully achieved for all but two of the sixteen fragments generated by FAFLP and demonstrated that, by using this technique, insertion sites can be mapped onto the genomes of M.”


The news correspondents report that additional information may be obtained from K. Moganeradj, Microbiology Services, Dept. of Bioanalysis and Horizon Technologies, Health Protection Agency, 61 Colindale Avenue, London NW9 5EQ, UK. (2013 Mar 08)
University of Basel: Putative Compensatory Mutations in the rpoC Gene of Rifampin-Resistant Mycobacterium tuberculosis Are Associated with Ongoing Transmission

By a News Reporter-Staff News Editor at Biotech Week – Current study results on Chemotherapy have been published. According to news originating from Basel, Switzerland, by NewsRx correspondents, research stated, “Rifampin resistance in clinical isolates of Mycobacterium tuberculosis arises primarily through the selection of bacterial variants harboring mutations in the 81-bp rifampin resistance-determining region of the rpoB gene. While these mutations were shown to infer a fitness cost in the absence of antibiotic pressure, compensatory mutations in rpoA and rpoC were identified which restore the fitness of rifampin-resistant bacteria carrying mutations in rpoB.”

Our news journalists obtained a quote from the research from the University of Basel, “To investigate the epidemiological relevance of these compensatory mutations, we analyzed 286 drug-resistant and 54 drug-susceptible clinical M. tuberculosis isolates from the Western Cape, South Africa, a high-incidence setting of multidrug-resistant tuberculosis. Sequencing of a portion of the RpoA-RpoC interaction region of the rpoC gene revealed that 23.5% of all rifampin-resistant isolates tested carried a nonsynonymous mutation in this region. These putative compensatory mutations in rpoC were associated with transmission, as 30.8% of all rifampin-resistant isolates with an IS6110 restriction fragment length polymorphism (RFLP) pattern belonging to a recognized RFLP cluster harbored putative rpoC mutations. Such mutations were present in only 9.4% of rifampin-resistant isolates with unique RFLP patterns (P < 0.01). Moreover, these putative compensatory mutations were associated with specific strain genotypes and the rpoB S531L rifampin resistance mutation. Among isolates harboring this rpoB mutation, 44.1% also harbored rpoC mutations, while only 4.1% of the isolates with other rpoB mutations exhibited mutations in rpoC (P < 0.001).”

According to the news editors, the research concluded: “Our study supports a role for rpoC mutations in the transmission of multidrug-resistant tuberculosis and illustrates how epistatic interactions between drug resistance-conferring mutations, compensatory mutations, and different strain genetic backgrounds might influence compensatory evolution in drug-resistant M. tuberculosis.”

For more information on this research see: Putative Compensatory Mutations in the rpoC Gene of Rifampin-Resistant Mycobacterium tuberculosis Are Associated with Ongoing Transmission. Antimicrobial Agents and Chemotherapy, 2013;57(2):827-832. Antimicrobial Agents and Chemotherapy can be contacted at: Amer Soc Microbiology, 1752 N
University of Tennessee, Knoxville: Understanding TB latency using computational and dynamic modelling procedures

By a News Reporter-Staff News Editor at Biotech Week – Investigators publish new report on Mycobacterium Infections. According to news originating from Knoxville, Tennessee, by NewsRx correspondents, research stated, “The *Mycobacterium tuberculosis* bacilli’s potency to cause persistent latent infection that is unresponsive to the current cocktail of TB drugs is strongly associated with its ability to adapt to changing intracellular environments, and tolerating, evading and subverting host defence mechanisms. We applied a combination of bioinformatics and mathematical modelling methods to enhance the understanding of TB latency dynamics.”

Our news journalists obtained a quote from the research from the University of Tennessee, “Analysis of time course microarray gene expression data was carried out and gene profiles for bacilli adaptation and survival in latency, simulated by hypoxia were determined. Reverse network engineering techniques were used to predict gene dependencies and regulatory interactions. Biochemical systems theory was applied to mathematically model the inferred gene regulatory networks. Significant regulatory genes involved in latency were determined by a combination of systems biology procedures and mathematical modelling of the inferred regulatory networks. Analysis of gene clusters of the inferred networks in the stationary and non-replicating phases of the bacilli predicted probable functions of some of the latency genes to be associated with latency genes of known functions. The systems biology approach and mathematical computational deletion experiments predicted key genes in the TB latency/dormancy program that may be possible TB drug targets.”

According to the news editors, the research concluded: “However, these gene candidates require experimental testing and validation.”

The news correspondents report that additional information may be obtained from G. Magombedze, National Institute for Mathematical and Biological Synthesis, 1534 White Ave, University of Tennessee, Knoxville, TN 37996-1527, United States. (2013 Mar 06)

Health Protection Agency, Leicester: Whole-genome sequencing to delineate Mycobacterium tuberculosis outbreaks: a retrospective observational study

By a News Reporter-Staff News Editor at Life Science Weekly – Data detailed on Infectious Diseases have been presented. According to news reporting from Leicester, United Kingdom, by NewsRx journalists, research stated, “Tuberculosis incidence in the UK has risen in the past decade. Disease control depends on epidemiological data, which can be difficult to obtain.”

The news correspondents obtained a quote from the research from Health Protection Agency, “Whole-genome sequencing can detect microevolution within Mycobacterium tuberculosis strains. We aimed to estimate the genetic diversity of related M tuberculosis strains in the UK Midlands and to investigate how this measurement might be used to investigate community outbreaks. In a retrospective observational study, we used Mumina technology to sequence M tuberculosis genomes from an archive of frozen cultures. We characterised isolates into four groups: cross-sectional, longitudinal, household, and community. We measured pairwise nucleotide differences within hosts and between hosts in household outbreaks and estimated the rate of change in DNA sequences. We used the findings to interpret network diagrams constructed from 11 community clusters derived from mycobacterial interspersed repetitive-unit variable-number tandem-repeat data. We sequenced 390 separate isolates from 254 patients, including representatives from all five major lineages of M tuberculosis. The estimated rate of change in DNA sequences was 0.5 single nucleotide polymorphisms (SNPs) per genome per year (95% CI 0.3-0.7) in longitudinal isolates from 30 individuals and 25 families. Divergence is rarely higher than five SNPs in 3 years. 109 (96%) of 114 paired isolates from individuals and households differed by five or fewer SNPs. More than five SNPs separated isolates from none of 69 epidemiologically linked patients, two (15%) of 13 possibly linked patients, and 13 (17%) of 75 epidemiologically unlinked patients (three-way comparison exact p<0.0001). Genetic trees and clinical and epidemiological data suggest that superspreaders were present in two community clusters. Whole-genome sequencing can delineate outbreaks of tuberculosis and allows inference about direction of transmission between cases.”
According to the news reporters, the research concluded: “The techni-
nique could identify super-spreaders and predict the existence of undi-
agnosed cases, potentially leading to early treatment of infectious pa-
tients and their contacts.”

For more information on this research see: Whole-genome sequencing
to delineate Mycobacterium tuberculosis outbreaks: a retrospec-
tive observational study. Lancet Infectious Diseases, 2013;13(2):137-
146. Lancet Infectious Diseases can be contacted at: Elsevier Sci-
ence Inc, 360 Park Ave South, New York, NY 10010-1710, USA. (El-
elsevier.com/wps/product/cws_home/622214)

Our news journalists report that additional information may be ob-
tained by contacting T.M. Walker, Hlth Protect Agcy, Leicester, Leics,
United Kingdom. (2013 Mar 05)

Zahedan University of Medical Sciences: Association of P2X7 gene polymorphisms with susceptibility to pulmonary tuberculosis in Zahedan, Southeast Iran

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – A new study on Genetic Research is now available. According to news originating from Zahedan, Iran, by NewsRx correspondents, research stated, “Susceptibility to tuberculosis may be influenced by vari-
ations in human genes. The P2X7 receptor is an ATP-gated cation chan-
nel expressed in immune cells, and it influences the release of proin-
flammatory cytokines from monocytes and macrophages.”

Our news journalists obtained a quote from the research from the Zahedan University of Medical Sciences, “In the present study, we aimed to evaluate the impact of P2X7 gene rs2393799 (-762T/C) and rs1718119 (Thr348Ala) polymorphisms on patient susceptibility to pul-
monary tuberculosis (PTB) in a sample of the Iranian population. This case-control study was performed using 150 PTB cases and 150 con-
trols. P2X7 receptor polymorphisms were determined using tetra-
amplification refractory mutation system-polymerase chain reaction. Genotype and allelic frequencies of the rs2393799 variant within the P2X7 gene were significantly higher in the PTB patients than in the healthy controls. The genotypes were CC in 71, CT in 54, and TT in 25 PTB patients. The genotypes were CC in 104, CT in 40, and TT in 6 healthy controls. The results indicate a significant association be-
 tween rs2393799 polymorphism of the P2X7 gene and susceptibility to PTB (CT vs CC: OR=6.5, 95%CI=2.5-16.9, p<0.0001; TT vs CC: OR=3.3, 95%CI=1.2-8.9, p=0.018; TC+TT vs CC: OR=2.56, 95%CI=1.59-
4.12, p<0.0001). The rs2393799 T allele is a risk factor for predispo-
sition to PTB (OR=2.53, 95%CI=1.73-3.71, p<0.0001). No association
between the rs1718119 polymorphism and PTB was found.”
According to the news editors, the research concluded: “The rs2393799 polymorphism in the P2X7 gene may contribute to patient susceptibility to PTB in our study population.”


The news correspondents report that additional information may be obtained from G. Bahari, Research Center for Infectious Diseases and Tropical Medicine, Zahedan University of Medical Sciences, Zahedan, Iran. (2013 Mar 04)

**Global Health Institute, Lausanne: Genome-wide definition of the SigF regulon in Mycobacterium tuberculosis**

By a News Reporter-Staff News Editor at Health & Medicine Week – Research findings on Bacteriology are discussed in a new report. According to news originating from Lausanne, Switzerland, by NewsRx correspondents, research stated, “In *Mycobacterium tuberculosis* the alternative sigma factor SigF controls the expression of a particular subset of genes by altering RNA polymerase specificity. Here, we utilize two genome-wide approaches to identify SigF-binding sites: chromatin immunoprecipitation (ChIP-on-chip) and microarray analysis of SigF-mediated transcripts.”

Our news journalists obtained a quote from the research from Global Health Institute, “Since SigF is not an abundant protein in the logarithmic phase of growth, a pristinamycin IA-inducible system was used to control its expression. We identified 67 high-affinity SigF-binding sites and 16 loci where a SigF promoter directs the expression of a transcript. These loci include sigF itself, genes involved in lipid and intermediary metabolism and virulence, and at least one transcriptional regulator (Rv2884), possibly acting downstream of SigF. In addition, SigF was also found to direct the transcription of the gene for small RNA F6. Many loci were also found where SigF may be involved in antisense transcription, and in two cases (Rv1358 and Rv1870c) the SigF-dependent promoter was located within the predicted coding sequence. Quantitative PCR confirmed the microarray findings and 5'-rapid amplification of cDNA ends was used to map the SigF-specific transcriptional start points. A canonical SigF consensus promoter sequence GGTTT-N((15-17))-GGGTA was found prior to 11 genes.”

According to the news editors, the research concluded: “Together, these data help to define the SigF regulon and show that SigF not only governs expression of proteins such as the virulence factor, HbhA, but also impacts novel functions, such as noncoding RNAs and antisense transcripts.”

The news correspondents report that additional information may be obtained from R.C. Hartkoorn, Global Health Institute, Ecole Polytechnique Federale de Lausanne, Lausanne, Switzerland. (*2013 Mar 01*)

**Institute Pasteur, Paris: After the bottleneck: Genome-wide diversification of the Mycobacterium tuberculosis complex by mutation, recombination, and natural selection**

By a News Reporter-Staff News Editor at Health & Medicine Week – Current study results on Genomics have been published. According to news reporting originating in Paris, France, by NewsRx journalists, research stated, “Many of the most virulent bacterial pathogens show low genetic diversity and sexual isolation. Accordingly, *Mycobacterium tuberculosis*, the deadliest human pathogen, is thought to be clonal and evolve by genetic drift.”

The news reporters obtained a quote from the research from Institute Pasteur, “Yet, its genome shows few of the concomitant signs of genome degradation. We analyzed 24 genomes and found an excess of genetic diversity in regions encoding key adaptive functions including the type VII secretion system and the ancient horizontally transferred virulence-related regions. Four different approaches showed evident signs of recombination in *M. tuberculosis*. Recombination tracts add a high density of polymorphisms, and many are thus predicted to arise from outside the clade. Some of these tracts match *Mycobacterium canettii* sequences. Recombination introduced an excess of non-synonymous diversity in general and even more in genes expected to be under positive or diversifying selection, e.g., cell wall component genes. Mutations leading to non-synonymous SNPs are effectively purged in MTBC, which shows dominance of purifying selection. MTBC mutation bias toward AT nucleotides is not compensated by biased gene conversion, suggesting the action of natural selection also on synonymous changes. Together, all of these observations point to a strong imprint of recombination and selection in the genome affecting both non-synonymous and synonymous positions.”

According to the news reporters, the research concluded: “Hence, contrary to some other pathogens and previous proposals concerning *M. tuberculosis*, this lineage may have come out of its ancestral bottleneck as a very successful pathogen that is rapidly diversifying by the action of mutation, recombination, and natural selection.”
For more information on this research see: After the bottleneck: Genome-wide diversification of the Mycobacterium tuberculosis complex by mutation, recombination, and natural selection. Genome Research, 2012;22(4):721-34.

Our news correspondents report that additional information may be obtained by contacting A. Namouchi, Unite de Genetique Mycobacterienne, Institut Pasteur, 75015 Paris, France. (2013 Mar 01)

University of Louisville School of Medicine: High proportion of fluoroquinolone-resistant Mycobacterium tuberculosis isolates with novel gyrase polymorphisms and a gyrA region associated with fluoroquinolone susceptibility

By a News Reporter-Staff News Editor at Health & Medicine Week – Fresh data on Mycobacterium Infections are presented in a new report. According to news reporting from Louisville, Kentucky, by NewsRx journalists, research stated, “Fluoroquinolone resistance in Mycobacterium tuberculosis can be conferred by mutations in gyrA or gyrB. The prevalence of resistance mutations outside the quinolone resistance-determining region (QRDR) of gyrA or gyrB is unclear, since such regions are rarely sequenced. M. tuberculosis isolates from 1,111 patients with newly diagnosed culture-confirmed tuberculosis diagnosed in Tennessee from 2002 to 2009 were screened for phenotypic ofloxacin resistance (&gt;2 g/ml).”

The news correspondents obtained a quote from the research from the University of Louisville School of Medicine, “For each resistant isolate, two ofloxacin-susceptible isolates were selected: one with antecedent fluoroquinolone exposure and one without. The complete gyrA and gyrB genes were sequenced and compared with M. tuberculosis H37Rv. Of 25 ofloxacin-resistant isolates, 11 (44%) did not have previously reported resistance mutations. Of these, 10 had novel polymorphisms: 3 in the QRDR of gyrA, 1 in the QRDR of gyrB, and 6 outside the QRDR of gyrA or gyrB; 1 did not have any gyrase polymorphisms. Polymorphisms in gyrA codons 1 to 73 were more common in fluoroquinolone-susceptible than in fluoroquinolone-resistant strains (20% versus 0%; p=0.016).”

According to the news reporters, the research concluded: “In summary, almost half of fluoroquinolone-resistant M. tuberculosis isolates did not have previously described resistance mutations, which has implications for genotypic diagnostic tests.”

For more information on this research see: High proportion of fluoroquinolone-resistant Mycobacterium tuberculosis isolates with novel gyrase polymorphisms and a gyrA region associated with
University of London: Microevolution of extensively drug-resistant tuberculosis in Russia

By a News Reporter-Staff News Editor at Biotech Week – Fresh data on Mycobacterium Infections are presented in a new report. According to news reporting originating from London, United Kingdom, by NewsRx correspondents, research stated, “Extensively drug-resistant (XDR) tuberculosis (TB), which is resistant to both first-and second-line antibiotics, is an escalating problem, particularly in the Russian Federation. Molecular fingerprinting of 2348 Mycobacterium tuberculosis isolates collected in Samara Oblast, Russia, revealed that 72% belonged to the Beijing lineage, a genotype associated with enhanced acquisition of drug resistance and increased virulence.”

Our news editors obtained a quote from the research from the University of London, “Whole-genome sequencing of 34 Samaran isolates, plus 25 isolates representing global M. tuberculosis complex diversity, revealed that Beijing isolates originating in Eastern Europe formed a monophyletic group. Homoplastic polymorphisms within this clade were almost invariably associated with antibiotic resistance, indicating that the evolution of this population is primarily driven by drug therapy. Resistance genotypes showed a strong correlation with drug susceptibility phenotypes. A novel homoplastic mutation in rpoC, found only in isolates carrying a common rpoB rifampicin-resistance mutation, may play a role in fitness compensation. Most multidrug-resistant (MDR) isolates also had mutations in the promoter of a virulence gene, eis, which increase its expression and confer kanamycin resistance. Kanamycin therapy may thus select for mutants with increased virulence, helping preserve bacterial fitness and promoting transmission of drug-resistant TB strains. The East European clade was dominated by two MDR clusters, each disseminated across Samara.”

According to the news editors, the research concluded: “Polymorphisms conferring fluoroquinolone resistance were independently acquired multiple times within each cluster, indicating that XDR TB is currently not widely transmitted.”

For more information on this research see: Microevolution of extensively drug-resistant tuberculosis in Russia. Genome Research, 2012;22(4):735-45.

The news editors report that additional information may be obtained by contacting N. Casali, National Mycobacterium Reference Laboratory,
Blizard Institute, Queen Mary, University of London, London E1 2AT, UK. (2013 Feb 27)

McMaster University, Hamilton: Global Gene Transcriptome Analysis in Vaccinated Cattle Revealed a Dominant Role of IL-22 for Protection against Bovine Tuberculosis

By a News Reporter-Staff News Editor at Life Science Weekly – Fresh data on Mycobacterium Infections are presented in a new report. According to news reporting out of Hamilton, Canada, by NewsRx editors, research stated, “Bovine tuberculosis (bTB) is a chronic disease of cattle caused by Mycobacterium bovis, a member of the Mycobacterium tuberculosis complex group of bacteria. Vaccination of cattle might offer a long-term solution for controlling the disease and priority has been given to the development of a cattle vaccine against bTB.”

Our news journalists obtained a quote from the research from McMaster University, “Identification of biomarkers in tuberculosis research remains elusive and the goal is to identify host correlates of protection. We hypothesized that by studying global gene expression we could identify in vitro predictors of protection that could help to facilitate vaccine development. Calves were vaccinated with BCG or with a heterologous BCG prime adenovirally vectored subunit boosting protocol. Protective efficacy was determined after M. bovis challenge. RNA was prepared from PPD-stimulated PBMC prepared from vaccinated-protected, vaccinated-unprotected and unvaccinated control cattle prior to M. bovis challenge and global gene expression determined by RNA-seq. 668 genes were differentially expressed in vaccinated-protected cattle compared with vaccinated-unprotected and unvaccinated control cattle. Cytokine-cytokine receptor interaction was the most significant pathway related to this dataset with IL-22 expression identified as the dominant surrogate of protection besides INF-gamma. Finally, the expression of these candidate genes identified by RNA-seq was evaluated by RT-qPCR in an independent set of PBMC samples from BCG vaccinated and unvaccinated calves.”

According to the news editors, the research concluded: “This experiment confirmed the importance of IL-22 as predictor of vaccine efficacy.”

From multidrug-resistant to extensively drug-resistant tuberculosis in Lisbon, Portugal: the stepwise mode of resistance acquisition

By a News Reporter-Staff News Editor at Health & Medicine Week – Current study results on Antimicrobials have been published. According to news reporting from Lisbon, Portugal, by NewsRx journalists, research stated, “The development and transmission of extensively drug-resistant (XDR) tuberculosis (TB) constitutes a serious threat to the effective control of TB in several countries. Here, in an attempt to further elucidate the dynamics of the acquisition of resistance to second-line drugs and investigate an eventual role for eis promoter mutations in aminoglycoside resistance, we have studied a set of multidrug-resistant (MDR)/XDR-TB isolates circulating in Lisbon, Portugal.”

The news correspondents obtained a quote from the research, “Forty-four MDR-TB or XDR-TB isolates were genotyped and screened for mutations in genes associated with second-line drug resistance, namely tlyA, gyrA, rrs and eis. The most prevalent mutations found in each gene were Ins755GT in tlyA, A1401G in rrs, G-10A in eis and S91P in gyrA. Additionally, two genetic clusters were found in this study: Lisboa3 and Q1. The characteristic mutational profile found among recent XDR-TB circulating in Lisbon was also found in MDR-TB strains isolated in the 1990s. Also investigated was the resistance level conferred by eis G-10A mutations, revealing that eis G-10A mutations may result in amikacin resistance undetectable by widely used phenotypic assays. The analysis of the distribution of the mutations found by genetic clustering showed that in the Q1 cluster, two mutations, gyrA D94A and rrs A1401G, were enough to ensure development of XDR-TB from an MDR strain.”

According to the news reporters, the research concluded: “Moreover, in the Lisboa3 cluster it was possible to elaborate a model in which the development of low-level kanamycin resistance was at the origin of the emergence of XDR-TB strains that can be discriminated by tlyA mutations.”

Institute of Systems Biology, Seattle: Global analysis of mRNA stability in *Mycobacterium tuberculosis*

By a News Reporter-Staff News Editor at Health & Medicine Week – A new study on Nucleic Acids Research is now available. According to news reporting originating from Seattle, Washington, by NewsRx correspondents, research stated, “*Mycobacterium tuberculosis* (MTB) is a highly successful pathogen that infects over a billion people. As with most organisms, MTB adapts to stress by modifying its transcriptional profile.”

Our news editors obtained a quote from the research from the Institute of Systems Biology, “Remodeling of the transcriptome requires both altering the transcription rate and clearing away the existing mRNA through degradation, a process that can be directly regulated in response to stress. To understand better how MTB adapts to the harsh environs of the human host, we performed a global survey of the decay rates of MTB mRNA transcripts. Decay rates were measured for 2139 of the similar to 4000 MTB genes, which displayed an average half-life of 9.5 min. This is nearly twice the average mRNA half-life of other prokaryotic organisms where these measurements have been made. The transcriptome was further stabilized in response to lowered temperature and hypoxic stress.”

According to the news editors, the research concluded: “The generally stable transcriptome described here, and the additional stabilization in response to physiologically relevant stresses, has far-ranging implications for how this pathogen is able to adapt in its human host.”


The news editors report that additional information may be obtained by contacting T.R. Rustad, Inst Syst Biol, Seattle, WA 98109, United States. (2013 Feb 08)
Shandong University, Jinan: MprAB Regulates the espA Operon in Mycobacterium tuberculosis and Modulates ESX-1 Function and Host Cytokine Response

By a News Reporter-Staff News Editor at Health & Medicine Week –

Data detailed on Bacteriology have been presented. According to news reporting out of Jinan, People’s Republic of China, by NewsRx editors, research stated, “The ESX-1 secretion system exports the immunomodulatory protein ESAT-6 and other proteins important in the pathogenesis of Mycobacterium tuberculosis. Components and substrates of ESX-1 are encoded at several loci, but the regulation of the encoding genes is only partially understood.”

Our news journalists obtained a quote from the research from Shandong University, “In this study, we investigated the role of the MprAB two-component system in the regulation of ESX-1 activity. We determined that MprAB directly regulates the espA gene cluster, a locus necessary for ESX-1 function. Transcript mapping determined that the five genes in the cluster form an operon with two transcriptional start points, and several MprA binding sites were detected in the espA promoter. Expression analyses and promoter constructs indicated that MprAB represses the espA operon. However, the MprAB mutant Rv-D981 secreted lower levels of EspA, ESAT-6, and the ESX-1 substrate EspB than control strains. Secretion of CFP10, which is normally cosecreted with ESAT-6, was similar in Rv-D981 and control strains, further demonstrating aberrant ESX-1 activity in the mutant. ESAT-6 induces proinflammatory cytokines, and macrophages infected with Rv-D981 elicited lower levels of interleukin 1β (IL-1β) and tumor necrosis factor alpha (TNF-α), consistent with the reduced levels of ESAT-6.”

According to the news editors, the research concluded: “These findings indicate that MprAB modulates ESX-1 function and reveal a new role for MprAB in host-pathogen interactions.”

For more information on this research see: MprAB Regulates the espA Operon in Mycobacterium tuberculosis and Modulates ESX-1 Function and Host Cytokine Response. Journal of Bacteriology, 2013;195(1):66-75. (American Society for Microbiology - www.asm.org; Journal of Bacteriology - jb.asm.org)

Our news journalists report that additional information may be obtained by contacting X. Pang, The State Key Laboratory of Microbial Technology, Shandong University, Jinan, People’s Taiwan. (2013 Feb 08)
University of California, Berkeley: Elucidation and chemical modulation of sulfolipid-1 biosynthesis in Mycobacterium tuberculosis

By a News Reporter-Staff News Editor at Health & Medicine Week – Researchers detail new data in Mycobacterium Infections. According to news reporting originating in Berkeley, California, by NewsRx journalists, research stated, “Mycobacterium tuberculosis possesses unique cell-surface lipids that have been implicated in virulence. One of the most abundant is sulfolipid-1 (SL-1), a tetraacyl-sulfotrehalose glycolipid.”

The news reporters obtained a quote from the research from the University of California, “Although the early steps in SL-1 biosynthesis are known, the machinery underlying the final acylation reactions is not understood. We provide genetic and biochemical evidence for the activities of two proteins, Chp1 and Sap (corresponding to gene loci rv3822 and rv3821), that complete this pathway. The membrane-associated acyltransferase Chp1 accepts a synthetic diacyl sulfolipid and transfers an acyl group regioselectively from one donor substrate molecule to a second acceptor molecule in two successive reactions to yield a tetraacylated product. Chp1 is fully active in vitro, but in M. tuberculosis, its function is potentiated by the previously identified sulfolipid transporter MmpL8. We also show that the integral membrane protein Sap and MmpL8 are both essential for sulfolipid transport. Finally, the lipase inhibitor tetrahydrolipstatin disrupts Chp1 activity in M. tuberculosis, suggesting an avenue for perturbing SL-1 biosynthesis in vivo.”

According to the news reporters, the research concluded: “These data complete the SL-1 biosynthetic pathway and corroborate a model in which lipid biosynthesis and transmembrane transport are coupled at the membrane-cytosol interface through the activity of multiple proteins, possibly as a macromolecular complex.”


Our news correspondents report that additional information may be obtained by contacting J.C. Seeliger, Dept. of Chemistry, University of California, Berkeley, California 94720-1460, United States. (2013 Feb 08)
Indian Institute of Science, Bangalore: Functional analysis of DNA replication fork reversal catalyzed by Mycobacterium tuberculosis RuvAB proteins

By a News Reporter-Staff News Editor at Health & Medicine Week – Investigators publish new report on Biological Chemistry. According to news originating from Bangalore, India, by NewsRx correspondents, research stated, “Initially discovered in Escherichia coli, RuvAB proteins are ubiquitous in bacteria and play a dual role as molecular motor proteins responsible for branch migration of the Holliday junction(s) and reversal of stalled replication forks. Despite mounting genetic evidence for a crucial role of RuvA and RuvB proteins in reversal of stalled replication forks, the mechanistic aspects of this process are still not fully understood.”

Our news journalists obtained a quote from the research from the Indian Institute of Science, “Here, we elucidate the ability of Mycobacterium tuberculosis RuvAB (MtRuvAB) complex to catalyze the reversal of replication forks using a range of DNA replication fork substrates. Our studies show that MtRuvAB, unlike E. coli RuvAB, is able to drive replication fork reversal via the formation of Holliday junction intermediates, suggesting that RuvAB-catalyzed fork reversal involves concerted unwinding and annealing of nascent leading and lagging strands. We also demonstrate the reversal of replication forks carrying hemi-replicated DNA, indicating that MtRuvAB complex-catalyzed fork reversal is independent of symmetry at the fork junction. The fork reversal reaction catalyzed by MtRuvAB is coupled to ATP hydrolysis, is processive, and culminates in the formation of an extended reverse DNA arm. Notably, we found that sequence heterology failed to impede the fork reversal activity of MtRuvAB.”

According to the news editors, the research concluded: “We discuss the implications of these results in the context of recognition and processing of varied types of replication fork structures by RuvAB proteins.”


The news correspondents report that additional information may be obtained from J.S. Khanduja, Dept. of Biochemistry, Indian Institute of Science, Bangalore 560012, India. (2013 Feb 01)
University of Birmingham: Identification of Novel Imidazo[1,2-a]pyridine Inhibitors Targeting M. tuberculosis QcrB

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators publish new report on Life Science Research. According to news reporting from Birmingham, United Kingdom, by NewsRx journalists, research stated, “Mycobacterium tuberculosis is a major human pathogen and the causative agent for the pulmonary disease, tuberculosis (TB). Current treatment programs to combat TB are under threat due to the emergence of multi-drug and extensively-drug resistant TB.”

The news correspondents obtained a quote from the research from the University of Birmingham, “Through the use of high throughput whole cell screening of an extensive compound library a number of imidazo[1,2-a]pyridine (IP) compounds were obtained as potent lead molecules active against M. tuberculosis and Mycobacterium bovis BCG. The IP inhibitors (1-4) demonstrated minimum inhibitory concentrations (MICs) in the range of 0.03 to 5 M against a panel of M. tuberculosis strains. M. bovis BCG spontaneous resistant mutants were generated against IP 1, 3, and 4 at 5 x MIC and subsequent whole genome sequencing identified a single nucleotide polymorphism (937)ACC &gt;(937)GCC (T313A) in qcrB, which encodes the b subunit of the electron transport ubiquinol cytochrome C reductase. This mutation also conferred cross-resistance against IP 1, 3 and 4 demonstrating a common target. Gene dosage experiments confirmed M. bovis BCG QcrB as the target where over-expression in M. bovis BCG led to an increase in MIC from 0.5 to &gt;8 M for IP 3.”

According to the news reporters, the research concluded: “An acute murine model of TB infection established bacteriostatic activity of the IP series, which await further detailed characterization.”

For more information on this research see: Identification of Novel Imidazo[1,2-a]pyridine Inhibitors Targeting M. tuberculosis QcrB. Plos One, 2012;7(12):e52951. (Public Library of Science - www.plos.org; Plos One - www.plosone.org)

Our news journalists report that additional information may be obtained by contacting K.A. Abrahams, School of Biosciences, University of Birmingham, Edgbaston, Birmingham, UK. (2013 Jan 29)
University Hospital, Santander: Mannose-binding lectin promoter polymorphisms and gene variants in pulmonary tuberculosis patients from cantabria (northern Spain)

By a News Reporter-Staff News Editor at Tuberculosis Week – Current study results on Tuberculosis have been published. According to news reporting from Santander, Spain, by NewsRx journalists, research stated, “Mannose-binding lectin is a central molecule of the innate immune system. Mannose-binding lectin 2 promoter polymorphisms and structural variants have been associated with susceptibility to tuberculosis.”

The news correspondents obtained a quote from the research from University Hospital, “However, contradictory results among different populations have been reported, resulting in no convincing evidence of association between mannose-binding lectin 2 and susceptibility to tuberculosis. For this reason, we conducted a study in a well genetically conserved Spanish population in order to shed light on this controversial association. We analysed the six promoter and structural mannose-binding lectin 2 gene variants in 107 patients with pulmonary tuberculosis and 441 healthy controls. Only D variant and HYPD haplotype were significantly more frequent in controls which would indicate that this allele could confer protection against pulmonary tuberculosis, but this difference disappeared after statistical correction. Neither the rest of alleles nor the haplotypes were significantly associated with the disease. These results would indicate that mannose-binding lectin promoter polymorphisms and gene variants would not be associated with an increased risk to pulmonary tuberculosis.”

According to the news reporters, the research concluded: “Despite the slight trend of the D allele and HYPD haplotype in conferring protection against pulmonary tuberculosis, susceptibility to this disease would probably be due to other genetic factors, at least in our population.”

For more information on this research see: Mannose-binding lectin promoter polymorphisms and gene variants in pulmonary tuberculosis patients from cantabria (northern Spain). *Pulmonary Medicine*, 2012;2012():469128. (Hindawi Publishing - www.hindawi.com; Pulmonary Medicine - http://www.hindawi.com/journals/pm/)

Our news journalists report that additional information may be obtained by contacting J.G. Ocejo-Vinyals, Servicio de Inmunologia, Hospital Universitario Marques de Valdecilla, Avenida de Valdecilla s, n, 39008 Santander, Spain. (2013 Jan 28)
University of Strathclyde, Glasgow: Synthesis, antitubercular activity and mechanism of resistance of highly effective thiacetazone analogues

By a News Reporter-Staff News Editor at Tuberculosis Week – Current study results on Life Science Research have been published. According to news reporting originating in Glasgow, United Kingdom, by NewsRx journalists, research stated, “Defining the pharmacological target(s) of currently used drugs and developing new analogues with greater potency are both important aspects of the search for agents that are effective against drug-sensitive and drug-resistant Mycobacterium tuberculosis. Thiacetazone (TAC) is an anti-tubercular drug that was formerly used in conjunction with isoniazid, but removed from the antitubercular chemotherapeutic arsenal due to toxic side effects.”

The news reporters obtained a quote from the research from the University of Strathclyde, “However, several recent studies have linked the mechanisms of action of TAC to mycolic acid metabolism and TAC-derived analogues have shown increased potency against M. tuberculosis. To obtain new insights into the molecular mechanisms of TAC resistance, we isolated and analyzed 10 mutants of M. tuberculosis that were highly resistant to TAC. One strain was found to be mutated in the methyltransferase MmaA4 at Gly101, consistent with its lack of oxygenated mycolic acids. All remaining strains harbored missense mutations in either HadA (at Cys61) or HadC (at Val85, Lys157 or Thr123), which are components of the &#223;-hydroxyacyl-ACP dehydratase complex that participates in the mycolic acid elongation step. Separately, a library of 31 new TAC analogues was synthesized and evaluated against M. tuberculosis. Two of these compounds, 15 and 16, exhibited minimal inhibitory concentrations 10-fold lower than the parental molecule, and inhibited mycolic acid biosynthesis in a dose-dependent manner. Moreover, overexpression of HadAB HadBC or HadABC in M. tuberculosis led to high level resistance to these compounds, demonstrating that their mode of action is similar to that of TAC.”

According to the news reporters, the research concluded: “In summary, this study uncovered new mutations associated with TAC resistance and also demonstrated that simple structural optimization of the TAC scaffold was possible and may lead to a new generation of TAC-derived drug candidates for the potential treatment of tuberculosis as mycolic acid inhibitors.”

S. Raffaele Scientific Institute, Milan: Genome-Wide Discovery of Small RNAs in Mycobacterium tuberculosis

By a News Reporter-Staff News Editor at Health & Medicine Week – A new study on Life Science Research is now available. According to news originating from Milan, Italy, by NewsRx correspondents, research stated, “Only few small RNAs (sRNAs) have been characterized in Mycobacterium tuberculosis and their role in regulatory networks is still poorly understood. Here we report a genome-wide characterization of sRNAs in M. tuberculosis integrating experimental and computational analyses.”

Our news journalists obtained a quote from the research from S. Raffaele Scientific Institute, “Global RNA-seq analysis of exponentially growing cultures of M. tuberculosis H37Rv had previously identified 1373 sRNA species. In the present report we show that 258 (19%) of these were also identified by microarray expression. This set included 22 intergenic sRNAs, 84 sRNAs mapping within 5'/3' UTRs, and 152 antisense sRNAs. Analysis of promoter and terminator consensus sequences identified sigma A promoter consensus sequences for 121 sRNAs (47%), terminator consensus motifs for 22 sRNAs (8.5%), and both motifs for 35 sRNAs (14%). Additionally, 20/23 candidates were visualized by Northern blot analysis and 5' end mapping by primer extension confirmed the RNA-seq data. We also used a computational approach utilizing functional enrichment to identify the pathways targeted by sRNA regulation. We found that antisense sRNAs preferentially regulated transcription of membrane-bound proteins.”

According to the news editors, the research concluded: “Genes putatively regulated by novel cis-encoded sRNAs were enriched for two-component systems and for functional pathways involved in hydrogen transport on the membrane.”

For more information on this research see: Genome-Wide Discovery of Small RNAs in Mycobacterium tuberculosis. PloS One, 2012;7(12):e51950. (Public Library of Science - www.plos.org; Plos One - www.plosone.org)

The news correspondents report that additional information may be obtained from P. Miotto, Emerging Bacterial Pathogens Unit, S Raffaele Scientific Institute, Milan, Italy. (2013 Jan 25)
Northwest Polytechnic University, Shaanxi: CYP2E1 RsaI/PstI polymorphism and risk of anti-tuberculosis drug-induced liver injury: a meta-analysis

By a News Reporter-Staff News Editor at Life Science Weekly – Data detailed on Tuberculosis and Lung Disease have been presented. According to news reporting out of Shaanxi, People’s Republic of China, by NewsRx editors, research stated, “A number of studies have evaluated the association between cytochrome P450 2E1 (CYP2E1) RsaI/PstI polymorphism and the risk of anti-tuberculosis drug-induced liver injury (ATDILI). However, the results were inconsistent.”

Our news journalists obtained a quote from the research from Northwest Polytechnic University, “We conducted a meta-analysis to clarify the role of this polymorphism in ATDILI. Two authors independently searched the PubMed, Medline, EMBASE and Chinese National Knowledge Infrastructure databases for studies on the association of CYP2E1 RsaI/PstI polymorphism with risk of ATDILI. Summary odds ratios (ORs) with their corresponding 95% confidence intervals (CIs) were calculated. The combined results showed that the CYP2E1 c1/c1 genotype was associated with increased ATDILI risk compared to variant genotypes (c1/c2+c2/c2) (OR 1.36, 95%CI 1.09-1.69). When stratifying for study population, statistically significant results were observed in Chinese (OR 1.47, 95%CI 1.12-1.92) and Korean populations (OR 1.85, 95%CI 1.04-3.30). In comparison with CYP2E1 c1/c2 or c2/c2 with rapid/intermediate acetylators, the risk of ATDILI increased from 1.88 (95%CI 1.14-3.09) for CYP2E1 c1/c1 with rapid/intermediate acetylators to 6.44 (95%CI 3.47-11.97) for CYP2E1 c1/c1 with slow acetylators.”

According to the news editors, the research concluded: “This meta-analysis suggests that CYP2E1 RsaI/PstI polymorphism may affect susceptibility to ATDILI, particularly among Chinese and Korean populations.”


Our news journalists report that additional information may be obtained by contacting R. Deng, NW Polytechnic Univ, Sch Life Sci, Dept. of Pharmacol, Xian 710072, Shaanxi, People’s Republic of China. (2013 Jan 22)
University of Szeged: A Case of Spinal Tuberculosis From the Middle Ages in Transylvania (Romania)

By a News Reporter-Staff News Editor at TB & Outbreaks Week – A new study on Mycobacterium Infections is now available. According to news reporting originating from Szeged, Hungary, by NewsRx correspondents, research stated, “Case report. To characterize the paleopathology presented in the skeleton of a 45- to 50-year-old man indicative of tuberculous spondylitis and to confirm by the detection of ancient DNA.”

Our news editors obtained a quote from the research from the University of Szeged, “Summary of Background Data. Tuberculosis (TB) is an infectious disease prevalent in both present and ancient human populations. The disease is primarily located within the lungs; although characteristic bone lesions can lead to a clear diagnosis, skeletal TB occurs in only 5% to 6% of TB infections, even in historical cases. In addition, the visual appearance of human skeletal remains may be influenced by the environmental conditions at the burial site. However, it is important to recognize ancient skeletal TB because it can provide important data on the history of Mycobacterium tuberculosis and give a unique opportunity for physicians to observe the natural outcome of the infection of the preantibiotic era. Paleopathological analysis was carried out using careful visual observation supported by ancient DNA analysis. Approximately 60 mg of bone powder from rib fragments was examined and DNA from the M. tuberculosis complex was detected by polymerase chain reaction (PCR) targeting specific genetic loci of the IS6110 and IS1081 regions. The skeleton is part of a human osteoarchaeological collection (n = 274) from the 12th- to 13th-century Transylvanian archaeological site of Peteni, in modern-day Romania. The individual, a 45- to 50-year-old man, showed gross pathology typical of tuberculous spondylitis. The paleopathological diagnosis was supported by analysis for M. tuberculosis complex ancient DNA.”

According to the news editors, the research concluded: “This case demonstrates that TB was present in Transylvania (Romania) during the 12th and 13th centuries and adds to the growing body of knowledge on the history of this disease.”

For more information on this research see: A Case of Spinal Tuberculosis From the Middle Ages in Transylvania (Romania). SPINE, 2012;37(25):E1598-E1601. SPINE can be contacted at: Lippincott Williams & Wilkins, 530 Walnut St, Philadelphia, PA 19106-3621, USA. (Lippincott Williams and Wilkins - www.lww.com; SPINE - http://journals.lww.com/spinejournal/pages/default.aspx)

The news editors report that additional information may be obtained by contacting T. Hajdu, University of Szeged, Szeged, Hungary. (2013 Jan 15)
College of Health Sciences, Mwanza: Albinism and disease causing pathogens in Tanzania: Are alleles that are associated with OCA2 being maintained by balancing selection?

By a News Reporter-Staff News Editor at TB & Outbreaks Week – Investigators discuss new findings in Medical Hypotheses. According to news reporting originating from Mwanza, Tanzania, by NewsRx correspondents, research stated, “Oculocutaneous albinism type 2 (OCA2) is present at significantly higher frequencies in sub-Saharan African populations compared to populations in other regions of the world. In Tanzania and other sub-Saharan countries, most OCA2 is associated with a common 2.7 kb deletion allele.”

Our news editors obtained a quote from the research from the College of Health Sciences, “Leprosy is also in high prevalence in sub-Saharan African populations. The infectious agent of leprosy, Mycobacterium leprae, contains a gene, 38L, that is similar to OCA2. Hypopigmented patches of skin are early symptoms that present with infection of leprosy. In consideration of both the genetic similarity of OCA2 and the 38L gene of M. leprae and the involvement of pigmentation in both disorders, we hypothesized that the high rates of OCA2 may be due to heterozygote advantage. Hence, we hypothesized that carriers of the 2.7 kb deletion allele of OCA2 may provide a protective advantage from infection with leprosy. We tested this hypothesis by determining the carrier frequency of the 2.7 kb deletion allele from a sample of 240 individuals with leprosy from Tanzania. The results were inconclusive due to the small sample size; however, they enabled us to rule out a large protective effect, but perhaps not a small advantage. Mycobacterium tuberculosis is another infectious organism prevalent in sub-Saharan Africa that contains a gene, arsenic-transport integral membrane protein that is also similar to OCA2. Interestingly, chromosomal region 15q11-13, which also contains OCA2, was reported to be linked to tuberculosis susceptibility. Although variants within OCA2 were tested for association, the 2.7 kb deletion allele of OCA2 was not tested. This led us to hypothesize that the deletion allele may confer resistance to susceptibility. Confirmation of our hypothesis would enable development of novel pharmacogenetic therapies for the treatment of tuberculosis, which in turn, may enable development of drugs that target other pathogens that utilize a similar infection mechanism as M. tuberculosis.”

According to the news editors, the research concluded: “From an evolutionary perspective, confirmation of our hypothesis may provide another example of heterozygote advantage.”

For more information on this research see: Albinism and disease causing pathogens in Tanzania: Are alleles that are associated with

The news editors report that additional information may be obtained by contacting A.M. Tuli, Weill Bugando Univ Coll Hlth Sci, Mwanza, Tanzania. (2013 Jan 08)

**University of Surrey, Guildford: A microfluidic system for long-term time-lapse microscopy studies of mycobacteria**

By a News Reporter-Staff News Editor at Health & Medicine Week – Researchers detail new data in Tuberculosis and Lung Disease. According to news reporting from Guildford, United Kingdom, by NewsRx journalists, research stated, “Phenotypic heterogeneity in bacterial populations is thought to contribute to a number of important phenomena including sporulation and persistence. The latter has clinical implications in many diseases such as tuberculosis, where persistence of *Mycobacterium tuberculosis* within the human host is believed to be the root cause of latent tuberculosis and the ability of a minority population of cells to survive antibiotic exposure, despite being genetically identical to the bulk population that are killed.”

The news correspondents obtained a quote from the research from the University of Surrey, “However, phenotypic variations caused by non-genetic mechanisms are difficult to study because of the transient nature of the persistent state and thereby the requirement to observe individual cells in real-time. Recently, microfluidics, combined with time-lapse microscopy, has become a powerful tool for studying population heterogeneity in bacteria. However, growth and replication of mycobacterial cells provide particular problems for the development of microfluidic systems due to their tendency to grow in three dimensions. We here describe a novel microfluidic device for the observation of growth and antibiotic killing in individual mycobacterial cells. We constructed a microfluidic device suitable for studying single cell behavior in mycobacteria. The growth of single cells of *Mycobacterium smegmatis* expressing green fluorescent protein was monitored using a confocal laser scanning microscope. Within the device *M. smegmatis* cells were tightly confined within a hydrogel matrix thus promoting planar growth. Cell growth and killing was observed in the device with dead cells highlighted by uptake of propidium iodide.”

According to the news reporters, the research concluded: “We demonstrate that our device allows real-time analysis and long-term culture of single cells of mycobacteria, and is able to support the study
of cell death during the application of antibiotics. The device will allow observation of individual cells’ cell genealogy to be determined and direct observation of rare states, such as persistence.”


Our news journalists report that additional information may be obtained by contacting S.A. Golchin, University of Surrey, Fac Engn & Phys Sci, Adv Technol Inst, Guildford GU2 7HX, Surrey, United Kingdom. (2012 Dec 28)

**University of Hong Kong: Genomic sequence based scanning for drug resistance-associated mutations and evolutionary analysis of multidrug-resistant and extensively drug-resistant Mycobacterium tuberculosis**

By a News Reporter-Staff News Editor at Life Science Weekly – Research findings on Infection Research are discussed in a new report. According to news reporting originating from Hong Kong, People’s Republic of China, by NewsRx correspondents, research stated, “To better understand the molecular mechanisms and evolution of drug resistance in Mycobacterium tuberculosis (M. tuberculosis), we performed a genomic sequence based scanning of drug resistance-associated loci for multidrug-resistant (MDR) and extensively drug-resistant (XDR) M. tuberculosis strains. Forty-five pairs of primers covering known drug resistance-associated loci compiled in the TBDReaMDB database were designed to perform the analysis of drug resistance-associated mutations for 14 M. tuberculosis clinical isolates from TB patients in China.”

Our news editors obtained a quote from the research from the University of Hong Kong, “Genetic diversity and evolutionary analysis was done using concatenated nucleotide sequences of drug resistance-associated loci. Forty-four types of mutations were identified in 14 M. tuberculosis clinical isolates. Average nucleotide diversity for drug resistance-associated loci increased in the M. tuberculosis isolates as the drug resistance increased (pi = 0, pi = 0.00021, and pi = 0.00028 for susceptible, MDR, and XDR isolates, respectively). The dN/dS ratios for coding regions of drug resistance-associated genes in MDR and XDR isolates were 2.73 and 1.83, respectively. MDR and XDR isolates were distributed sporadically on different branches in the phylogenetic trees.”
According to the news editors, the research concluded: “Our study provides supporting evidence to demonstrate that the MDR- and XDR-M. tuberculosis strains have evolved independently driven by positive selection.”


The news editors report that additional information may be obtained by contacting C.H. Liu, University of Hong Kong, Dept. of Microbiol, State Key Lab Emerging Infect Dis, Hong Kong, Hong Kong, People’s Republic of China. (2012 Dec 18)

**Indian Institute of Science, Bangalore: Mycobacterium leprae RecA is structurally analogous but functionally distinct from Mycobacterium tuberculosis RecA protein**

By a News Reporter-Staff News Editor at Health & Medicine Week – A new study on Mycobacterium Infections is now available. According to news reporting originating from Bangalore, India, by NewsRx correspondents, research stated, “Mycobacterium leprae is closely related to Mycobacterium tuberculosis, yet causes a very different illness. Detailed genomic comparison between these two species of mycobacteria reveals that the decaying *M. leprae* genome contains less than half of the *M. tuberculosis* functional genes.”

Our news editors obtained a quote from the research from the Indian Institute of Science, “The reduction of genome size and accumulation of pseudogenes in the *M. leprae* genome is thought to result from multiple recombination events between related repetitive sequences, which provided the impetus to investigate the recombination-like activities of RecA protein. In this study, we have cloned, over-expressed and purified *M. leprae* RecA and compared its activities with that of *M. tuberculosis* RecA. Both proteins, despite being 91% identical at the amino acid level, exhibit strikingly different binding profiles for single-stranded DNA with varying GC contents, in the ability to catalyze the formation of D-loops and to promote DNA strand exchange. The kinetics and the extent of single-stranded DNA-dependent ATPase and coprotease activities were nearly equivalent between these two recombinases. However, the degree of inhibition exerted by a range of ATP:ADP ratios was greater on strand exchange promoted by *M. leprae* RecA compared to
its *M. tuberculosis* counterpart. Taken together, our results provide insights into the mechanistic aspects of homologous recombination and coprotease activity promoted by *M. lepare* RecA, and further suggests that it differs from the *M. tuberculosis* counterpart.”

According to the news editors, the research concluded: “These results are consistent with an emerging concept of DNA-sequence influenced structural differences in RecA nucleoprotein filaments and how these differences reflect on the multiple activities associated with RecA protein.”

For more information on this research see: Mycobacterium leprae RecA is structurally analogous but functionally distinct from *Mycobacterium tuberculosis* RecA protein. *Biochimica Et Biophysica Acta*, 2011;1814(12):1802-11.

The news editors report that additional information may be obtained by contacting K.N. Patil, Dept. of Biochemistry, Indian Institute of Science, Bangalore, India. (2012 Dec 14)

**Department of Biological Research, Norwich: Structure of Streptomyces maltosyltransferase GlgE, a homologue of a genetically validated anti-tuberculosis target**

By a News Reporter-Staff News Editor at Tuberculosis Week – New research on Biological Chemistry is the subject of a report. According to news reporting originating from Norwich, United Kingdom, by NewsRx correspondents, research stated, “GlgE is a recently identified (1?4)-a-d-glucan:phosphate a-d-maltosyltransferase involved in a-glucan biosynthesis in bacteria and is a genetically validated anti-tuberculosis drug target. It is a member of the GH13.3 CAZy subfamily for which no structures were previously known.”

Our news editors obtained a quote from the research from the Department of Biological Research, “We have solved the structure of GlgE isoform I from Streptomyces coelicolor and shown that this enzyme has the same catalytic and very similar kinetic properties to GlgE from *Mycobacterium tuberculosis*. The S. coelicolor enzyme forms a homodimer with each subunit comprising five domains, including a core catalytic a-amylase-type domain A with a (ß/a)(8) fold. This domain is elaborated with domain B and two inserts that are specifically configured to define a well conserved donor pocket capable of binding maltose. Domain A, together with domain N from the neighboring subunit, forms a hydrophobic patch that is close to the maltose-binding site and capable of binding cyclodextrins. Cyclodextrins competitively inhibit the binding of maltooligosaccharides to the S. coelicolor enzyme, showing that the hydrophobic patch overlaps with the acceptor binding site. This patch is incompletely conserved in the *M. tuberculosis* enzyme such that
cyclodextrins do not inhibit this enzyme, despite acceptor length specificity being conserved. The crystal structure reveals two further domains, C and S, the latter being a helix bundle not previously reported in GH13 members.”

According to the news editors, the research concluded: “The structure provides a framework for understanding how GlgE functions and will help guide the development of inhibitors with therapeutic potential.”


The news editors report that additional information may be obtained by contacting K. Syson, Dept. of Biological, John Innes Centre, Norwich Research Park, Norwich, Norfolk NR4 7UH, UK. (2012 Dec 03)

University of British Columbia, Vancouver: WhiB7, a transcriptional activator that coordinates physiology with intrinsic drug resistance in Mycobacterium tuberculosis

By a News Reporter-Staff News Editor at Health & Medicine Week – Research findings on Mycobacterium Infections are discussed in a new report. According to news reporting out of Vancouver, Canada, by NewsRx editors, research stated, “Current tuberculosis treatment regimens are notoriously limited, lengthy and becoming increasingly ineffective due to the emergence of drug-resistant mutant strains of Mycobacterium tuberculosis. The intrinsic resistance of M. tuberculosis to the majority of available drugs relies both on the impermeability of its cell envelope, and its ability to activate specific genes and physiological states.”

Our news journalists obtained a quote from the research from the University of British Columbia, “WhiB7 is a transcriptional regulatory protein underlying this adaptive process. Transcription of the whiB7 gene is upregulated in response to a variety of antibiotics having different structures and targets, as well as in response to metabolic signals. The whiB7 regulon activates various systems of intrinsic drug resistance involving antibiotic export, antibiotic inactivation (by chemical modifications of the drug or its target) and significant changes to thiol redox balance.”

According to the news editors, the research concluded: “Drugs have been identified that inactivate resistance determinants in the whiB7 regulon, thereby potentiating the activities of diverse antibiotics against M.”
For more information on this research see: WhiB7, a transcriptional activator that coordinates physiology with intrinsic drug resistance in Mycobacterium tuberculosis. *Expert Review of Anti-infective Therapy*, 2012;10(9):1037-47.

Our news journalists report that additional information may be obtained by contacting J. Burian, Dept. of Microbiology and Immunology, University of British Columbia, Vancouver, BC V6T 1Z3, Canada. (2012 Nov 30)

**University of Toronto: Targeting the global regulator Lsr2 as a novel approach for anti-tuberculosis drug development**

By a News Reporter-Staff News Editor at Tuberculosis Week – Current study results on Antiinfectives have been published. According to news reporting originating in Toronto, Canada, by NewsRx journalists, research stated, “Leprosy serum reactive clone 2 (Lsr2; Rv3597c) is a recently identified nucleoid-associated protein that acts as a global transcriptional regulator of *Mycobacterium tuberculosis*. Strikingly, Lsr2 appears to play a critical role in controlling the expression of virulence-associated genes.”

The news reporters obtained a quote from the research from the University of Toronto, “Here the authors outline the current knowledge concerning this novel global regulator and its potential as a target for chemotherapeutic intervention. Compounds that induce high level expression of lsr2 may lead to abolishment of virulence traits and render the bacterium incapable of causing infection and/or disease.”

According to the news reporters, the research concluded: “Alternatively, compounds that either silence lsr2 expression or block the protein’s function could be lethal since it has been postulated that lsr2 is essential in M.”


Our news correspondents report that additional information may be obtained by contacting J. Liu, Dept. of Molecular Genetics, University of Toronto, 1 King’s College Circle, Toronto, ON M5S 1A8, Canada. (2012 Nov 26)
San Raffaele Scientific Institute, Milano: GenoType MTBDRsl performance on clinical samples with diverse genetic background

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – Current study results on Respiratory Medicine have been published. According to news originating from Milano, Italy, by NewsRx correspondents, research stated, “We evaluate the performance of the GenoType® MTBDRsl (Hain Lifescience Nehren, Germany) for the detection of second-line resistant tuberculosis and we correlate the frequency of mutations to different Mycobacterium tuberculosis genotypes. We tested 175 strains and 59 clinical specimens interpreting the results according to the Standards for Reporting of Diagnostic Accuracy recommendations.”

Our news journalists obtained a quote from the research from San Raffaele Scientific Institute, “All the strains were also investigated by spoligotyping and Mycobacterial Interspersed Repetitive Units-Variable Number of Tandem Repeats typing. The performances of the MTBDRsl in detecting resistance to fluoroquinolones (FQ), second-line injectable drugs (SLID), and ethambutol (EMB) on clinical isolates were similar (specificity ~ 99%, sensitivity ~ 70%, and positive predictive value (PPV) ~ 99%). Of the 59 respiratory specimens, three samples were classified as ‘indeterminate’. The specificity in detecting resistances was similar for FQs and EMB 100% (95% CI 92.7-100%) and 100% (95% CI 83.9-100%), respectively with a PPV of 100% (95% CI 64.6-100%) and 100% (95% CI 87.9-100%), respectively. Detection of SLID showed a specificity of 89.1% (95% CI 77.0-95.3%) and a PPV of 58.3% (95% CI 32.0-80.7%). Sensitivity for FQ-resistance detection was 100% (95% CI 64.6-100%), whereas for SLID and EMB it was 89.1% (95% CI 77.0-95.3%) and 86.1% (95% CI 71.3-93.9%), respectively. We detected a significant association between mutations in the rrs gene and Beijing lineage. The MTBDRsl can be used to ‘rule in’ extensively drug-resistant strains of tuberculosis in a high risk group; the low sensitivity and negative predicted value (NPV) make confirmation by conventional drug susceptibility testing mandatory when mutations are not identified.”

According to the news editors, the research concluded: “NPV for SLID is higher in Beijing strains, showing that the predictive values of the molecular tests are related to the genetic background.”

For more information on this research see: GenoType MTBDRsl performance on clinical samples with diverse genetic background. European Respiratory Review, 2012;40(3):690-8.

The news correspondents report that additional information may be obtained from P. Miotto, Emerging Bacterial Pathogens Unit, Division of Immunology, Transplantation and Infectious Diseases, San Raffaele
University of Cape Town, Western Cape: A new crystal form of MshB from Mycobacterium tuberculosis with glycerol and acetate in the active site suggests the catalytic mechanism

By a News Reporter-Staff News Editor at Health & Medicine Week – A new study on Biological Crystallography is now available. According to news reporting out of Western Cape, South Africa, by NewsRx editors, research stated, “MshB, a zinc-based deacetylase, catalyses a step in the mycothiol biosynthetic pathway that involves the deacetylation of 1-O-(2-acetamido-2-deoxy-α-D-glucopyranosyl)-D-myo-inositol (GlcNAc-Ins), via cleavage of an amide bond, to 1-O-(2-amino-2-deoxy-α-D-glucopyranosyl)-D-myo-inositol (GlcN-Ins) and acetate. In this study, MshB was expressed, purified and crystallized.”

Our news journalists obtained a quote from the research from the University of Cape Town, “A new crystal form was encountered in 0.1 M sodium acetate, 0.2 M ammonium sulfate, 25% PEG 4000 pH 4.6. The crystals diffracted to 1.95 Å resolution and the resulting electron-density map revealed glycerol and the reaction product, acetate, in the active site. These ligands enabled the natural substrate GlcNAc-Ins to be modelled in the active site with some certainty. One acetate O atom is hydrogen bonded to Tyr142 and is located 2.5 Å from the catalytic zinc. The other acetate O atom is located 2.7 Å from a carboxylate O atom of Asp15. This configuration strongly suggests that Asp15 acts both as a general base catalyst in the nucleophilic attack of water on the amide carbonyl C atom and in its protonated form acts as a general acid to protonate the amide N atom.”

According to the news editors, the research concluded: “The configuration of Tyr142 differs from that observed previously in crystal structures of MshB (PDB entries 1q74 and 1q7t) and its location provides direct structural support for recently published biochemical and mutational studies suggesting that this residue is involved in a conformational change on substrate binding and contributes to the oxyanion hole that stabilizes the tetrahedral intermediate.”

For more information on this research see: A new crystal form of MshB from Mycobacterium tuberculosis with glycerol and acetate in the active site suggests the catalytic mechanism. *Acta Crystallographica Section D, Biological Crystallography*, 2012;68(Pt 11):1450-9.

Our news journalists report that additional information may be obtained by contacting S.G. Broadley, Dept. of Molecular and Cell Biology, University of Cape Town, University Avenue, Rondebosch, Western Cape 7700, South Africa. (2012 Nov 16)
Institute for Cancer Research and Treatment (IRCCS), Tradate: GenoType MTBDRs/ performance on clinical samples with diverse genetic background

By a News Reporter-Staff News Editor at Tuberculosis Week – Investigators discuss new findings in Respiratory Research. According to news reporting out of Tradate, Italy, by NewsRx editors, research stated, “We evaluate the performance of the GenoType ® MTBDRs/ (Hain Lifescience Nehren, Germany) for the detection of second-line resistant tuberculosis and we correlate the frequency of mutations to different Mycobacterium tuberculosis genotypes. We tested 175 strains and 59 clinical specimens interpreting the results according to the Standards for Reporting of Diagnostic Accuracy recommendations.”

Our news journalists obtained a quote from the research from Institute for Cancer Research and Treatment (IRCCS), “All the strains were also investigated by spoligotyping and Mycobacterial Interspersed Repetitive Units-Variable Number of Tandem Repeats typing. The performances of the MTBDRs/ in detecting resistance to fluoroquinolones (FQ), second-line injectable drugs (SLID), and ethambutol (EMB) on clinical isolates were similar (specificity similar to 99%, sensitivity similar to 70%, and positive predictive value (PPV) similar to 99%). Of the 59 respiratory specimens, three samples were classified as ‘indeterminate’. The specificity in detecting resistances was similar for FQs and EMB 100% (95% CI 92.7-100%) and 100% (95% CI 83.9-100%), respectively with a PPV of 100% (95% CI 64.6-100%) and 100% (95% CI 87.9-100%), respectively. Detection of SLID showed a specificity of 89.1% (95% CI 77.0-95.3%) and a PPV of 58.3% (95% CI 32.0-80.7%). Sensitivity for FQ-resistance detection was 100% (95% CI 64.6-100%), whereas for SLID and EMB it was 89.1% (95% CI 77.0-95.3%) and 86.1% (95% CI 71.3-93.9%), respectively. We detected a significant association between mutations in the rrs gene and Beijing lineage. The MTBDRs/ can be used to ‘rule in’ extensively drug-resistant strains of tuberculosis in a high risk group; the low sensitivity and negative predicted value (NPV) make confirmation by conventional drug susceptibility testing mandatory when mutations are not identified.”

According to the news editors, the research concluded: “NPV for SLID is higher in Beijing strains, showing that the predictive values of the molecular tests are related to the genetic background.”

Capital Medical University, Beijing: Functional polymorphisms in CYP2C19 & CYP3A5 genes associated with decreased susceptibility for paediatric tuberculosis

By a News Reporter-Staff News Editor at Pediatrics Week – Investigators publish new report on Mycobacterium Infections. According to news reporting originating from Beijing, People's Republic of China, by VerticalNews correspondents, research stated, “Tuberculosis (TB) bacilli ingested by macrophages evade host immune responses by multiple mechanisms including the inhibition of apoptosis. As the cytochrome-P-450 system (CYP) contributes to apoptosis it has been suggested that genetic variation in CYP may be associated with susceptibility to TB infection.”

Our news editors obtained a quote from the research from Capital Medical University, “This study was carried out to evaluate cytochrome P-450 polymorphisms in Chinese Han children and to investigate the effect of these polymorphisms in paediatric TB. Frequencies for the CYP2C19, CYP3A4, CYP3A5 and CYP2E1 mutated alleles and genotypes were compared between 142 Chinese paediatric TB patients and 150 non-infected controls by real time PCR genotyping on peripheral leukocyte DNA. CYP2C19 (636 G>A, rs4986893) A allele and AG genotype were associated with decreased susceptibility to TB (P = 0.006, OR= 0.33, 95% CI: 0.15-0.76; and P = 0.005, OR =0.31, 95% CI: 0.14-0.72 respectively), as were the CYP3A5 (6986A>G, rs776746) G allele and particularly homozygous GC (recessive mode) genotype (P = 0.004, OR=0.61, 95% CI: 0.43-0.85; and P=0.002, OR=0.47, 95% CI: 0.29-0.76). The data suggested that CYP2C19 and CYP3A5 polymorphisms affect susceptibility to paediatric TB.”

According to the news editors, the research concluded: “Further studies are indicated to confirm and elucidate these observations.”

For more information on this research see: Functional polymorphisms in CYP2C19 & CYP3A5 genes associated with decreased susceptibility for paediatric tuberculosis. Indian Journal of Medical Research, 2012;135(5):642-649. Indian Journal of Medical Research can be contacted at: Indian Council Medical Res, PO Box 4911 Ansari Nagar, New Delhi 110029, India.

The news editors report that additional information may be obtained by contacting W.X. Feng, Capital Med Univ, Beijing Childrens Hosp,
CSIR, Delhi: Footprints of genetic susceptibility to pulmonary tuberculosis: Cytokine gene variants in north Indians

By a News Reporter-Staff News Editor at Health & Medicine Week – Current study results on Mycobacterium Infections have been published. According to news reporting originating in Delhi, India, by NewsRx journalists, research stated, “Tuberculosis is (TB) responsible for high morbidity and mortality worldwide. Cytokines play a major role in defense against Mycobacterium tuberculosis infection.”

The news reporters obtained a quote from the research from CSIR, “Polymorphisms in the genes encoding the various pro- and anti-inflammatory cytokines have been associated with tuberculosis susceptibility. In this study we examined association of 25 sequence polymorphisms in six candidate cytokine genes namely IFNG, TNFB, IL4, IL1RA, IL1B and IL12 and their related haplotypes with risk of developing pulmonary tuberculosis (PTB) among north Indians. Pulmonary TB (n=110) patients and 215 healthy controls (HC) from north India were genotyped. Purified multiplex PCR products were subjected to mass spectrometry using Sequenom MassARRAY platform to generate the genotypes in a population-based case-control study. Using multiple corrections, significant overall risk against PTB was observed at seven loci which included variants in IFNG at rs1861493 and rs1861494; IL1RA at rs4252019, 11.4 variant rs2070874, IL12 variants rs3212220, rs2853694 and TNFB variant rs1041981. Analysis of gene structure revealed two haplotype blocks formed by IFNG variants rs1861493 and rs1861494. The TA haplotype was significantly over-represented (P=0.011) in the cases showing a two-fold risk in the current population (Odds ratio=1.59 CI=1.101 to 2.297) and TNFB variants at rs2229094 and rs1041981 contributed to two haplotypes which were in strong linkage disequilibrium (LD) with AT haplotype showing a three-fold risk (P=0.0011, Odds ratio=3, CI=0.1939 to 0.7445) of developing PTB in north Indians. Our study showed six novel associations of cytokine gene variants with susceptibility to PTB in north Indians.”

According to the news reporters, the research concluded: “Variants of IFNG and TNFB emerged as factors imposing a significant risk of developing PTB in north Indians apart from risk indicated by IL1RA, IL4 and IL12.”

For more information on this research see: Footprints of genetic susceptibility to pulmonary tuberculosis: Cytokine gene variants in north
Ohio State University, Columbus: Innate Immune Gene Polymorphisms in Tuberculosis

By a News Reporter-Staff News Editor at Health & Medicine Week – Investigators publish new report on Immunology. According to news reporting originating in Columbus, Ohio, by NewsRx journalists, research stated, “Tuberculosis (TB) is a leading cause worldwide of human mortality attributable to a single infectious agent. Recent studies targeting candidate genes and control’ association have revealed numerous polymorphisms implicated in host susceptibility to TB.”

The news reporters obtained a quote from the research from Ohio State University, “Here, we review current progress in the understanding of causative polymorphisms in host innate immune genes associated with TB pathogenesis. We discuss genes encoding several types of proteins: macrophage receptors, such as the mannose receptor (MR, CD206), dendritic cell-specific ICAM-3-grabbing nonintegrin (DC-SIGN, CD209), Dectin-1, Toll-like receptors (TLRs), complement receptor 3 (CR3, CD11b/CD18), nucleotide oligomerization domain 1 (NOD1) and NOD2, CD14, P2X7, and the vitamin D nuclear receptor (VDR); soluble C-type lectins, such as surfactant protein-A (SP-A), SP-D, and mannose-binding lectin (MBL); phagocyte cytokines, such as tumor necrosis factor (TNF), interleukin-1 beta (IL-1 beta), IL-6, IL-10, IL-12, and IL-18; chemokines, such as IL-8, monocyte chemoattractant protein 1 (MCP-1), RANTES, and CXCL10; and other important innate immune molecules, such as inducible nitric oxide synthase (iNOS) and solute carrier protein 11A1 (SLC11A1). Polymorphisms in these genes have been variably associated with susceptibility to TB among different populations. This apparent variability is probably accounted for by evolutionary selection pressure as a result of long-term host-pathogen interactions in certain regions or populations and, in part, by lack of proper study design and limited knowledge of molecular and functional effects of the implicated genetic variants.”

According to the news reporters, the research concluded: “Finally, we discuss genomic technologies that hold promise for resolving questions regarding the evolutionary paths of the human genome, functional effects of polymorphisms, and corollary impacts of adaptation on human health, ultimately leading to novel approaches to controlling TB.”
For more information on this research see: Innate Immune Gene Polymorphisms in Tuberculosis. *Infection and Immunity*, 2012;80(10):3343-3359. *Infection and Immunity* can be contacted at: Amer Soc Microbiology, 1752 N St NW, Washington, DC 20036-2904, USA. (American Society for Microbiology - www.asm.org; Infection and Immunity - iai.asm.org)

Our news correspondents report that additional information may be obtained by contacting A.K. Azad, Ohio State University, Dept. of Pharmacol, Program Pharmacogenom, Columbus, OH 43210, United States. (2012 Nov 09)

**University of Arkansas, Fayetteville: Capillary electrophoresis-single strand conformation polymorphism for the detection of multiple mutations leading to tuberculosis drug resistance**

By a News Reporter-Staff News Editor at Biotech Week – Researchers detail new data in Microbiology. According to news originating from Fayetteville, Arkansas, by NewsRx correspondents, research stated, “Drug resistant tuberculosis (TB) is a major health problem in both developed and developing countries. Mutations in the Mycobacterium (M.) tuberculosis bacterial genome, such as those to the rpoB gene and mabA-inhA promoter region, have been linked to TB drug resistance in against rifampicin and isoniazid, respectively.”

Our news journalists obtained a quote from the research from the University of Arkansas, “The rapid, accurate, and inexpensive identification of these and other mutations leading to TB drug resistance is an essential tool for improving human health. Capillary electrophoresis (CE) single strand conformation polymorphism (SSCP) can be a highly sensitive technique for the detection of genetic mutation that has not been previously explored for drug resistance mutations in *M. tuberculosis*. This work explores the potential of CE-SSCP through the optimization of variables such as polymer separation matrix concentration, capillary wall coating, electric field strength, and temperature on resolution of mutation detection. The successful detection of an rpoB gene mutation and two mabA-inhA promoter region mutations while simultaneously differentiating a TB-causing mycobacteria from a non-TB bacteria was accomplished using the optimum conditions of 4.5% (w/v) PDMA in a PDMA coated capillary at 278V/cm.”

According to the news editors, the research concluded: “This multiplexed analysis that can be completed in a few hours demonstrates the potential of CE-SSCP to be an inexpensive and rapid analysis method.”
Zhejiang University, Hangzhou: Association of CD14 G(-1145)A and C(-159)T polymorphisms with reduced risk for tuberculosis in a Chinese Han population

By a News Reporter-Staff News Editor at Life Science Weekly – Research findings on Genetic Research are discussed in a new report. According to news reporting originating from Hangzhou, People’s Republic of China, by NewsRx correspondents, research stated, “Although the role of CD14 in mediating signals from Toll-like receptors to recognize Mycobacterium tuberculosis is known, how polymorphisms in this gene affect the susceptibility to develop tuberculosis are still not clear. We examined whether single nucleotide polymorphisms at positions -1145 and -159 in the promoter region of the CD14 gene are associated with tuberculosis in a Chinese Han population in a case-control study of 432 Chinese patients with tuberculosis and 404 ethnically matched healthy controls.”

Our news editors obtained a quote from the research from Zhejiang University, “Genotyping was performed to identify polymorphisms of the CD14 gene by PCR-DNA sequencing. Both the frequency of allele T in the C(-159)T polymorphism (odds ratio (OR)=1.4; 95% confidence interval (95%CI)=1.148-1.708) and allele G in the G(-1145)A polymorphism (OR=1.512; 95%CI=1.236-1.849) were significantly more frequent in cases than in controls. The frequencies of genotypes CC and CT in the C(-159)T polymorphism, as well as the frequencies of genotypes AA and AG, were lower in cases than in controls.”

According to the news editors, the research concluded: “Based on our results, we conclude that G(-1145)A and C(-159)T polymorphisms of CD14 are associated with decreased risk for the development of tuberculosis in the Chinese Han population.”

The news editors report that additional information may be obtained by contacting M.Y. Zhao, Institute of Cell Biology, Zhejiang University, Hangzhou, People’s Taiwan. *(2012 Nov 06)*

**Institute of Microbial Technology, Chandigarh: The mechanism of redox sensing in Mycobacterium tuberculosis**

By a News Reporter-Staff News Editor at Health & Medicine Week – Researchers detail new data in Free Radical Research. According to news reporting originating in Chandigarh, India, by NewsRx journalists, research stated, “Tuberculosis epidemics have defied constraint despite the availability of effective treatment for the past half-century. *Mycobacterium tuberculosis*, the causative agent of TB, is continually exposed to a number of redox stressors during its pathogenic cycle. The mechanisms used by Mtb to sense redox stress and to maintain redox homeostasis are central to the success of Mtb as a pathogen.”

The news reporters obtained a quote from the research from the Institute of Microbial Technology, “Careful analysis of the Mtb genome has revealed that Mtb lacks classical redox sensors such as FNR, FixL, and OxyR. Recent studies, however, have established that Mtb is equipped with various sophisticated redox sensors that can detect diverse types of redox stress, including hypoxia, nitric oxide, carbon monoxide, and the intracellular redox environment. Some of these sensors, such as heme-based DosS and DosT, are unique to mycobacteria, whereas others, such as the WhiB proteins and anti-s factor RsrA, are unique to actinobacteria.”

According to the news reporters, the research concluded: “This article provides a comprehensive review of the literature on these redox-sensory modules in the context of TB pathogenesis.”


Our news correspondents report that additional information may be obtained by contacting S.A. Bhat, Council of Scientific and Industrial Research, Institute of Microbial Technology, Chandigarh 160036, India. *(2012 Nov 02)*
National Institute for Medical Research, London: Whole-genome sequencing of rifampicin-resistant Mycobacterium tuberculosis strains identifies compensatory mutations in RNA polymerase genes

By a News Reporter-Staff News Editor at Health & Medicine Week – Fresh data on Mycobacterium Infections are presented in a new report. According to news originating from London, United Kingdom, by NewsRx correspondents, research stated, “Epidemics of drug-resistant bacteria emerge worldwide, even as resistant strains frequently have reduced fitness compared to their drug-susceptible counterparts. Data from model systems suggest that the fitness cost of antimicrobial resistance can be reduced by compensatory mutations; however, there is limited evidence that compensatory evolution has any significant role in the success of drug-resistant bacteria in human populations.”

Our news journalists obtained a quote from the research from National Institute for Medical Research, “Here we describe a set of compensatory mutations in the RNA polymerase genes of rifampicin-resistant \textit{M. tuberculosis}, the etiologic agent of human tuberculosis (TB). \textit{M. tuberculosis} strains harboring these compensatory mutations showed a high competitive fitness in vitro. Moreover, these mutations were associated with high fitness in vivo, as determined by examining their relative clinical frequency across patient populations. Of note, in countries with the world’s highest incidence of multidrug-resistant (MDR) TB, more than 30% of MDR clinical isolates had this form of mutation.”

According to the news editors, the research concluded: “Our findings support a role for compensatory evolution in the global epidemics of MDR TB.”


The news correspondents report that additional information may be obtained from I. Comas, Division of Mycobacterial Research, Medical Research Council, National Institute for Medical Research, London, UK. (2012 Nov 02)
University of Texas Health Science Center, Tyler:
Replacement of Mycobacterium smegmatis dnaA gene by Mycobacterium tuberculosis homolog results in temperature sensitivity

By a News Reporter-Staff News Editor at Health & Medicine Week – Research findings on Tuberculosis are discussed in a new report. According to news reporting originating in Tyler, Texas, by NewsRx journalists, research stated, “The genetic aspects of DnaA mediated initiation of oriC replication in mycobacteria are largely unknown. To get insights into the replication initiation process in mycobacteria, we characterized Mycobacterium tuberculosis DnaA and its interactions with oriC.”

The news reporters obtained a quote from the research from the University of Texas Health Science Center, “We show that the replacement of Mycobacterium smegmatis dnaA with the M. tuberculosis counterpart expressed from its native promoter resulted in temperature-sensitive (TS) phenotype. However, the TS phenotype was abolished when the M. tuberculosis dnaA was expressed from the inducible amidae promoter, which produces elevated levels of DnaA. We provide evidence that M. tuberculosis dnaA promoter activity was unaffected at non-permissive temperature, but the DnaA protein was found to be unstable indicating that protein factors stabilizing M. tuberculosis DnaA are absent in M. smegmatis. Finally, we show by surface plasmon resonance that the M. tuberculosis DnaA interacts with M. smegmatis oriC, similar to its cognate oriC indicating that the binding interactions between in vitro folded DnaA and oriC are unaffected.”

According to the news reporters, the research concluded: “Our results suggest that Mtb DnaA functions as a partially active protein in M. smegmatis, hence is not as proficient as M. smegmatis counterpart in optimally driving the M. smegmatis oriC replication machinery.”


Our news correspondents report that additional information may be obtained by contacting M. Madiraju, The University of Texas Health Science Center, 11937 US HwY @ 271, Tyler, TX 75703, United States. (2012 Nov 02)
Leiden University Medical Center: Genome-wide expression profiling identifies type 1 interferon response pathways in active tuberculosis

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators discuss new findings in Life Science Research. According to news reporting out of Leiden, Netherlands, by NewsRx editors, research stated, “Tuberculosis (TB), caused by Mycobacterium tuberculosis (M.tb), remains the leading cause of mortality from a single infectious agent. Each year around 9 million individuals newly develop active TB disease, and over 2 billion individuals are latently infected with M.tb worldwide, thus being at risk of developing TB reactivation disease later in life.”

Our news journalists obtained a quote from the research from Leiden University Medical Center, “The underlying mechanisms and pathways of protection against TB in humans, as well as the dynamics of the host response to M.tb infection, are incompletely understood. We carried out whole-genome expression profiling on a cohort of TB patients longitudinally sampled along 3 time-points: during active infection, during treatment, and after completion of curative treatment. We identified molecular signatures involving the upregulation of type-1 interferon (α/β) mediated signaling and chronic inflammation during active TB disease in an Indonesian population, in line with results from two recent studies in ethnically and epidemiologically different populations in Europe and South Africa. Expression profiles were captured in neutrophil-depleted blood samples, indicating a major contribution of lymphocytes and myeloid cells. Expression of type-1 interferon (α/β) genes mediated was also upregulated in the lungs of M.tb infected mice and in infected human macrophages. In patients, the regulated gene expression-signature normalized during treatment, including the type-1 interferon mediated signaling and a concurrent opposite regulation of interferon-gamma. Further analysis revealed IL15RA, UBE2L6 and GBP4 as molecules involved in the type-I interferon response in all three experimental models.”

According to the news editors, the research concluded: “Our data is highly suggestive that the innate immune type-I interferon signaling cascade could be used as a quantitative tool for monitoring active TB disease, and provide evidence that components of the patient’s blood gene expression signature bear similarities to the pulmonary and macrophage response to mycobacterial infection.”

For more information on this research see: Genome-wide expression profiling identifies type 1 interferon response pathways in active tuberculosis. Plos One, 2012;7(9):e45839. (Public Library of Science - www.plos.org; Plos One - www.plosone.org)
Our news journalists report that additional information may be obtained by contacting T.H. Ottenhoff, Dept. of Infectious Diseases, Leiden University Medical Center, Leiden, Netherlands. (2012 Oct 23)

Washington University School of Medicine, St. Louis: Interaction of CarD with RNA Polymerase Mediates Mycobacterium tuberculosis Viability, Rifampin Resistance, and Pathogenesis

By a News Reporter-Staff News Editor at Health & Medicine Week – Data detailed on Mycobacterium Infections have been presented. According to news reporting from St. Louis, Missouri, by NewsRx journalists, research stated, “Mycobacterium tuberculosis infection continues to cause substantial human suffering. New chemotherapeutic strategies, which require insight into the pathways essential for \textit{M. tuberculosis} pathogenesis, are imperative.”

The news correspondents obtained a quote from the research from the Washington University School of Medicine, “We previously reported that depletion of the CarD protein in mycobacteria compromises viability, resistance to oxidative stress and fluoroquinolones, and pathogenesis. CarD associates with the RNA polymerase (RNAP), but it has been unknown which of the diverse functions of CarD are mediated through the RNAP; this question must be answered to understand the CarD mechanism of action. Herein, we describe the interaction between the \textit{M. tuberculosis} CarD and the RNAP \&#223; subunit and identify point mutations that weaken this interaction. The characterization of mycobacterial strains with attenuated CarD/RNAP \&#223; interactions demonstrates that the CarD/RNAP \&#223; association is required for viability and resistance to oxidative stress but not for fluoroquinolone resistance. Weakening the CarD/RNAP \&#223; interaction also increases the sensitivity of mycobacteria to rifampin and streptomycin. Surprisingly, depletion of the CarD protein did not affect sensitivity to rifampin. These findings define the CarD/RNAP interaction as a new target for chemotherapeutic intervention that could also improve the efficacy of rifampin treatment of tuberculosis.”

According to the news reporters, the researchers concluded: “In addition, our data demonstrate that weakening the CarD/RNAP \&#223; interaction does not completely phenocopy the depletion of CarD and support the existence of functions for CarD independent of direct RNAP binding.”

Our news journalists report that additional information may be obtained by contacting L.A. Weiss, Dept. of Molecular Microbiology, Washington University School of Medicine, St Louis, Missouri, United States. (2012 Oct 19)

Medical College of Wisconsin, Milwaukee: MprA and DosR Coregulate a Mycobacterium tuberculosis Virulence Operon Encoding Rv1813c and Rv1812c

By a News Reporter-Staff News Editor at Health & Medicine Week – Current study results on Immunology have been published. According to news reporting originating from Milwaukee, Wisconsin, by NewsRx correspondents, research stated, “Mycobacterium tuberculosis remains a significant global pathogen, causing extensive morbidity and mortality worldwide. This bacterium persists within granulomatous lesions in a poorly characterized, nonreplicating state.”

Our news editors obtained a quote from the research from the Medical College of Wisconsin, “The two-component signal transduction systems MprAB and DosRS-DosT (DevRS-Rv2027c) are responsive to conditions likely to be present within granulomatous lesions and mediate aspects of M. tuberculosis persistence in vitro and in vivo. Here, we describe a previously uncharacterized locus, Rv1813c-Rv1812c, that is coregulated by both MprA and DosR. We demonstrate that MprA and DosR bind to adjacent and overlapping sequences within the promoter region of Rv1813c and direct transcription from an initiation site located several hundred base pairs upstream of the Rv1813 translation start site. We further show that Rv1813c and Rv1812c are cotranscribed, and that the genomic organization of this operon is specific to M. tuberculosis and Mycobacterium bovis. Although Rv1813c is not required for survival of M. tuberculosis in vitro, including under conditions in which MprAB and DosRST signaling are activated, an M. tuberculosis Delta Rv1813c mutant is attenuated in the low-dose aerosol model of murine tuberculosis, where it exhibits a lower bacterial burden, delayed time to death, and decreased ability to stimulate proinflammatory cytokines interleukin-1 beta (IL-1 beta) and IL-12. Interestingly, overcomplementation of these phenotypes is observed in the M. tuberculosis Delta Rv1813c mutant expressing both Rv1813c and Rv1812c, but not Rv1813c alone, in trans.”

According to the news editors, the researchers concluded: “Therefore, Rv1813c and Rv1812c may represent general stress-responsive elements that are necessary for aspects of M. tuberculosis virulence and the host immune response to infection.”

For more information on this research see: MprA and DosR Coregulate a Mycobacterium tuberculosis Virulence Operon Encoding Rv1813c and Rv1812c. Infection and Immunity, 2012;80(9):3018-3033. Infection
Indian Institute of Science, Bangalore: Distinct and Contrasting Transcription Initiation Patterns at Mycobacterium tuberculosis Promoters

By a News Reporter-Staff News Editor at Health & Medicine Week – A new study on Life Science Research is now available. According to news originating from Bangalore, India, by NewsRx correspondents, research stated, “Although sequencing of Mycobacterium tuberculosis genome lead to better understanding of transcription units and gene functions, interactions occurring during transcription initiation between RNA polymerase and promoters is yet to be elucidated. Different stages of transcription initiation include promoter specific binding of RNAP, isomerization, abortive initiation and promoter clearance.”

Our news journalists obtained a quote from the research from the Indian Institute of Science, “We have now analyzed these events with four promoters of M. tuberculosis viz. P(gyrB1), P(gyrR), P(rrnPCL1) and P(metU). The promoters differed from each other in their rates of open complex formation, decay, promoter clearance and abortive transcription. The equilibrium binding and kinetic studies of various steps revealed distinct rate limiting events for each of the promoter, which also differed markedly in their characteristics from the respective promoters of Mycobacterium smegmatis. Surprisingly, the transcription at gyr promoter was enhanced in the presence of initiating nucleotides and decreased in the presence of alarmone, pppGpp, a pattern typically seen with rRNA promoters studied so far. The gyr promoter of M. smegmatis, on the other hand, was not subjected to pppGpp mediated regulation. The marked differences in the transcription initiation pathway seen with rrn and gyr promoters of M. smegmatis and M. tuberculosis suggest that such species specific differences in the regulation of expression of the crucial housekeeping genes could be one of the key determinants contributing to the differences in growth rate and lifestyle of the two organisms.”

According to the news editors, the researchers concluded: “Moreover, the distinct rate limiting steps during transcription initiation of each one of the promoters studied point at variations in their intracellular regulation.”

For more information on this research see: Distinct and Contrasting Transcription Initiation Patterns at Mycobacterium tuberculosis

The news correspondents report that additional information may be obtained from P. Tare, Dept. of Microbiology and Cell Biology, Indian Institute of Science, Bangalore, India. *2012 Oct 05*

**Scientific Institute of Public Health, Brussels: Systematic Analysis of Pyrazinamide-Resistant Spontaneous Mutants and Clinical Isolates of Mycobacterium tuberculosis**

By a News Reporter-Staff News Editor at Health & Medicine Week – Investigators publish new report on Antimicrobial Agents and Chemotherapy. According to news reporting originating in Brussels, Belgium, by NewsRx journalists, research stated, “Pyrazinamide (PZA) is a first-line antitubercular drug known for its activity against persistent *Mycobacterium tuberculosis* bacilli. We set out to systematically determine the PZA susceptibility profiles and mutations in the pyrazinamidase (*pncA*) gene of a collection of multidrug-resistant tuberculosis (MDR-TB) clinical isolates and PZA-resistant (PZA(r)) spontaneous mutants.”

The news reporters obtained a quote from the research from the Scientific Institute of Public Health, “The frequency of acquired resistance to PZA was determined to be 10(-5) bacilli in vitro. Selection at a lower concentration of PZA yielded a significantly larger number of spontaneous mutants. The methodical approach employed allowed for determination of the frequency of the PZA(r) phenotype correlated with mutations in the *pncA* gene, which was 87.5% for the laboratory-selected spontaneous mutants examined in this study. As elucidated by structural analysis, most of the identified mutations were foreseen to affect protein activity through either alteration of an active site residue or destabilization of protein structure, indicating some preferential mutation site rather than random scattering.”

According to the news reporters, the researchers concluded: “Twelve percent of the PZA(r) mutants did not have a *pncA* mutation, strongly indicating the presence of at least one other mechanism(s) of PZA(r).”


Our news correspondents report that additional information may be obtained by contacting K. Stoffels, Tuberculosis and Mycobacteria, Communicable & Infectious Diseases, Scientific Institute of Public Health, Brussels, Belgium. *2012 Oct 05*
University of Paris: “Spoligoriftpying,” a dual-priming-oligonucleotide-based direct-hybridization assay for tuberculosis control with a multianalyte microbead-based hybridization system

By a News Reporter-Staff News Editor at Life Science Weekly – Research findings on Clinical Microbiology are discussed in a new report. According to news originating from Paris, France, by NewsRx correspondents, research stated, “We developed ‘spoligoriftpying,’ a 53-plex assay based on two preexisting methods, the spoligotyping and ‘rifoligotyping’ assays, by combining them into a single assay. Spoligoriftpying allows simultaneous spoligotyping (i.e., clustered regularly interspaced short palindromic repeat [CRISPR]-based genotyping) and characterization of the main rifampin drug resistance mutations on the rpoB hot spot region in a few hours.”

Our news journalists obtained a quote from the research from the University of Paris, “This test partly uses the dual-priming-oligonucleotide (DPO) principle, which allows simultaneous efficient amplifications of rpoB and the CRISPR locus in the same sample. We tested this method on a set of 114 previously phenotypically and genotypically characterized multidrug-resistant (MDR) Mycobacterium tuberculosis or drug-susceptible M. tuberculosis DNA extracted from clinical isolates obtained from patients from Bulgaria, Nigeria, and Germany. We showed that our method is 100% concordant with rpoB sequencing results and 99.95% (3,911/3,913 spoligotype data points) correlated with classical spoligotyping results. The sensitivity and specificity of our assay were 99 and 100%, respectively, compared to those of phenotypic drug susceptibility testing.”

According to the news editors, the researchers concluded: “Such assays pave the way to the implementation of locally and specifically adapted methods of performing in a single tube both drug resistance mutation detection and genotyping in a few hours.”


The news correspondents report that additional information may be obtained from M.K. Gomgnimbou, Institut de Genetique et Microbiologie, UMR8621, CNRS-Universite Paris-Sud, IGEPE Team, Paris, France. (2012 Oct 02)
Huazhong Agricultural University, Wuhan: ClpR protein-like regulator specifically recognizes RecA protein-independent promoter motif and broadly regulates expression of DNA damage-inducible genes in mycobacteria

By a News Reporter-Staff News Editor at Tuberculosis Week – A new study on Biological Chemistry is now available. According to news reporting out of Wuhan, People’s Republic of China, by NewsRx editors, research stated, “The RecA-dependent DNA damage response pathway (SOS response) appears to be the major DNA repair mechanism in most bacteria, but it has been suggested that a RecA-independent mechanism is responsible for controlling expression of most damage-inducible DNA repair genes in Mycobacterium tuberculosis. The specific reparative responses and molecular mediators involved in the DNA repair mechanism remain largely unclear in this pathogen and its related species.”

Our news journalists obtained a quote from the research from Huazhong Agricultural University, “In this study, a mycobacterial ClpR-like regulator, corresponding to Rv2745c in M. tuberculosis and to Ms2694 in M. smegmatis mc(2)155, was found to interact with the promoter regions of multiple damage-inducible DNA repair genes. Specific binding of the ClpR-like factor to the conserved RecA-independent promoter RecA-NDp motif was then confirmed using in vitro electrophoretic mobility shift assays as well as in vivo chromatin immunoprecipitation experiments. The ClpR knock-out experiments, in combination with quantitative real time PCR assays, demonstrated that the expression of these RecA-independent genes were significantly down-regulated in the mutant strain of M. smegmatis in response to a DNA-damaging agent compared with the wild type strain. Furthermore, the ClpR-like factor was shown to contribute to mycobacterial genomic stability.”

According to the news editors, the researchers concluded: “These results enhance our understanding of the function of the ClpR regulator and the regulatory mechanism of RecA-independent DNA repair in mycobacteria.”


Our news journalists report that additional information may be obtained by contacting Y. Wang, National Key Laboratory of Agricultural
National University of Singapore: Interaction of Mycobacterium tuberculosis RshA and SigH Is Mediated by Salt Bridges

By a News Reporter-Staff News Editor at Health & Medicine Week – Current study results on Mycobacterium Infections have been published. According to news reporting from Singapore, Singapore, by NewsRx journalists, research stated, “The alternate sigma factor sigH of Mycobacterium tuberculosis is expressed under stress and acts as a major regulator of several genes, including some other sigma factors and redox systems. While it is auto-regulated by its own promoter at the transcriptional level, its regulation at the post-translational level is through its cognate protein, an anti-sigma factor, RshA.”

The news correspondents obtained a quote from the research from the National University of Singapore, “Hither before RshA was believed to be a zinc-associated anti-sigma factor (ZAS) and the binding of RshA to SigH is redox dependent. Here, we show that RshA coordinates a [2Fe-2S] cluster using cysteines as ligands and native RshA has more affinity to [2Fe-2S] cluster than to zinc. Furthermore, we used amide hydrogen deuterium exchange mass spectrometry (HDX-MS), followed by site-directed mutagenesis in SigH and RshA, to elucidate the interaction mechanism of RshA and SigH and the potential role of metal ion clustering in SigH regulation. Three regions in SigH, comprising of residues 1-25, 58-69, 90-111, 115-132 and 157-196 and residues 35-57 of RshA show decreased deuterium exchange and reflect decreased solvent accessibility upon complexation with SigH. Of the three RshA mutants, created based on the HDX results, the RshA E37A mutant shows stronger interaction with SigH, relative to WT RshA, while the H49A mutant abolishes interactions and the C(53)XXC(56)AXXA mutant has no effect on complexation with SigH. The D22A, D160A and E162 SigH mutants show significantly decreased binding to RshA and the E168A mutant completely abolished interactions with RshA, indicating that the SigH-RshA interaction is mediated by salt bridges. In addition, SigH-RshA interaction does not require clustering of metal ions.”

According to the news reporters, the researchers concluded: “Based on our results, we propose a molecular model of the SigH-RshA interaction.”

For more information on this research see: Interaction of Mycobacterium tuberculosis RshA and SigH Is Mediated by Salt Bridges. Plos
Our news journalists report that additional information may be obtained by contacting S. Kumar, Dept. of Biological Sciences, National University of Singapore, Singapore, Singapore. (2012 Sep 28)

**Peking University, Beijing: NAT2 genetic polymorphisms and anti-tuberculosis drug-induced hepatotoxicity in Chinese community population**

By a News Reporter-Staff News Editor at Gastroenterology Week – Investigators discuss new findings in Hepatology Research. According to news reporting out of Beijing, People’s Republic of China, by NewsRx editors, research stated, “Background. Anti-tuberculosis drug-induced hepatotoxicity (ATDH) is one of the most prevalent and serious adverse drug reactions in the course of anti-tuberculosis (TB) treatment.”

Our news journalists obtained a quote from the research from Peking University, “Some researchers suggested that determination of N-acetyltransferase 2 (NAT2) genotype may be clinically useful to identify patients at high risk of developing ATDH. To evaluate whether the NAT2 genotype could be as a predictor for ATDH in Chinese community TB population. A total of 4304 community-based TB patients were followed up six to nine months prospectively. A nested case-control study was designed. Each ATDH case was 1:4 matched with controls by age (within 5 years old), gender, treatment history, disease severity and drug dosage. The polymorphisms of NAT2 were determined using polymerase chain reaction with restriction fragment length polymorphism. Conditional Logistic regression model was used to calculate odds ratio (OR) and 95% confidence interval (CI), as well as corresponding P-values. A total of 89 ATDH cases and 356 controls were included in this study. Allele frequency of NAT2*5, NAT2*6 and NAT2*7 in cases and controls were 4.5 and 3.2%, 25.3 and 26.5%, and 13.5 and 13.5%, respectively. Frequencies of genotypes and alleles of NAT2*5, NAT2*6 and NAT2*7 did not differ significantly between cases and controls. The OR of intermediate acetylator and slow acetylator compared with rapid acetylator was 1.040 (95%CI 0.616-1.758) and 0.990 (95%CI 0.509-1.925), respectively. The NAT2 haplotype distribution in cases was similar to controls. we did not find significant association between NAT2 genotype and ATDH in community-based Chinese population.”

According to the news editors, the researchers concluded: “It may be deficient to take NAT2 genotype as a predictor for ATDH in Chinese community TB patients.”

Our news journalists report that additional information may be obtained by contacting X. Lv, Dept. of Epidemiology and Biostatistics, School of Public Health, Peking University Health Science Center, Beijing, People’s Taiwan. (2012 Sep 24)

Chongqing Medical University: SP110 gene polymorphisms and tuberculosis susceptibility: A systematic review and meta-analysis based on 10 624 subjects

By a News Reporter-Staff News Editor at Health & Medicine Week – Fresh data on Mycobacterium Infections are presented in a new report. According to news reporting originating in Chongqing, People’s Republic of China, by NewsRx journalists, research stated, “Tuberculosis (TB), caused by infection of Mycobacterium tuberculosis, is a major challenge to global public health. The SP110 (Speckled 110) gene, which is considered as a host genetic susceptibility to TB, has been widely studied in recent years, yet the results were somewhat contradictory and indeterminate.”

The news reporters obtained a quote from the research from Chongqing Medical University, “We systematically searched published literatures on SP110 polymorphisms and tuberculosis risk until January 2012 in relevant databases, selected studies by previously defined criteria, extracted key data and quantitatively summarized associations of the most extensively studied polymorphisms through meta-analysis. A total of 10 624 subjects from seven case-control studies were included in the present study. In overall meta-analysis, pooled odds ratio of polymorphisms rs1135791, rs9061, rs11556887, rs3948464, rs1346311 were 1.01 (95% CI: 0.71-1.44), 0.86 (95% CI: 0.70-1.04), 0.99 (95% CI: 0.67-1.47), 1.29 (CI: 0.89-1.89) and 0.95 (CI: 0.86-1.04) respectively; the summary odds ratio of sensitivity analysis specifically on pulmonary TB were 1.02 (95% CI: 0.65-1.54) for rs1135791, 0.84 (95% CI: 0.68-1.02) for rs9061, 0.88 (95% CI: 0.57-1.36) for rs11556887, 0.94 (95% CI: 0.85-1.04) for rs1346311; and in the ethnicity stratified analysis, the estimated odds ratio were 0.97 (95% CI: 0.54-1.73) for rs1135791 and 0.86 (95% CI: 0.70-1.04) for rs9061 among Asians. None of the target polymorphisms in SP110 gene observed in the present quantitative synthesis was detected to be significantly associated with TB susceptibility.”

According to the news reporters, the researchers concluded: “Given the moderate strength of the results, the complexities of pulmonary and extra-pulmonary host genetic polymorphisms, gene-gene and gene-environment interactions, and the cross-species difference between human and mice, it would not be robust to remark that SP110 has no role in TB progress.”

Our news correspondents report that additional information may be obtained by contacting X. Lei, School of Public Health and Health Management, Chongqing Medical University, Chongqing 400016, People’s Taiwan. (2012 Sep 21)

**University of Pisa: Large Sequence Polymorphisms of the Euro-American lineage of Mycobacterium tuberculosis: A phylogenetic reconstruction and evidence for convergent evolution in the DR locus**

By a News Reporter-Staff News Editor at Life Science Weekly – Researchers detail new data in Molecular Epidemiology and Evolutionary Genetics. According to news reporting from Pisa, Italy, by NewsRx journalists, research stated, “The Euro-American lineage of the *Mycobacterium tuberculosis* complex consists of 10 sublineages, each defined by a deletion of a large genomic region (RD, region of difference); by spoligotyping, that probes the polymorphism of the Direct Repeat (DR) locus, the Euro-American strains are classified into 5 lineages (T, Haarlem, LAM, S and X) and 34 sublineages, but the relationships between the RD-defined sublineages and the spoligotype groupings are largely unclear. By testing a global sample of 158 Euro-American strains, mutually exclusive deletions of RD115, RD122, RD174, RD182, RD183, RD193, RD219, RD726 or RD761 were found in 122 strains; deletion of RD724, typical of strains from Central Africa, was not found.”

The news correspondents obtained a quote from the research from the University of Pisa, “The RD-defined sublineages, tested for katG463/gyrA95 polymorphism, belonged to Principal Genotypic Group (PGG) 2, with the exception of RD219 sublineage belonging to PGG3; the 36 strains with no deletion were of either PGG2 or 3. Based on these polymorphisms, a phylogenetic reconstruction of the Euro-American lineage, that integrates the previously reported phylogeny, is proposed. Although certain deletions were found to be associated to certain spoligotype lineages (i.e., deletion RD115 to T and LAM, RD174 to LAM, RD182 to Haarlem, RD219 to T), our analysis indicates a general lack of concordance between RD-defined sublineages and spoligotype groupings. Moreover, of the 42 spoligotypes detected among the study strains, sixteen were shared by strains belonging to different RD sublineages. IS6110-RFLP analysis of strains sharing spoligotypes confirmed a poor
genetic relatedness between strains of different RD sublineages. These findings provide evidence for the occurrence of a high degree of homoplasy in the DR locus leading to convergent evolution to identical spoligotypes.”

According to the news reporters, the researchers concluded: “The incongruence between Large Sequence Polymorphism and spoligotype polymorphism argues against the use of spoligotyping for establishing phylogenetic relationships within the Euro-American lineage.”


Our news journalists report that additional information may be obtained by contacting L. Rindi, Dipartimento di Patologia Sperimentale, Biotecnologie Mediche, Infettivologia ed Epidemiologia, Universita di Pisa, I-56127 Pisa, Italy. (2012 Sep 18)

Broad Institute of MIT and Harvard, Cambridge: Identification of Novel Inhibitors of M. tuberculosis Growth Using Whole Cell Based High-Throughput Screening

By a News Reporter-Staff News Editor at Health & Medicine Week – Data detailed on Mycobacterium Infections have been presented. According to news originating from Cambridge, Massachusetts, by NewsRx correspondents, research stated, “Despite the urgent need for new antitubercular drugs, few are on the horizon. To combat the problem of emerging drug resistance, structurally unique chemical entities that inhibit new targets will be required.”

Our news journalists obtained a quote from the research from the Broad Institute of MIT and Harvard, “Here we describe our investigations using whole cell screening of a diverse collection of small molecules as a methodology for identifying novel inhibitors that target new pathways for Mycobacterium tuberculosis drug discovery. We find that conducting primary screens using model mycobacterial species may limit the potential for identifying new inhibitors with efficacy against M. tuberculosis. In addition, we confirm the importance of developing in vitro assay conditions that are reflective of in vivo biology for maximizing the proportion of hits from whole cell screening that are likely to have activity in vivo. Finally, we describe the identification and characterization of two novel inhibitors that target steps in M. tuberculosis cell wall biosynthesis. The first is a novel benzimidazole that targets mycobacterial membrane protein large 3 (MmpL3), a proposed transporter for cell wall mycolic acids. The second is a nitro-triazole that
inhibits decaprenylphosphoryl-\(\beta\)-d-ribose 2’-epimerase (DprE1),
an epimerase required for cell wall biosynthesis. These proteins are
both among the small number of new targets that have been identified
by forward chemical genetics using resistance generation coupled with
genome sequencing.”

According to the news editors, the researchers concluded: “This sug-
gests that methodologies currently employed for screening and target
identification may lead to a bias in target discovery and that alterna-
tive methods should be explored.”

For more information on this research see: Identification of Novel
Inhibitors of M. tuberculosis Growth Using Whole Cell Based High-
(American Chemical Society - www.acs.org; Acs Chemical Biology -
http://www.pubs.acs.org/journal/acbcct)

The news correspondents report that additional information may be
obtained from S.A. Stanley, The Broad Institute, 7 Cambridge Center,
Cambridge, Massachusetts 02142, United States. (2012 Sep 14)

Institute of Microbial Technology, Chandigarh: Equilibrium
binding and kinetic characterization of putative
tetracycline repressor family transcription regulator Fad35R
from Mycobacterium tuberculosis

By a News Reporter-Staff News Editor at Health & Medicine Week –
Investigators publish new report on Mycobacterium Infections. Accord-
ing to news originating from Chandigarh, India, by NewsRx correspon-
dents, research stated, “Fatty acids play critical role in the survival and
virulence of Mycobacterium tuberculosis (Mt b). Activation of fatty acids
by acyl-CoA synthetases (Fad) into fatty acyl-CoA is the first and one of
the crucial steps in fatty acid metabolism.”

Our news journalists obtained a quote from the research from the
Institute of Microbial Technology, “Mt b possesses 36 fatty acyl-CoA
synthetases, unlike Escherichia coli, which has single enzyme. However,
the mechanisms by which the expression of these multiple Fad
genes is regulated remain uncharacterized. We characterized the DNA-
and ligand-binding properties of a putative tetracycline repressor fam-
ily regulator, named Fad35R, located upstream of the Fad35 gene and
ScoA-citE operon. We identified a palindromic regulatory motif up-
stream of Fad35 and characterized the binding of Fad35R to this motif.
Equilibrium binding studies show that Fad35R binds to this motif with
high affinity (K(d) \~ 0.033 m) and the specificity of binding was con-
firmed by an electromobility gel shift assay. Kinetic studies indicate
that faster association (k(a,avg) \~ 5.4 x 10(4) m(-1) s(-1)) and slower
dissociation rates (k(d,avg) \~ 5.84 x 10(-4) s(-1)) confer higher affinity.
The affinity for the promoter is maximum at 300 mm NaCl but decreases rapidly beyond this range. Ligand-binding studies indicate that Fad35R binds specifically to tetracycline and also binds to fatty acid derivatives. The promoter-binding affinity is decreased significantly in the presence of palmitoyl-CoA, suggesting that Fad35R can sense the levels of activated fatty acids and alter its DNA-binding activity. Our results suggest that Fad35R may be the functional homologue of FadR and controls the expression of genes in a metabolite-dependent manner.

According to the news editors, the researchers concluded: “Structured digital abstract? Fad35R binds to palindromic sequence shown by surface plasmon resonance? Fad35R binds to tetracycline and activated fatty acids as shown by fluorescence spectroscopy.”


The news correspondents report that additional information may be obtained from S. Anand, Council of Scientific and Industrial Research, India, Institute of Microbial Technology, Chandigarh, India.

The publisher’s contact information for the *The Febs Journal* is: Blackwell Publishing Inc, 350 Main St, Malden, MA 02148, USA. (2012 Sep 14)

**Farhat Hached University Teaching Hospital, Sousse: IL23R(Arg381Gln) Functional Polymorphism Is Associated with Active Pulmonary Tuberculosis Severity**

By a News Reporter-Staff News Editor at Health & Medicine Week – Fresh data on Mycobacterium Infections are presented in a new report. According to news originating from Sousse, Tunisia, by NewsRx correspondents, research stated, “The purpose of our study was to investigate the association between a functional single nucleotide polymorphism (SNP) in the interleukin-23 receptor gene (IL23R; rs11209026, 1142 G(wild type) ? A(reduced function), Arg381Gln) and disease severity outcome in pulmonary tuberculosis (TB) in the Tunisian population. SNP was investigated in a population of 168 patients with active pulmonary TB (cases were stratified into patients with minimal/moderate lung involvement, i.e., patients with minimal/moderate disease [Pmd], and patients with extensive lung involvement, i.e., patients with active disease [Pad]) and 150 healthy subjects.”

Our news journalists obtained a quote from the research from Farhat Hached University Teaching Hospital, “Genotype analyses were carried out using the PCR-restriction fragment length polymorphism method.
We have found that the IL23R reduced-function allele 1142A and genotypes AA and AG were overrepresented, especially in the Pad subgroup compared with the control group (51% versus 18% \([p=10^{-8}]\), 33% versus 5% \([p=10^{-8}]\), and 36% versus 26% \([p=5 \times 10^{-3}]\), respectively). Additionally, comparison of the Pad and the Pmd groups showed that the A allele and AA genotype seemed to be associated with 2.79-fold \((p=4 \times 10^{-5})\) and 7.74-fold \((p=10^{-5})\) increased risks of TB with minimal/moderate lung involvement, respectively.

According to the news editors, the researchers concluded: “Our results demonstrate that the reduced-function polymorphism 1142G \(\rightarrow\) A encoded by IL23R influences the outcome of disease severity of active pulmonary TB in Tunisian patients.”

For more information on this research see: IL23R(Arg381Gln) Functional Polymorphism Is Associated with Active Pulmonary Tuberculosis Severity. *Clinical and Vaccine Immunology*, 2012;19(8):1188-92. (American Society for Microbiology - www.asm.org; Clinical and Vaccine Immunology - cdli.asm.org)

The news correspondents report that additional information may be obtained from W. Ben-Selma, Laboratory of Microbiology and Immunology, Farhat Hached University Hospital, Sousse, Tunisia. (2012 Aug 24)

Institute of Microbiology, Beijing: A marine-derived Streptomyces sp. MS449 produces high yield of actinomycin X(2) and actinomycin D with potent anti-tuberculosis activity

By a News Reporter-Staff News Editor at China Weekly News – Research findings on Mycobacterium Infections are discussed in a new report. According to news reporting originating in Beijing, People’s Republic of China, by VerticalNews journalists, research stated, “In the course of our screening program for anti-*Mycobacterium bovis* bacillus Calmette-Guerin (BCG) and anti-*Mycobacterium tuberculosis* H37Rv (MTB H37Rv) agents from our marine natural product library, a newly isolated actinomycete strain, designated as MS449, was picked out for further investigation. The strain MS449, isolated from a sediment sample collected from South China Sea, produced actinomycin X(2) and actinomycin D in substantial quantities, which showed strong inhibition of BCG and MTB H37Rv.”

The news reporters obtained a quote from the research from the Institute of Microbiology, “The structures of actinomycins were elucidated by nuclear magnetic resonance and mass spectrometric analysis. The strain MS449 was taxonomically characterized on the basis of morphological and phenotypic characteristics, genotypic data, and phylogenetic
analysis. The 16S rRNA gene sequence of the strain was determined and a database search indicated that the strain was closely associated with the type strain of Streptomyces avermitilis (99.7% 16S rRNA gene similarity). S. avermitilis has not been previously reported to produce actinomycins. The marine-derived strain of Streptomyces sp. MS449 produced notably higher quantities of actinomycin X(2) (1.92 mg/ml) and actinomycin D (1.77 mg/ml) than previously reported actinomycins producing strains.

According to the news reporters, the researchers concluded: “Thus, MS449 was considered of great potential as a new industrial producing strain of actinomycin X(2) and actinomycin D.”

For more information on this research see: A marine-derived Streptomyces sp. MS449 produces high yield of actinomycin X(2) and actinomycin D with potent anti-tuberculosis activity. Applied Microbiology and Biotechnology, 2012;95(4):919-27. (Springer - www.springer.com; Applied Microbiology and Biotechnology - http://www.springerlink.com/content/0175-7598/)

Our news correspondents report that additional information may be obtained by contacting C. Chen, Key Laboratory of Pathogenic Microbiology and Immunology, Institute of Microbiology, Chinese Academy of Sciences, Beijing, 100190, People’s Taiwan. (2012 Aug 21)

University of Cape Town: Function Prediction and Analysis of Mycobacterium tuberculosis Hypothetical Proteins

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators publish new report on Gram-Positive Bacteria. According to news reporting out of Cape Town, South Africa, by NewsRx editors, research stated, “High-throughput biology technologies have yielded complete genome sequences and functional genomics data for several organisms, including crucial microbial pathogens of humans, animals and plants. However, up to 50% of genes within a genome are often labeled ‘unknown’, ‘uncharacterized’ or ‘hypothetical’, limiting our understanding of virulence and pathogenicity of these organisms.”

Our news journalists obtained a quote from the research from the University of Cape Town, “Even though biological functions of proteins encoded by these genes are not known, many of them have been predicted to be involved in key processes in these organisms. In particular, for Mycobacterium tuberculosis, some of these ‘hypothetical’ proteins, for example those belonging to the Pro-Glu or Pro-Pro-Glu (PE/PPE) family, have been suspected to play a crucial role in the intracellular lifestyle of this pathogen, and may contribute to its survival in different environments. We have generated a functional interaction network for Mycobacterium tuberculosis proteins and used this to predict functions for many of its hypothetical proteins. Here we performed functional
enrichment analysis of these proteins based on their predicted biological functions to identify annotations that are statistically relevant, and analysed and compared network properties of hypothetical proteins to the known proteins. From the statistically significant annotations and network information, we have tried to derive biologically meaningful annotations related to infection and disease.”

According to the news editors, the researchers concluded: “This quantitative analysis provides an overview of the functional contributions of Mycobacterium tuberculosis ‘hypothetical’ proteins to many basic cellular functions, including its adaptability in the host system and its ability to evade the host immune response.”

For more information on this research see: Function Prediction and Analysis of Mycobacterium tuberculosis Hypothetical Proteins. *International Journal of Molecular Sciences*, 2012;13(6):7283-7302. *International Journal of Molecular Sciences* can be contacted at: Mdp Ag, Postfach, Ch-4005 Basel, Switzerland.

Our news journalists report that additional information may be obtained by contacting G.K. Mazandu, University of Cape Town, Inst Infect Dis & Mol Med, Dept. of Clin Lab Sci, Computat Biol Grp, ZA-7925 Cape Town, South Africa. (2012 Aug 14)

**Institute of Microbial Technology, Chandigarh:**

**WhiB2/Rv3260c, a cell division-associated protein of Mycobacterium tuberculosis H37Rv, has properties of a chaperone**

By a News Reporter-Staff News Editor at Health & Medicine Week – Investigators discuss new findings in Mycobacterium Infections. According to news reporting from Chandigarh, India, by NewsRx journalists, research stated, “whiB-like genes have been found in all actinomycetes sequenced so far. The amino-acid sequences of WhiB proteins of *Mycobacterium tuberculosis* H37Rv are highly conserved and participate in several cellular functions.”

The news correspondents obtained a quote from the research from the Institute of Microbial Technology, “Unlike other WhiB proteins of *M. tuberculosis* that have properties of protein disulfide reductases, WhiB2 showed properties like a chaperone as it suppressed the aggregation of several model substrates (e.g. citrate synthase, rhodanese and luciferase). Suppression of aggregation of the model substrates did not require ATP. Four cysteine residues of WhiB2 form two intramolecular disulfide bonds; however, chaperone function was unaffected by the redox state of the cysteines. WhiB2 also restored the activity of chemically denatured citrate synthase and did not require either ATP or a co-chaperone for refolding. The results indicate that WhiB2, which
has been shown to be associated with cell division in mycobacteria and streptomycetes, has evolved independently of other WhiBs, although it retains basic properties of this group of proteins."

According to the news reporters, the researchers concluded: "This is the first report to show that a WhiB protein has chaperone-like function; therefore, this report will have major implications in attempts to understand the role of WhiB proteins in mycobacteria, particularly in cell division."

For more information on this research see: WhiB2/Rv3260c, a cell division-associated protein of Mycobacterium tuberculosis H37Rv, has properties of a chaperone. The Febs Journal, 2012;279(15):2781-92. The Febs Journal can be contacted at: Blackwell Publishing Inc, 350 Main St, Malden, MA 02148, USA.

Our news journalists report that additional information may be obtained by contacting M. Konar, Institute of Microbial Technology (CSIR), Chandigarh, India.

Publisher contact information for the The Febs Journal is: Blackwell Publishing Inc, 350 Main St, Malden, MA 02148, USA. (2012 Aug 10)

Radboud University, Nijmegen: Polymorphisms in SP110 are not associated with pulmonary tuberculosis in Indonesians

By a News Reporter-Staff News Editor at Health & Medicine Week – Data detailed on Mycobacterium Infections have been presented. According to news reporting originating in Nijmegen, Netherlands, by NewsRx journalists, research stated, “Despite being high transmissible, Mycobacterium tuberculosis (M. tuberculosis) infection causes active disease in only 5-10% of disease-susceptible individuals. This has instigated interest in studying potentially underlying genetic host factors and mechanisms in tuberculosis (TB).”

The news reporters obtained a quote from the research from Radboud University, “The recent identification of the Intracellular pathogen resistance 1 (Ipr1) gene, which plays a major role in controlling M. tuberculosis susceptibility and infection severity in mice (Pan et al., 2005), has prompted studies on its human homolog; SP110 in humans. Association of SP110 SNPs with pulmonary TB were first reported in a study on West African families (Tosh et al., 2006). Subsequent attempts to replicate these findings in other populations, including another West African (Ghanaian) cohort (Thye et al., 2006), however, were unsuccessful. Here we have genotyped 20 SNPs located in the SP110 gene, including the previously TB associated variants; rs2114592 and rs3948464, for the first time in a South East Asian cohort from Indonesia. Our study did not reveal any statistically significant associations between SP110 SNPs and pulmonary TB.”
According to the news reporters, the researchers concluded: “In addition, a meta-analysis of the two previously TB associated SNPs revealed that these are not associated with TB, further confirming the lack of convincing evidence for SP110 to be implicated in TB susceptibility, as yet in humans.”

For more information on this research see: Polymorphisms in SP110 are not associated with pulmonary tuberculosis in Indonesians. Infection Genetics and Evolution, 2012;12(6):1319-1323. Infection Genetics and Evolution can be contacted at: Elsevier Science Bv, PO Box 211, 1000 Ae Amsterdam, Netherlands.

Our news correspondents report that additional information may be obtained by contacting E. Png, Radboud University, Nijmegen Med Center, Dept. of Med, Nijmegen, Netherlands. (2012 Aug 10)

Colorado State University, Fort Collins: Translating basic science insight into public health action for multidrug- and extensively drug-resistant tuberculosis

By a News Reporter-Staff News Editor at Health & Medicine Week – Current study results on Mycobacterium Infections have been published. According to news originating from Fort Collins, Colorado, by NewsRx correspondents, researchers stated “Multidrug (MDR)- and extensively drug-resistant (XDR) tuberculosis (TB) impose a heavy toll of human suffering and social costs. Controlling drug-resistant TB is a complex global public health challenge.”

Our news journalists obtained a quote from the research from Colorado State University, “Basic science advances including elucidation of the genetic basis of resistance have enabled development of new assays that are transforming the diagnosis of MDR-TB. Molecular epidemiological approaches have provided new insights into the natural history of TB with important implications for drug resistance. In the future, progress in understanding Mycobacterium tuberculosis strain-specific human immune responses, integration of systems biology approaches with traditional epidemiology and insight into the biology of mycobacterial persistence have potential to be translated into new tools for diagnosis and treatment of MDR- and XDR-TB.”

According to the news editors, the researchers concluded: “We review recent basic sciences developments that have contributed or may contribute to improved public health response.”

Purdue University, West Lafayette: An Outbreak Of Tuberculosis By Mycobacterium Bovis In Coatis (nasua Nasua)

By a News Reporter-Staff News Editor at Life Science Weekly – A new study on Gram-Positive Bacteria is now available. According to news reporting from West Lafayette, Indiana, by NewsRx journalists, researchers stated “Mycobacterium tuberculosis complex, which includes Mycobacterium bovis, infrequently causes severe or lethal disease in captive wildlife populations. A dead coati from a wildlife triage center showing pulmonary lesions compatible with tuberculosis had raised suspicion of a potential disease caused by mycobacteria species and was further investigated.”

The news correspondents obtained a quote from the research from Purdue University, “Four native coatis (Nasua nasua) with suspected mycobacterial infection were sedated, and bronchoalveolar lavages and tuberculin skin tests (TSTs) were performed. All animals tested positive upon TST. Mycobacterial culturing, Ziehl-Neelsen staining, and genetic testing were performed on postmortem samples and the etiologic agent was identified as M. bovis.”

According to the news reporters, the researchers concluded: “Molecular genetic identification using a polymerase chain reaction panel was crucial to achieving a definitive diagnosis.”

For more information on this research see: An Outbreak Of Tuberculosis By Mycobacterium Bovis In Coatis (nasua Nasua). Journal of Zoo and Wildlife Medicine, 2012;43(2):338-341. Journal of Zoo and Wildlife Medicine can be contacted at: Amer Assoc Zoo Veterinarians, 581705 White Oak Road, Yulee, FL 32097, USA.

Our news journalists report that additional information may be obtained by contacting P.S. Murakami, Purdue University, West Lafayette, IN 47907, United States. (2012 Jul 31)
Center for Disease Control and Prevention, Nanjing: Association between the CD209 promoter -336A/G polymorphism and susceptibility to tuberculosis: A meta-analysis

By a News Reporter-Staff News Editor at Health & Medicine Week – Current study results on Mycobacterium Infections have been published. According to news reporting originating from Nanjing, People’s Republic of China, by NewsRx correspondents, researchers stated “Dendritic cell-specific intracellular adhesion molecule-3 grabbing nonintegrin (DC-SIGN), encoded by the CD209 gene, is a major Mycobacterium tuberculosis receptor on human dendritic cells. The potentially functional -336A/G polymorphism in the CD209 promoter region has been associated with susceptibility to tuberculosis (TB), but the results have been inconclusive.”

Our news editors obtained a quote from the research by the authors from Center for Disease Control and Prevention, “We performed a meta-analysis to clarify the relationship between the CD209-336A/G variant and the risk of TB. Ten studies involving a total of 2598 TB patients and 2614 control subjects were systematically reviewed, and the data were quantitatively synthesized by meta-analysis. The Q-test was applied to assess the heterogeneity of associations among the studies, and Egger’s regression test was used to assess potential publication bias. No significant association was identified between the CD209-336A/G polymorphism and risk of TB (G allele vs A allele: odds ratio (OR) 1.02, 95% confidence interval (CI) 0.90-1.15). Moreover, no significant association was observed in populations of African ethnicity (OR 1.01, 95% CI 0.87-1.17) or among individuals who were negative for the human immunodeficiency virus (OR 0.98, 95% CI 0.84-1.15).”

According to the news editors, the researchers concluded: “This meta-analysis has indicated that the CD209-336A/G polymorphism may not contribute to susceptibility to TB.”


The news editors report that additional information may be obtained by contacting R. Miao, Dept. of Chronic Communicable Disease, Nanjing Municipal Center for Disease Control and Prevention, Nanjing, People’s Taiwan. (2012 Jul 27)
Farhat Hached University Teaching Hospital, Sousse: Age- and gender-specific effects on NRAMP1 gene polymorphisms and risk of the development of active tuberculosis in Tunisian populations

By a News Reporter-Staff News Editor at Health & Medicine Week – Investigators publish new report on Mycobacterium Infections. According to news reporting originating from Sousse, Tunisia, by NewsRx correspondents, researchers stated “Studies that have assessed NRAMP1 polymorphisms and their association with susceptibility to tuberculosis (TB) in humans have yielded conflicting results. In this study, we evaluated the association between NRAMP1 gene polymorphisms and the risk of the development of active TB in Tunisian populations.”

Our news editors obtained a quote from the research by the authors from Farhat Hached University Teaching Hospital, “The distribution of 3'-UTR and D543N polymorphisms in 223 TB patients (168 patients with pulmonary TB (PTB) and 55 patients with extrapulmonary TB (EPTB)) and 150 healthy donors was determined by PCR-restriction fragment length polymorphism (RFLP) method. We found that AA and AG genotypes appeared to be associated with susceptibility to PTB (odds ratio (OR) 10.8, 95% confidence interval (CI) 1.37-230.8; p corrected for the number of genotypes (pc) = 0.018) and EPTB (OR 4.37, 95% CI 1.64-11.82; pc = 0.0024), respectively, in patients aged less than 30 years. However, wild-type GG genotype appeared to be associated with resistance against PTB in females (OR 0.1, 95% CI 0.01-0.74; pc = 0.03). The 3'-UTR del/del genotype appeared to be associated with susceptibility to PTB in patients aged less than 30 years (OR 3.75, 95% CI 1.5-9.52; pc = 0.003). In contrast, TGTG+/del might be associated with resistance against the development of active PTB (OR 0.23, 95% CI 0.08-0.65; pc = 0.003). A-del haplotype appeared to be associated with susceptibility to PTB (OR 1.79, 95% CI 1.11-2.9; pc = 0.04).”

According to the news editors, the researchers concluded: “Collectively, our results suggest an association of NRAMP1 3'-UTR and D543N polymorphisms with susceptibility to mycobacterial infection in Tunisian populations in relation to age and sex.”

Howard Hughes Medical Institute, Chevy Chase: MetaMerge: scaling up genome-scale metabolic reconstructions with application to Mycobacterium tuberculosis

By a News Reporter-Staff News Editor at Health & Medicine Week – Data detailed on Mycobacterium Infections have been presented. According to news reporting out of Chevy Chase, Maryland, by NewsRx editors, researchers stated “Reconstructed models of metabolic networks are widely used for studying metabolism in various organisms.”

Our news journalists obtained a quote from the research by the authors from Howard Hughes Medical Institute, “Many different reconstructions of the same organism often exist concurrently, forcing researchers to choose one of them at the exclusion of the others. We describe MetaMerge, an algorithm for semi-automatically reconciling a pair of existing metabolic network reconstructions into a single metabolic network model.”

According to the news editors, the researchers concluded: “We use MetaMerge to combine two published metabolic networks for Mycobacterium tuberculosis into a single network, which allows many reactions that could not be active in the individual models to become active, and predicts essential genes with a higher positive predictive value.”


Our news journalists report that additional information may be obtained by contacting L. Chindelevitch, Howard Hughes Med Inst, Chevy Chase, MD 20815, United States. (2012 Jul 27)
Sotiria Chest Diseases Hospital, Athens: HLA-A and HLA-DRB1 amino acid polymorphisms are associated with susceptibility and protection to pulmonary tuberculosis in a Greek population

By a News Reporter-Staff News Editor at Health & Medicine Week – New research on Mycobacterium Infections is the subject of a report. According to news reporting from Athens, Greece, by NewsRx journalists, researchers stated “Pulmonary tuberculosis remains the single deadliest infectious disease causing high mortality in humans leading to 1.4 million deaths annually. Inherited genetic factors may explain why some people resist infection more successfully than others.”

The news correspondents obtained a quote from the research by the authors from Sotiria Chest Diseases Hospital, “The polymorphisms of HLA-class I (-A, -B) and class II (-DRB1, -DQB1) genes have been evaluated using DNA-based typing in a population of 86 non-immunosuppressed, unrelated Greek patients with PTb and 46 healthy unrelated people without a history of PTb, who were all tested purified protein derivative positive (&gt;14 mm). The HLA-A R-114 and HLA-DR beta N-37 residues are associated with susceptibility. They operate independently from each other and their effect is detected when the population is evaluated for their concurrent presence (A R-114 positive or DR beta N-37 positive or A R-114 and DR beta N-37 positive). Furthermore the HLA-A S-77 appears to have a protective role, however in the presence of the DR beta N-37, the A-S-77 does not exert its protective effect. The HLA residues A-S-77, A-R-114 and DR beta N-37 in combination with PTb antigenic elements possibly modulate T-cell responses against MTb that lead to either protection or susceptibility.”

According to the news reporters, the researchers concluded: “The HLA-A and -DRB1-dependent T-cell networks may interact among themselves and influence each other resulting in different PTb phenotypes.”

For more information on this research see: HLA-A and HLA-DRB1 amino acid polymorphisms are associated with susceptibility and protection to pulmonary tuberculosis in a Greek population. Human Immunology, 2012;73(6):641-646. Human Immunology can be contacted at: Elsevier Science Inc, 360 Park Ave South, New York, NY 10010-1710, USA. (Elsevier - www.elsevier.com; Human Immunology - http://www.elsevier.com/wps/product/cws_home/505763)

Our news journalists report that additional information may be obtained by contacting E.E. Magira, Sotiria Chest Dis Hosp, Dept. of Pulm Clin 6, Athens 11527, Greece. (2012 Jul 20)
Chapter 3  Genetics

Department of Radiation Medicine, Damascus: Characterization of mutations causing rifampicin and isoniazid resistance of Mycobacterium tuberculosis in Syria

By a News Reporter-Staff News Editor at Tuberculosis Week – Current study results on Microbiology have been published. According to news reporting originating from Damascus, Syria, by NewsRx correspondents, researchers stated “In order to characterize mutations causing rifampicin and isoniazid resistance of *M. tuberculosis* in Syria, 69 rifampicin resistant (Rif(r)) and 72 isoniazid resistant (Inh(r)) isolates were screened for point mutations in hot spots of the rpoB, katG and inhA genes by DNA sequencing and real time PCR. Of 69 Rif(r) isolates, 62 (90%) had mutations in the rifampin resistance determining region (RRDR) of the rpoB gene, with codons 531 (61%), 526 (13%), and 516 (8.7%) being the most commonly mutated.”

Our news editors obtained a quote from the research by the authors from the Department of Radiation Medicine, “We found two new mutations (Asp516Thr and Ser531Gly) described for the first time in the rpoB-RRDR in association with rifampicin resistance. Only one mutation (Ile572Phe) was found outside the rpoB-RRDR. Of 72 Inh(r) strains, 30 (41.6%) had a mutation in katGcodon315 (with Ser315Thr being the predominant alteration), and 23 (32%) harbored the inhA(-15C→T) mutation. While the general pattern of rpoB-RRDR and katG mutations reflected those found worldwide, the prevalence of the inhA(-15C→T) mutation was above the value found in most other countries, emphasizing the great importance of testing the inhA(-15C→T) mutation for prediction of isoniazid resistance in Syria. Sensitivity of a rapid test using real time PCR and 3’-Minor groove binder (MGB) probes in detecting Rif(r) and Inh(r) isolates was 90% and 69.4%, respectively.”

According to the news editors, the researchers concluded: “This demonstrates that a small set of MGB-probes can be used in real time PCR in order to detect most mutations causing resistance to rifampicin and isoniazid.”


The news editors report that additional information may be obtained by contacting A. Madania, Dept. of Radiation Medicine, Atomic Energy Commission, PO 6091, Damascus, Syria. (2012 Jul 16)
Albert Einstein College of Medicine, Bronx: NXL104 Irreversibly Inhibits the beta-Lactamase from Mycobacterium tuberculosis

By a News Reporter-Staff News Editor at Health & Medicine Week – Data detailed on Biochemistry have been presented. According to news originating from Bronx, New York, by NewsRx correspondents, researchers stated “NXL104 is a novel beta-lactamase inhibitor with a non-lactam structural scaffold. Our kinetic and mass spectrometric analysis demonstrates that NXL104 quantitatively inhibits BlaC, the only chromosomally encoded beta-lactamase from Mycobacterium tuberculosis, by forming a carbamyl adduct with the enzyme.”

Our news journalists obtained a quote from the research by the authors from the Albert Einstein College of Medicine, “The inhibition efficiency (k(2)/K) of NXL104 was shown to be more than 100-fold lower than that of clavulanate, a classical beta-lactamase inhibitor, which is probably caused by the bulky rings of NXL104. However, the decarbamylation rate constant (k(3)) was determined to be close to zero. The BlaC NXL104 adduct remained stable for at least 48 h, while the hydrolysis of the BlaC-clavulanate adduct was observed after 2 days. The three-dimensional crystal structure of the BlaC-NXL104 carbamyl adduct was determined at a resolution of 2.3 angstrom. Interestingly, the sulfate group of NXL104 occupies the position of a phosphate ion in the structure of the BlaC-clavulanate adduct and is hydrogen bonded to residues Ser128, Thr237, and Thr239. Favorable interactions are also seen in the electrostatic potential map.”

According to the news editors, the researchers concluded: “We propose that these additional interactions, as well as the intrinsic stability of the carbamyl linkage, contribute to the extraordinary stability of the BlaC-NXL104 adduct.”


The news correspondents report that additional information may be obtained from H. Xu, Albert Einstein College of Medicine, Dept. of Biochem, Bronx, NY 10461, United States. (2012 Jul 13)
University of Sheffield: Mycobacterium tuberculosis WhiB1 represses transcription of the essential chaperonin GroEL2

By a News Reporter-Staff News Editor at Tuberculosis Week – Researchers detail new data in Mycobacterium Infections. According to news originating from Sheffield, United Kingdom, by NewsRx correspondents, researchers stated “A central feature of TB pathogenesis is the formation of Mycobacterium tuberculosis latent infections that can persist for decades. Nitric oxide produced by infected lung macrophages promotes expression of genes associated with dormancy, and impaired nitric oxide production can lead to reactivation of latent disease.”

Our news journalists obtained a quote from the research by the authors from the University of Sheffield, “Recently, WhiB1 was identified as a nitric oxide-responsive transcription factor. Here it is shown that apo-WhiB1 binds to groEL2 (Rv0440) promoter DNA. Apo-WhiB1 inhibited transcription from the groEL2 promoter in vitro and the transcript start was located ~181 bases upstream of the groEL2 start codon. Electrophoretic mobility shift assays with sub-fragments of the groEL2 promoter indicated that the complete Rv0439c-Rv0440 intergenic region was required for WhiB1 binding, suggesting that this region possessed more than one WhiB1-binding site. DNase I footprinting identified a WhiB1-binding region that overlapped the -35 element of the groEL2 promoter. The CRP-family transcription factor Cmr (Rv1675c) was shown to bind the groEL2 promoter and activate transcription in vitro in the presence or absence of cAMP.”

According to the news editors, the researchers concluded: “Therefore, it is suggested that WhiB1 acts to oppose Cmr-mediated cAMP-independent activation of groEL2 expression in the presence of nitric oxide by promoter occlusion.”


The news correspondents report that additional information may be obtained from M.R. Stapleton, Dept. of Molecular Biology and Biotechnology, University of Sheffield, Sheffield S10 2TN, UK. (2012 Jul 09)
Institute of Genomics and Integrative Biology, Delhi: Structural and functional characterization of Rv2966c protein reveals an RsmD-like methyltransferase from Mycobacterium tuberculosis and the role of its N-terminal domain in target recognition

By a News Reporter-Staff News Editor at Life Science Weekly – New research on Mycobacterium tuberculosis is the subject of a report. According to news originating from Delhi, India, by NewsRx correspondents, researchers stated “Nine of ten methylated nucleotides of Escherichia coli 16S rRNA are conserved in Mycobacterium tuberculosis. All the 10 different methyltransferases are known in E. coli, whereas only TlyA and GidB have been identified in mycobacteria.”

Our news journalists obtained a quote from the research by the authors from the Institute of Genomics and Integrative Biology, “Here we have identified Rv2966c of M. tuberculosis as an ortholog of RsmD protein of E. coli. We have shown that rv2966c can complement rsmD-deleted E. coli cells. Recombinant Rv2966c can use 30 S ribosomes purified from rsmD-deleted E. coli as substrate and methylate G966 of 16S rRNA in vitro. Structure determination of the protein shows the protein to be a two-domain structure with a short hairpin domain at the N terminus and a C-terminal domain with the S-adenosylmethionine-MT-fold. We show that the N-terminal hairpin is a minimalist functional domain that helps Rv2966c in target recognition. Deletion of the N-terminal domain prevents binding to nucleic acid substrates, and the truncated protein fails to carry out the m<sup>2</sup>G966 methylation on 16S rRNA.”

According to the news editors, the researchers concluded: “The N-terminal domain also binds DNA efficiently, a property that may be utilized under specific conditions of cellular growth.”


The news correspondents report that additional information may be obtained from A. Kumar, Institute of Genomics and Integrative Biology (Council of Scientific and Industrial Research), Delhi, India. (2012 Jul 03)
Distinct clinical and epidemiological features of tuberculosis in New York City caused by the RDRio Mycobacterium tuberculosis sublineage

By a News Reporter-Staff News Editor at Business & Finance Week – A new study on Tuberculosis is now available. According to news reporting out of Albany, New York, by VerticalNews editors, researchers stated “Genetic tracking of Mycobacterium tuberculosis is a cornerstone of tuberculosis (TB) control programs. The RDRio M. tuberculosis sublineage was previously associated with TB in Brazil. We investigated 3847 M. tuberculosis isolates and registry data from New York City (NYC) (2001-2005) to: (1) affirm the position of RDRio strains within the M. tuberculosis phylogenetic structure, (2) determine its prevalence, and (3) define transmission, demographic, and clinical characteristics associated with RDRio TB.”

Our news journalists obtained a quote from the research by the authors, “Isolates classified as RDRio or non-RDRio M. tuberculosis by multiplex PCR were further classified as clustered (>= 2 isolates) or unique based primarily upon IS6110-RFLP patterns and lineage-specific cluster proportions were calculated. The secondary case rate of RDRio was compared with other prevalent M. tuberculosis lineages. Genotype data were merged with the data from the NYC TB Registry to assess demographic and clinical characteristics. RDRio strains were found to: (1) be restricted to the Latin American-Mediterranean family, (2) cause approximately 8% of TB cases in NYC, and (3) be associated with heightened transmission as shown by: (i) a higher cluster proportion compared to other prevalent lineages, (ii) a higher secondary case rate, and (iii) cases in children. Furthermore, RDRio strains were significantly associated with US-born Black or Hispanic race, birth in Latin American and Caribbean countries, and isoniazid resistance. The RDRio genotype is a single M. tuberculosis strain population that is emerging in NYC.”

According to the news editors, the researchers concluded: “The findings suggest that expanded RDRio case and exposure identification could be of benefit due to its association with heightened transmission.”

For more information on this research see: Distinct clinical and epidemiological features of tuberculosis in New York City caused by the RDRio Mycobacterium tuberculosis sublineage. Infection Genetics and Evolution, 2012;12(4):664-670. Infection Genetics and Evolution can be contacted at: Elsevier Science Bv, PO Box 211, 1000 Ae Amsterdam, Netherlands.

Our news journalists report that additional information may be obtained by contacting S.A. Weisenberg, New York State Dept. of Hlth, Bur TB Control, Albany, NY, United States. (2012 Jun 30)
National Jewish Health, Denver: Are phylogenetic position, virulence, drug susceptibility and in vivo response to treatment in mycobacteria interrelated?

By a News Reporter-Staff News Editor at Health & Medicine Week – Current study results on Tuberculosis have been published. According to news originating from Denver, Colorado, by NewsRx correspondents, researchers stated “Phylogenetic analyses on the basis of multiple house-keeping genes and whole genome sequences have offered new insights in the phylogeny of the genus Mycobacterium. This genus yields obligate pathogens, the M. tuberculosis complex and M. leprae, as well as opportunistic pathogens (e.g. M. avium, M. intracellulare, M. kansasii, M. marinum, M. malmoense) and saprophytes (e.g. M. phlei, M. sphagni, M. gordonae).”

Our news journalists obtained a quote from the research by the authors from National Jewish Health, “The most virulent mycobacteria, the M. tuberculosis complex, M. leprae and the M. kansasii-M. szulgai-M. marinum-M. ulcerans group are phylogenetically related and infections by these organisms are better treatable than those caused by less virulent and phylogenetically more distantly related Mycobacterium species. The most virulent Mycobacterium species are also characterized by high levels of natural drug susceptibility. In this paper, we review studies of phylogeny, drug susceptibility, and clinical significance to support our hypothesis that drug susceptibility in mycobacteria is acquired and reflects the low level of competition in- and adaptation to-a closer-to-human (environmental) niche.”

According to the news editors, the researchers concluded: “In turn, mycobacteria that inhabit the most competitive environmental niches are the least adapted to humans, thus of low clinical significance, but most tolerant to antibiotics derived from microbes with which they share their habitat, lowering the chances of cure in case of infection.”

For more information on this research see: Are phylogenetic position, virulence, drug susceptibility and in vivo response to treatment in mycobacteria interrelated? Infection Genetics and Evolution, 2012;12(4):832-837. Infection Genetics and Evolution can be contacted at: Elsevier Science Bv, PO Box 211, 1000 Ae Amsterdam, Netherlands.

The news correspondents report that additional information may be obtained from J. van Ingen, Natl Jewish Hlth, Adv Diagnost Labs ADx, Dept. of Mycobacteriol, Denver, CO 80206, United States. (2012 Jun 29)
University of New South Wales, Sydney: Impact of homoplasy on variable numbers of tandem repeats and spoligotypes in Mycobacterium tuberculosis

By a News Reporter-Staff News Editor at Health & Medicine Week – Fresh data on Tuberculosis are presented in a new report. According to news reporting out of Sydney, Australia, by NewsRx editors, researchers stated “Homoplasy is the occurrence of genotypes that are identical by state but not by descent. It arises through a number of means including convergent and reverse evolution, and horizontal gene transfer.”

Our news journalists obtained a quote from the research by the authors from the University of New South Wales, “When using molecular markers that are based on sequences possessing a finite number of character states, such as VNTR or spoligotypes, this is an unavoidable phenomenon. Here we discuss the extent of homoplasy and its impact on inferences drawn from spoligotypes and VNTR in epidemiological studies of tuberculosis. To further explore this problem, we developed a computer simulation model combining the processes of mutation and transmission. Our results show that while the extent of homoplasy is not negligible, its effect on the proportion of isolates clustered (‘n - 1 method’) is likely to be relatively low for spoligotyping. For VNTR-typing, homoplasy occurs at a low rate provided the number of loci used is high and the mutation rate is relatively high.”

According to the news editors, the researchers concluded: “However, deep phylogenetic inferences using spoligotypes or VNTRs with a small number of loci are likely to be unreliable.”

For more information on this research see: Impact of homoplasy on variable numbers of tandem repeats and spoligotypes in Mycobacterium tuberculosis. Infection Genetics and Evolution, 2012;12(4):811-818. Infection Genetics and Evolution can be contacted at: Elsevier Science Bv, PO Box 211, 1000 Ae Amsterdam, Netherlands.

Our news journalists report that additional information may be obtained by contacting J.F. Reyes, University of New South Wales, Evolut & Ecol Res Center, Sydney, NSW, Australia. (2012 Jun 29)

Morehouse School of Medicine, Atlanta: Molecular epidemiology and genetic diversity of Mycobacterium tuberculosis complex in the Cross River State, Nigeria

By a News Reporter-Staff News Editor at TB & Outbreaks Week – Researchers detail new data in Tuberculosis. According to news reporting from Atlanta, Georgia, by NewsRx journalists, researchers stated “This
study provides with a first insight on Mycobacterium tuberculosis complex epidemiology and genetic diversity in the Cross River State, Nigeria. Starting with 137 smear positive patients recruited over a period of 12 months (June 2008 to May 2009), we obtained 97 pure mycobacterial isolates out of which 81 (83.5%) were identified as M. tuberculosis complex.”

The news correspondents obtained a quote from the research by the authors from the Morehouse School of Medicine, “Genotyping revealed a total of 27 spoligotypes patterns with 10 clusters (n = 64% or 79% of clustered isolates, 2-32 isolates/cluster), with patients in the age group range 25-34 years being significantly associated with shared-type pattern SIT61 (p = 0.019). Comparison with SITVIT2 database showed that with the exception of a single cluster (SIT727/H1), all other clusters observed were representative of West Africa; the two main lineages involved were LAM10-CAM (n = 42/81% or 51.8%) of M. tuberculosis and AFRI_2 sublineage of Mycobacterium africanum (n = 27/81% or 33.3%). Subsequent 12-loci MIRU typing resulted in a total of 13 SIT/MIT clusters (n = 52 isolates, 2-9 isolates per cluster), with a resulting recent n - 1 transmission rate of 48.1%. Available drug-susceptibility testing (DST) results for 58/81 clinical isolates revealed 6/58% or 10.4% cases of multiple drug-resistance (MDR); 5/6 MDR cases were caused by strains belonging to LAM10-CAM lineage (a specific cluster SIT61/MIT266 in 4/6 cases, and an orphan spoligotype pattern in 1/6 case). Additionally, MIT266 was associated with streptomycin resistance (p = 0.016). All the six MDRTB isolates were concomitantly resistance to streptomycin and ethambutol; however, 4/6 MDR strains with identical MIRU patterns were characterized by consecutive strain numbers hence the possibility of laboratory cross contamination could not be excluded in 3/4 serial cases.”

According to the news reporters, the researchers concluded: “The present preliminary study underlines the usefulness of spoligotyping and 12-loci MIRU-VNTRs to establish a baseline of circulating genotypic lineages of M. tuberculosis complex in Nigeria.”

For more information on this research see: Molecular epidemiology and genetic diversity of Mycobacterium tuberculosis complex in the Cross River State, Nigeria. Infection Genetics and Evolution, 2012;12(4):671-677. Infection Genetics and Evolution can be contacted at: Elsevier Science Bv, PO Box 211, 1000 Ae Amsterdam, Netherlands.

Our news journalists report that additional information may be obtained by contacting B.P. Thumamo, Morehouse Sch Med, Atlanta, GA 30310, United States. (2012 Jun 26)
Tongji University School of Medicine, Shanghai: A Rapid Loop-Mediated Isothermal Amplification Assay Targeting hspX for the Detection of Mycobacterium tuberculosis Complex

By a News Reporter-Staff News Editor at China Weekly News – Investigators discuss new findings in Tuberculosis. According to news reporting originating in Shanghai, People’s Republic of China, by Vertical-News journalists, researchers stated “A rapid, simple, and low-cost diagnostic tool for tuberculosis (TB) detection is urgently needed in countries with a high TB burden. Here, we report a novel loop-mediated isothermal amplification (LAMP) assay targeting the hspX gene for the rapid detection of Mycobacterium tuberculosis, M. bovis, M. africanum, and M. microti.”

The news reporters obtained a quote from the research by the authors from the Tongji University School of Medicine, “The specificity of this assay was evaluated using 4 reference strains of Mycobacterium tuberculosis complex (MTC), 22 species of non-tuberculous mycobacteria (NTM), 7 non-mycobacterial species, and 50 clinical M. tuberculosis isolates. All the reference MTC strains and M. tuberculosis clinical isolates were successfully detected by this method, and there were no false-positive results with NTM or non-mycobacterial species, which demonstrates the high specificity of this assay for MTC. The detection limit was 10 copies of MTC genome within 27 min, and the detection speed of this assay was higher than that of any other isothermal methods reported so far.”

According to the news reporters, the researchers concluded: “Because of its speed, simplicity, sensitivity, specificity, and inexpensiveness, the TB hspX LAMP assay is a potential gene diagnostic method for TB detection in developing countries with a high TB burden.”


Our news correspondents report that additional information may be obtained by contacting A. Bi, Shanghai Key Laboratory of Tuberculosis, Shanghai Pulmonary Hospital, Tongji University School of Medicine, Shanghai, People's Taiwan. (*2012 Jun 26*)
University of Stellenbosch, Tygerberg: Emergence and treatment of multidrug resistant (MDR) and extensively drug-resistant (XDR) tuberculosis in South Africa

By a News Reporter-Staff News Editor at Managed Care Weekly Digest – Current study results on Tuberculosis have been published. According to news reporting originating from Tygerberg, South Africa, by NewsRx correspondents, researchers stated “Drug resistant tuberculosis (TB) has reached alarming proportions in South Africa, draining valuable resources that are needed to fight drug susceptible TB. It is currently estimated that 9.6% of all TB cases have multi-drug resistant (MDR)-TB, thereby ranking South Africa as one of the highest MDR-TB burden countries in the world.”

Our news editors obtained a quote from the research by the authors from the University of Stellenbosch, “Molecular epidemiological studies have demonstrated the complexity of the epidemic and have clearly shown that the epidemic is driven by transmission as a consequence of low cases detection and diagnostic delay. The latter has in turn fueled the amplification of drug resistance, ultimately leading to the emergence of extensively drug resistant (XDR)-TB. Despite the introduction of new drugs to combat this scourge, culture conversion rates for XDR-TB remain below 20%. Failure to achieve cure may be explained from DNA sequencing results which have demonstrated mutations in 7 genes encoding resistance to at least 8 anti-TB drugs. This review shows how molecular epidemiology has provided novel insights into the MDR-TB epidemic in South Africa and thereby has highlighted the challenges that need to be addressed regarding the diagnosis and treatment of MDR-TB.”

According to the news editors, the researchers concluded: “An important step towards for curbing this epidemic will be collaboration between clinicians, laboratories and researchers to establish scientific knowledge and medical expertise to more efficiently guide public health policy.”

For more information on this research see: Emergence and treatment of multidrug resistant (MDR) and extensively drug-resistant (XDR) tuberculosis in South Africa. Infection Genetics and Evolution, 2012;12(4):686-694. Infection Genetics and Evolution can be contacted at: Elsevier Science Bv, PO Box 211, 1000 Ae Amsterdam, Netherlands.

The news editors report that additional information may be obtained by contacting E.M. Streicher, University of Stellenbosch, Fac Hlth Sci, Natl Hlth Lab Serv, Div Med Microbiol, ZA-7505 Tygerberg, South Africa. (2012 Jun 25)
St. George’s Hospital School of Medicine, London: The chemotherapy of tuberculosis: past, present and future

By a News Reporter-Staff News Editor at Life Science Weekly – Current study results on Tuberculosis have been published. According to news originating from London, United Kingdom, by NewsRx correspondents, researchers stated “The history of the development of modern chemotherapy for tuberculosis (TB), largely due to the British Medical Research Council, is first described. There is a current need to shorten the duration of treatment and to prevent and cure drug-resistant disease.”

Our news journalists obtained a quote from the research by the authors from the St. George’s Hospital School of Medicine, “These aims will only be achieved if the way in which multidrug treatment prevents resistance from emerging and the reasons for the very slow response to chemotherapy are understood. Consideration of mutation rates to resistance and the size of bacterial populations in lesions makes it very unlikely that resistance would emerge spontaneously, leaving irregularity in drug taking and inadequate dosage as the main reasons for its occurrence. Slow response to treatment seems due to the presence of persister populations whose natural history is only partly known. In the future, we need to explore the persister state in patients and in experimental murine TB, and to take it into account in the design of future mouse experiments. The activity of rifamycins and pyrazinamide is being increased by a rise in rifamycin dosage and the inhalation of pyrazinoic acid. New drugs are gradually being brought into use, initially TMC207 and the nitroimidazoles, PA824 and OPC67683.”

According to the news editors, the researchers concluded: “They will need to be tested in new combination regimens for drug-susceptible and multi-and extensively drug-resistant disease.”

For more information on this research see: The chemotherapy of tuberculosis: past, present and future. The International Journal of Tuberculosis and Lung Disease, 2012;16(6):724-32.

The news correspondents report that additional information may be obtained from D. Mitchison, Dept. of Cellular & Molecular Medicine, St George’s Hospital Medical School, London, UK. (2012 Jun 19)
University of Hong Kong: A Functional Single-Nucleotide Polymorphism in the Promoter of the Gene Encoding Interleukin 6 Is Associated With Susceptibility to Tuberculosis

By a News Reporter-Staff News Editor at Asia Business Newsweekly – Investigators publish new report on Tuberculosis. According to news reporting originating in Hong Kong, People’s Republic of China, by VerticalNews journalists, researchers stated “Genetic variation influences susceptibility or resistance to tuberculosis. Interleukin 6 (IL-6) contributes to protection against tuberculosis in mice.”

The news reporters obtained a quote from the research by the authors from the University of Hong Kong, “However, its role in regulating susceptibility or resistance to tuberculosis in humans is unclear. Genotyping of polymorphisms in IL-6 and IL-6R (CD126) genes was performed in 2 independent cohorts, an experimental population (495 cases and 358 controls) and a validation population (1383 cases and 1149 controls). The associations of the variants with tuberculosis were tested using 2 case-control association studies. In addition, the regulatory effects of single-nucleotide polymorphism rs1800796 (-572C > G) on IL-6 production in plasma and CD14(+) monocyte cultures stimulated with a Mycobacterium tuberculosis (M. tuberculosis) product were assessed. The rs1800796 polymorphism is associated with increased resistance to tuberculosis (odds ratio [OR], 0.771; 95% confidential interval, .684-.870). The rs1800796GG genotype is strongly associated with reduced risk to tuberculosis (OR, 0.621; 95% CI, .460-.838). Interestingly, CD14(+) monocytes isolated from individuals with rs1800796GG genotype produced significantly less IL-6 in response to M. tuberculosis 19-kDa lipoprotein than those with CC or CG genotype.”

According to the news reporters, the researchers concluded: “We identified a genetic polymorphism in the IL-6 promoter that regulates cytokine production and host resistance to pulmonary tuberculosis in Chinese populations.”


Our news correspondents report that additional information may be obtained by contacting G.L. Zhang, University of Hong Kong, LKS Fac Med, Dept. of Biochem, Pokfulam, Hong Kong, People’s Republic of China. (2012 Jun 19)
University of Oslo: Enzymatic Activities and DNA Substrate Specificity of Mycobacterium tuberculosis DNA Helicase XPB

By a News Reporter-Staff News Editor at Life Science Weekly – Researchers detail new data in Tuberculosis. According to news reporting originating from Oslo, Norway, by NewsRx correspondents, researchers stated “XPB, also known as ERCC3 and RAD25, is a 3′?5′ DNA repair helicase belonging to the superfamily 2 of helicases. XPB is an essential core subunit of the eukaryotic basal transcription factor complex TFIH.”

Our news editors obtained a quote from the research by the authors from the University of Oslo, “It has two well-established functions: in the context of damaged DNA, XPB facilitates nucleotide excision repair by unwinding double stranded DNA (dsDNA) surrounding a DNA lesion; while in the context of actively transcribing genes, XPB facilitates initiation of RNA polymerase II transcription at gene promoters. Human and other eukaryotic XPB homologs are relatively well characterized compared to conserved homologs found in mycobacteria and archaea. However, more insight into the function of bacterial helicases is central to understanding the mechanism of DNA metabolism and pathogenesis in general. Here, we characterized Mycobacterium tuberculosis XPB (Mtb XPB), a 3′?5′ DNA helicase with DNA-dependent ATPase activity. Mtb XPB efficiently catalyzed DNA unwinding in the presence of significant excess of enzyme. The unwinding activity was fueled by ATP or dATP in the presence of Mg(2+)/Mn(2+). Consistent with the 3′?5′ polarity of this bacterial XPB helicase, the enzyme required a DNA substrate with a 3′ overhang of 15 nucleotides or more. Although Mtb XPB efficiently unwound DNA model substrates with a 3′ DNA tail, it was not active on substrates containing a 3′ RNA tail. We also found that Mtb XPB efficiently catalyzed ATP-independent annealing of complementary DNA strands.”

According to the news editors, the researchers concluded: “These observations significantly enhance our understanding of the biological roles of Mtb XPB.”

For more information on this research see: Enzymatic Activities and DNA Substrate Specificity of Mycobacterium tuberculosis DNA Helicase XPB. Plos One, 2012;7(5):e36960. (Public Library of Science - www.plos.org; Plos One - www.plosone.org)

The news editors report that additional information may be obtained by contacting S.V. Balasingham, Centre for Molecular Biology and Neuroscience (CMBN) and Dept. of Microbiology, University of Oslo, Oslo, Norway. (2012 Jun 19)
Zahedan University of Medical Sciences: R620W functional polymorphism of protein tyrosine phosphatase non-receptor type 22 is not associated with pulmonary tuberculosis in Zahedan, southeast Iran

By a News Reporter-Staff News Editor at Life Science Weekly – Research findings on Pulmonary Tuberculosis are discussed in a new report. According to news reporting out of Zahedan, Iran, by NewsRx editors, researchers stated “The protein tyrosine phosphatase non-receptor type 22 (PTPN22) gene, which encodes an intracellular lymphoid-specific phosphatase, is considered an important regulator of T-cell activation. We investigated a possible association between the PTPN22 C1858T (R620W) polymorphism and pulmonary tuberculosis in an Iranian population.”

Our news journalists obtained a quote from the research by the authors from the Zahedan University of Medical Sciences, “Single nucleotide polymorphisms of PTPN22 C1858T (rs2476601) were genotyped in 172 pulmonary tuberculosis cases and 204 normal subjects from Zaheden, Iran. Frequencies of genotypes CC, CT and TT of the PTPN22 C1858T polymorphism were 98.3, 1.7 and 0% in the pulmonary tuberculosis patients, and 96.1, 3.9 and 0% in the control group, respectively (p=0.239). The frequency of the minor (T) allele was 0.8% in pulmonary tuberculosis patients and 2.0% in controls.”

According to the news editors, the researchers concluded: “Significant differences were not observed in genotype or allele frequencies of PTPN22 C1858T in the comparison between pulmonary tuberculosis patients and healthy subjects in our Iranian population sample.”

For more information on this research see: R620W functional polymorphism of protein tyrosine phosphatase non-receptor type 22 is not associated with pulmonary tuberculosis in Zahedan, southeast Iran. Genetics and Molecular Research [electronic Resource], 2012;11(2):1075-81.

Our news journalists report that additional information may be obtained by contacting H.R. Kouhpaye, Research Center for Infectious Diseases and Tropical Medicine, Zahedan University of Medical Sciences, Zahedan, Iran. (2012 Jun 19)
Impact of a 14-year screening programme on tuberculosis transmission among the homeless in Paris

By a News Reporter-Staff News Editor at Life Science Weekly – Data detailed on Tuberculosis have been presented. According to news originating from Paris, France, by NewsRx correspondents, researchers stated “To evaluate the impact of an active case-finding programme on tuberculosis (TB) transmission in homeless shelters in Paris, France. Between 1994 and 1997, an active case-finding programme was implemented in homeless shelters using a mobile radiological screening unit, and continued from 1997 to 2007.”

Our news journalists obtained a quote from the research by the authors, “During these periods, the strains isolated from TB cases diagnosed in the homeless were genotyped by restriction fragment length polymorphism analysis using the insertion sequence IS6110 as a probe. Between 1994 and 2007, 313 new TB cases were diagnosed among the homeless population: 179 through the programme among shelter users, and 134 among homeless people not using shelters. Half of the strains were clustered in 35 distinct patterns (2-48 cases/cluster). The clustering of TB cases steadily decreased in shelters during the 13 years of the survey, from 14.3 to 2.7 related cases per year (P < 0.01) and from 75% to 30% of related cases among all TB cases (P < 0.01). In contrast, there was only a slight trend towards a decrease in homeless people not using shelters. Active case finding in homeless shelters resulted in a decrease in case clustering, mainly in shelter users.”

According to the news editors, the researchers concluded: “Genotyping contributed to confirming the positive impact of the intervention.”


The news correspondents report that additional information may be obtained from C. Bernard, Direct Act Sociale Enfance & Sante, Paris, France. (2012 Jun 12)
Institute of Molecular Biology and Biophysics, Novosibirsk: Relationship between CYP2E1 polymorphism and increase of ALT activity during therapy of patients with pulmonary tuberculosis

By a News Reporter-Staff News Editor at Life Science Weekly – Current study results on Tuberculosis have been published. According to news reporting originating from Novosibirsk, Russia, by NewsRx correspondents, researchers stated “Association of CYP2E1 polymorphism with ALT activity increase was studied in patients with pulmonary tuberculosis receiving therapy by intermittent and daily protocols. The greatest increment of ALT activity in the group receiving therapy by intermittent protocol was seen in the patients with CYP2E1*7632TA genotype.”

Our news editors obtained a quote from the research by the authors from the Institute of Molecular Biology and Biophysics, “In patients with wild homozygotic 1C/1C (6/6) genotype, ALT activity significantly increased, but remained within the normal range (p=0.048). In the group on daily regimen, activity of ALT increased significantly in patients with all genotypes identified. A more pronounced elevation surpassing the median of the upper threshold of ALT norm was observed in patients with 7632TA genotype (p=0.0051) and in patients with 7632TA or -71GT or 1C/1D genotypes in combinations with wild type alleles by other detected polymorphisms (p=0.0277).”

According to the news editors, the researchers concluded: “Detection of the CYP2E1 gene 7632T &lt;A polymorphism was found to be the most informative test for prediction of the hepatotoxic reactions during therapy for tuberculosis.”


The news editors report that additional information may be obtained by contacting A.V. Kudryashov, Institute of Molecular Biology and Biophysics, Siberian Division of Russian Academy of Medical Sciences, Novosibirsk, Russia.

Publisher contact information for the journal Bulletin of Experimental Biology and Medicine is: Springer, 233 Spring Street, New York, NY 10013, USA. (2012 Jun 12)
Polymorphisms of NOD2 and the risk of tuberculosis: a validation study in the Chinese population

By a News Reporter-Staff News Editor at Asia Business Newsweekly

– Data detailed on Leprosy have been presented. According to news reporting originating in Zhenjiang, People’s Republic of China, by VerticalNews journalists, researchers stated “A genome-wide association study (GWAS) of leprosy reported four specific genetic polymorphisms of NOD2 that were associated with susceptibility to Mycobacterium leprae in China. Considering the role of NOD2 in innate immune defence, we performed a study in a Chinese population to determine whether the same SNPs of NOD2 that were associated with disease caused by M.leprae were also associated with disease caused by Mycobacterium tuberculosis.”

The news reporters obtained a quote from the research by the authors, “We performed a frequency-matched casecontrol study in 1043 patients with pulmonary tuberculosis and 808 unaffected controls. All subjects were >15 years old and were Han Chinese from Jiangsu Province. We extracted DNA from a blood sample from each study participant. SNPs of rs3135499, rs7194886, rs8057341 and rs9302752 in the NOD2 gene were genotyped using a TaqMan-based allelic discrimination system. Using all possible patients with tuberculosis as cases, no significant association was found between the four specific SNPs and the risk of tuberculosis. In a subgroup analysis restricted to cases with bacteriologically confirmed tuberculosis (sputum culture positive), the variant genotype of rs7194886 was significantly associated with an altered risk of tuberculosis. Compared with the CC genotype, individuals carrying the CT/TT genotype of rs7194886 had an increased risk [odds ratio (OR) 1.35, 95% confidence interval (CI) (1.05,1.72)]. The association was stronger among tobacco smokers and males. By haplotype analysis, rs9302752Crs7194886T was associated with an increased risk of bacteriologically confirmed tuberculosis (sputum culture positive) (P = 0.039), but it was not significant after correcting for multiple comparisons.”

According to the news reporters, the researchers concluded: “In summary, genetic polymorphisms of the SNP rs7194886 in the NOD2 gene, which were discovered in the GWAS of leprosy, might also be associated with the pulmonary tuberculosis in the Chinese population.”

Southwest University, Chongqing: Comparative genomic structures of Mycobacterium CRISPR-Cas

By a News Reporter-Staff News Editor at Life Science Weekly – New research on Tuberculosis is the subject of a report. According to news reporting originating from Chongqing, People’s Republic of China, by NewsRx correspondents, researchers stated “Clustered regularly interspaced short palindromic repeats (CRISPR) are inheritable genetic elements of many archaea and bacteria, conferring acquired immunity against invading nucleic acids. CRISPR might be indicative of the bacterial niche adaptation and evolutionary.”

Our news editors obtained a quote from the research by the authors from Southwest University, “Mycobacterium is an important genus occupying diverse niches with profound medical and environmental significance. To present a comparative genomic landscape of the Mycobacterium CRISPR, the feature of mycobacterium CRISPR structures with sequenced complete genomes were bioinformatically analyzed. The results show that CRISPR structures can be found among 14 mycobacteria, and all loci are chromosomally located. Long CRISPRs present in three species, namely M. tuberculosis, M. bovis, and M. avium. Integrated CRISPR-Cas system can only be found in M. tuberculosis and M. bovis, with highly conserved repeat sequences, very short leaders, and promoterless. M. tuberculosis and M. bovis repeat sequences cannot form stable RNA secondary structure, consistent with a Cas6-binding sequence. M. avium repeat sequences can form classical stem-loop structure.”

According to the news editors, the researchers concluded: “A three-step model of M. tuberculosis CRISPR-Cas system action was put forward based on the composition and function of cas genes cluster. M. tuberculosis and M. bovis CRISPRs might interfere with the invading nucleic acids, but have somehow lost the capacity to incorporate new spacers and co-evolve with corresponding mycobacteriophages.”

The news editors report that additional information may be obtained by contacting L. He, Institute of Modern Biopharmaceuticals, State Key Laboratory Breeding Base of Eco-Environment and Bio-Resource of the Three Gorges Area, School of Life Sciences, Southwest University, Beibei, Chongqing 400715, People’s Taiwan. (2012 Jun 12)

Jiwaji University, Gwalior: Genetic polymorphisms of CCL2, CCL5, CCR2 and CCR5 genes in Sahariya tribe of North Central India: An association study with pulmonary tuberculosis

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators publish new report on Tuberculosis. According to news reporting originating in Gwalior, India, by NewsRx journalists, researchers stated “The association of genetic variants of chemokines, CCL2 [MCP-1 (monocyte chemoattractant protein-1)], CCL5 [RANTES (regulated on activation, normal T-cell expressed and secreted)] and their receptors CCR2 and CCR5, respectively, earlier reported to be associated with susceptibility to pulmonary tuberculosis (PTB) in certain ethnic populations, were explored in Sahariya tribe, a primitive tribe of North Central India having a high prevalence of TB. We genotyped 215 cases and 215 controls of Sahariya tribe for polymorphisms in CCL2 (-2518A/G, -362G/C) by PCR-RFLP method and in CCR2 (V64I), CCL5 (-403G/A, -28C/G) and CCR5 (-59029G/A) by ARMS-PCR method.”

The news reporters obtained a quote from the research by the authors from Jiwaji University, “The frequencies of ‘AA’ genotype and ‘A’ allele of -403G/A were found significantly higher in cases than in controls (OR, 2.616 [95%CI, 1.302-5.320] and OR, 1.348 [95%CI, 0.980-1.853], respectively). Conversely, the frequencies of ‘AA’ genotype and ‘A’ allele of V64I were significantly (p=0.05 and 0.04, respectively) higher in controls than in cases. Also, the ‘AA’ genotype of V64I was found to provide significant (p=0.05) protection against high bacillary load (3+). Likewise, the comparison of frequencies of different combinations of these polymorphisms further strengthens the association of -403G/A with susceptibility and V64I with resistance to TB in Sahariya tribe. However, no significant association of other polymorphisms with either resistance or susceptibility to TB was found.”

According to the news reporters, the researchers concluded: “Thus, our findings support the association of -403G/A and V64I polymorphisms with genetic susceptibility and resistance to TB, respectively , alone or in combination with other polymorphisms in Sahariya tribe.”

For more information on this research see: Genetic polymorphisms of CCL2, CCL5, CCR2 and CCR5 genes in Sahariya tribe of

Our news correspondents report that additional information may be obtained by contacting G. Mishra, Centre for Genomics, Molecular and Human Genetics, Jiwaji University, Gwalior 474 011, India. (2012 Jun 05)

University of Michigan, Ann Arbor: Identification of factors for tuberculosis transmission via an integrated multidisciplinary approach

By a News Reporter-Staff News Editor at Life Science Weekly – New research on Tuberculosis is the subject of a report. According to news reporting originating from Ann Arbor, Michigan, by NewsRx correspondents, researchers stated “It was reported previously that the major fraction of the recent decrease of tuberculosis incident cases in Arkansas had been due to a decrease in the reactivated infections. Preventing transmission of Mycobacterium tuberculosis is the key to a continued decline in tuberculosis cases.”

Our news editors obtained a quote from the research by the authors from the University of Michigan, “In this study, we integrated epidemiological data analysis and comparative genomics to identify host and microbial factors important to tuberculosis transmission. A significantly higher proportion of cases in large clusters (containing &gt;10 cases) were non-Hispanic black, homeless, less than 65 years old, male sex, smear-positive sputum, excessive use of alcohol, and HIV sero-positive, compared to cases in small clusters (containing 2-5 cases) diagnosed within one year. However, being non-Hispanic black and homeless within the past year were the only two host characteristics that were identified as independent risk factors for being in large clusters. This finding suggests that social behavioral factors have a more important role in transmission of tuberculosis than does the infectiousness of the source.”

According to the news editors, the researchers concluded: “Comparing the genomic content of one of the large cluster strains to that of a non-clustered strain from the same community identified 25 genes that differed between the two strains, potentially contributing to the observed differences in transmission.”

For more information on this research see: Identification of factors for tuberculosis transmission via an integrated multidisciplinary approach. Tuberculosis, 2011;91(3):244-9. (Elsevier - www elsevier com; Tuberculosis - http://www elsevier com/wps/product/cws_home/638428)
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The news editors report that additional information may be obtained by contacting S. Talarico, Dept. of Epidemiology, School of Public Health, University of Michigan, M5124 SPH II, 1415 Washington Heights, Ann Arbor, MI 48109-2029, United States. (2012 Jun 05)

Patent Application Titled “Systems and Methods for Detecting Biomarkers of Interest” Published Online

By a News Reporter-Staff News Editor at Biotech Week – According to news reporting originating from Washington, D.C., by NewsRx journalists, a patent application by the inventors Seelig, Georg (Seattle, WA); Lutz, Barry (Seattle, WA), filed on September 4, 2012, was made available online on March 28, 2013.

No assignee for this patent application, patent application serial number 603298, has been made.

Reporters obtained the following quote from the background information supplied by the inventors: “Pathogen-derived proteins and nucleic acids have important roles as diagnostic markers for infectious diseases. For example, the detection of just a single molecular marker, such as a DNA sequence associated with the M. tuberculosis complex, can sometimes be indicative of a disease state. However, a reliable diagnosis and treatment decision often requires interpreting a combination of markers via complex algorithms. For example, in the case of DNA testing for tuberculosis (TB), the treatment decision requires interpretation of markers associated with the M. tuberculosis complex, TB antibiotic resistance and even HIV-coinfection (McNerney et al., 2011).

“DNA-based circuits and reaction networks may be designed that can be used for the analysis of complex molecular mixtures. Synthetic molecular circuits that are capable of information processing and computation have been built using a range of approaches. Examples include synthetic gene regulatory and signaling networks (Isaacs et al., 2006; Yeh et al., 2007; Win et al., 2008), computational networks using in vitro transcription (Kim et al., 2006; Simpson et al., 2009), digital logic circuits based on small molecules (de Silva et al., 2007) or peptides (Ashkenasy et al., 2004), and the nonlinear chemical reaction networks underlying the Belousov Zhabotinskii reaction and related phenomena (Epstein et al., 1998). In these circuits, information is stored in the concentrations, spatial localizations, and/or chemical properties of molecules; chemical reactions between molecules implement molecular information processing. Most of these systems lack the flexibility and modularity that would make them useful for biosensing applications. For proteins and small molecules in particular, the de novo design of individual functional molecular sensors and logic gates is difficult and integration of multiple elements into circuits is even more challenging.
“Because of the predictability of Watson-Crick base pairing, nucleic acid-based systems avoid some of these constraints and can be used to implement modular and scalable molecular computation. Initial demonstrations of nucleic acid logic circuits took advantage of enzyme or deoxyribozyme catalysis (Lu et al., 2006; Willner et al., 2008). Also, a DNA and enzyme-based molecular automaton was developed that could perform a computation where the outcome (the release of an antisense drug mimic) was dependent on the absence or presence of specific inputs (ssDNA with sequence analogous to diagnostically relevant mRNA) (Benenson et al., 2001; Benenson et al., 2004). Stojanovic and collaborators developed deoxyribozyme based logic gates (Stojanovic et al., 2002) and used these gates to form a variety of logic circuits (Stojanovic et al., 2003; Lederman et al., 2006; Yashin et al., 2007). Penchovsky and Breaker (Penchovsky et al., 2005) developed allosteric ribozymes that could implement cascaded logic using DNA inputs and RNA outputs. More recent work (Takahashi et al., 2006; Frezza et al., 2007; Cardelli et al., 2008; Qian et al., 2011; Seelig et al., 2006; Soloveichik et al., 2010), has relied on hybridization and strand displacement as a mechanism for implementing molecular logic.

“Although the field of DNA-based circuits and reaction networks has several promising approaches, such approaches are limited by their ability to discriminate between closely related molecules, especially when the sequence of the related molecules differs by a small number nucleotides. Thus, it would be desirable to design a system capable of robustly distinguishing molecules having related or similar sequences.”

In addition to obtaining background information on this patent application, NewsRx editors also obtained the inventors’ summary information for this patent application: “In one embodiment, a strand displacement system is provided. Such a system may include a first nucleic acid catalyst molecule; a nucleic acid gate molecule, wherein the first nucleic acid catalyst molecule binds the nucleic acid gate molecule forming a nucleic acid gate-catalyst complex and releases an output molecule; and a nucleic acid sink molecule. The nucleic acid sink molecule sequesters a putative second nucleic acid catalyst, wherein the second nucleic acid catalyst differs from the first nucleic acid catalyst molecule by at least one nucleotide. In some embodiments, the first nucleic acid catalyst includes a biomarker of interest, such as a DNA or RNA molecule. In other embodiments, the first nucleic acid catalyst is a nucleic acid aptamer which binds an amino acid-based biomarker of interest. The system may also include a nucleic acid fuel molecule, wherein the nucleic acid fuel molecule binds the nucleic acid gate/catalyst complex and releases the first nucleic acid catalyst molecule.

“In another embodiment, the strand displacement system may be part of a paper-based diagnostic tool. The paper-based diagnostic tool
may include a paper device that comprises a set of reaction components attached to at least one reaction zone, wherein the set of reaction components includes a nucleic acid gate molecule and a nucleic acid sink molecule; and a set of output capture probes attached to at least one detection zone, wherein the output capture probes are complementary to an output molecule released by the nucleic acid gate molecule.

"In other embodiments, methods for detecting a biomarker of interest in a biological sample are provided. Such methods may include a step of exposing the biological sample which contains or is suspected of containing a first nucleic acid catalyst molecule to a reaction zone of a paper-based diagnostic tool, wherein the first nucleic acid catalyst molecule comprises the biomarker of interest and the reaction zone comprises a set of reaction components which includes a nucleic acid gate molecule and a nucleic acid sink molecule, and. The methods may further include a step of detecting the biomarker of interest by visualizing a change in signal in a detection zone of the paper-based diagnostic tool, wherein the change in signal is produced when an output molecule binds a nucleic acid capture molecule that is attached to the detection zone.

BRIEF DESCRIPTION OF THE DRAWINGS

"FIG. 1 illustrates examples of double-stranded toehold exchange probes. (A) shows that hybridization is the binding process of complementary single-stranded nucleic acids. Formation of base pairs provides energy gain during hybridization. When there is a mismatch, the system will gain less energy, but the reaction still goes forward. (B) shows an example of strand displacement, which is the process of using one strand to displace another one. The single-stranded input binds to a double-stranded complex using partially single-stranded regions which are called toeholds (green). Because the black regions are identical for both top strands, a three way branch migration will start. The top strand, which originally binds the bottom strand, will fall off. (C) by adding a toehold on the other end (blue), the strand that fell off in (B) may re-bind the bottom strand, making the reaction reversible. This binding exchange is called toehold exchange. During this process, there is almost no enthalpy change and very few entropy change independent of environment. This method has been used to characterize nucleic acid dynamics, build catalysts, and make specific detection probes. (D) shows a four way strand displacement, which happens between four single-stranded nucleic acid and two sets of binding. The junction between four strands is called a holliday junction, and it represents an intermediate stage in genetic recombination.

"FIG. 2 illustrates how strand displacement can be used to detect single-stranded nucleic acids, according to some embodiments. (A) A strand displacement reaction where an input strand (1:2:3) displaces
an output strand (2:3:4) from a gate/sensor complex. DNA is represented as directional lines, with the arrow denoting the 3’ end. Domains are labeled by numbers, with _ denoting Watson-Crick complementarity. Multiple elementary steps are indicated: (1) binding of toeholds 1 and 1*; (2) a random walk branch migration process where domain 2 of strand 2: 3: 4 is partially displaced by domain 2 of strand 1: 2: 3; (3) the separation of domains 3 and 3* and release of an output strand. 

(B) The output strand of one strand displacement reaction can serve as an input to a downstream reaction. In this case, a reporter complex is used to detect the output strand released in the upstream reaction. The two strands in the reporter complex are chemically labeled with a fluorophore (magenta star) and a quencher (dark blue dot), respectively. Separation of the fluorophore and quencher lead to an increase in fluorescence. 

(C) Example kinetics traces for the two-step reaction sketched in (A) and (B). Gate complex is at 10 nM, readout at 13 nM, input concentration is varied from 0 nM to 10 nM. Reactions are run at 25°C. in TAE buffer with 12.5 mM Mg++. Domain 1 is 5 nucleotides (nt), domains 2 and 4 are 15 nt and domain 3 is 6 nt. The data can be fit well with a simple model assuming two sequential bimolecular reactions. 

(D) Strand displacement kinetics strongly depends on the free energy released when domains 1 and 1* hybridize. Reaction rates increase over several orders of magnitude as the toehold length is increased from 0-6 nt.

“FIG. 3 illustrates a catalytic system that includes a fuel molecule. The reaction starts with the toehold binding of the Gate and the Input (catalyst), followed by branch migration. The Output strand will be released from the Gate through branch migration, and the hidden toehold is exposed. A single-stranded Fuel molecule may bind on the exposed toehold and release the Input molecule. The Input can then be reused to trigger release of more Output strands to enhance the signal. The Output strands may react with a reporter to produce a signal.

“FIG. 4 illustrates that a seesaw gate may be used in a system for catalytic signal amplification, in accordance with some embodiments, which provides the basis for the biosensing systems provided herein. (A) The amplifier includes one double-stranded complex (‘gate’) and an auxiliary strand ‘fuel.’ The catalyst strand initiates the reaction by binding the gate through toehold mediated strand displacement. In the Examples provided herein, the role of the catalyst is played by a single-stranded biomarker of interest. 

(B) The reaction mechanism for the seesaw gate is initiated by the catalyst. The catalyst (1:2) binds the double stranded gate, resulting in release of the output (2:3:4). Next, the fuel strand (2:3) binds and releases the catalyst. See Qian et al., 2011 for more details regarding the seesaw gate system. (C) In this catalytic signal amplification experiment, the gate and fuel are at 10 nM.
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and the catalyst concentration is varied. A readout gate is used to detect release of the output strand. The concentration of the readout is 13 nM.

“FIG. 5 shows a logic circuit using a combination of microRNA and related precursor inputs and corresponding gates. (A) Signal propagation through an in vitro chemical circuit combining AND, OR, sequence translation, input amplification, and signal restoration. The five-layer circuit includes a total of 11 gates and accepts six inputs. Corresponding DNA structures are shown with the circuit diagram (inset). (B) Fluorescence traces of circuit operation without and with the signal restoration module (threshold plus amplifier). The traces for input conditions corresponding to a logical TRUE output (ON) are clearly distinguishable from the logical FALSE output (OFF). Cases tested include when all inputs are present, all cases in which exactly one input is missing, and combinations of inputs that turn off an OR clause.

“FIG. 6 is a schematic diagram showing a variety of diagnostic tests available, including lateral flow tests, instrumented PCR, line probe assays, and DNA/RNA microarrays. The diagnostics tests are arranged in accordance with their strengths and suitable use. Tests that are show farthest to the right are most suitable for a large numbers of markers that can improve diagnosis and provide comparative results, but require complex interpretation algorithms. Those shown toward the left are most suitable for use with single biomarkers and provide for easy to use, rapid results.

“FIG. 7 shows a series of multi-step processes in paper networks, according to some embodiments. (A) Sugar solutions dried on each leg create fluidic time delays that can be controlled by the sugar concentration. Each fluid source has a limited volume so it shuts off at a programmed time. The result is delivery of multiple fluids to a detection zone in a timed sequence. (B) A folding card design is used to contact fluid source pads to the network for a single step initiation of the fluid sequence. (C) Fluid from each leg is delivered in a timed sequence on a time scale appropriate for rapid point of care assays (30 minutes). Reagents can be stored in dry form on the pads, such that the user only adds a sample and buffer or water. Alternative designs have been used to perform automated assay sequences for wash steps and chemical signal amplification.

“FIG. 8 shows a mechanism of detecting mismatch discrimination according to some embodiments. (A) A combination of a seesaw amplifier and a ‘sink’ complex can be used to distinguish catalyst strand that differs by only a single base. (B) A seesaw amplifier without a sink can be used for kinetic discrimination of the inputs. However, end-point discrimination is not possible. Amplifier components are 10 nM, readouts are 13 nM and all catalysts are 5 nM. Experiments are performed in TAE with 12.5 mM Mg++. (C) The input can be inhibited by addition of
a sink. When the input binds the sink and completes branch migration, the input will not be released again. (D) Gates and sinks have different binding affinities for binding correct and mismatched targets. The correct input (catalyst) binds to the amplifier gate faster than it binds to the inhibitory sink. Although the input may be degraded slowly by the sink, a fast catalytic reaction of the input and gate ensures completion of amplification. The mutated input (catalyst with mismatched mutation) will be inhibited rapidly and thus almost no signal will be triggered. (E) Combining the seesaw amplifier with a sink enables endpoint discrimination. Reaction conditions are similar to those in (b). The sink concentration is 10 nM. (F) Kinetics with and without the mismatch can be predicted using binding energy. Reactions involving mis-binding are significantly slower. For idea rapid endpoint discrimination, the correct catalyst toehold binding should have energy around 10 kcal/mol.

“FIG. 9 shows a system for detection of DNA analogs of the let-7 family according to some embodiments. (A) The let-7 family is a set of miRNAs that have very similar sequences (SEQ ID NOs:1-9). (B) Experimental results from the let-7 detection system indicate that the catalytic system for let-A can be triggered by several other let-7 mismatched inputs. (C) The same catalytic system as shown in (B) is prepared using various sinks to sequester the mismatched let-7 family members. When sinks are added to the reaction, clear endpoint discrimination is seen for correct and mismatched inputs. With the sink, mismatched catalysts are degraded, producing little signal which is similar to that seen with a system leak. (D) Two catalytic systems, let-A and let-C, were run in parallel using different output channels, the results of which are shown in (E).

“FIG. 10 illustrates double-stranded toehold exchange probes. (A) shows a double toehold exchange probe P (or PtPb), which includes a fork shaped toehold. Such toeholds help initiate four-way branch migration. In this case, 5 new base pairs (orange and purple) are formed through the course of the reaction, and 4 base pairs (blue and green single-stranded regions) and a fluorophore-quencher interaction are broken. Toeholds before and after the reaction have similar lengths so that the standard free energy of the forward reaction is about 0 kcal/mol. Thus, when the correct target reacts with the probe, roughly equal amounts of reactant and products are seen at equilibrium. (B) shows a double-stranded toehold exchange reaction with a spurious target S (or StSb). This forward four-way branch migration at the mutated position is very slow and not favorable due to the energy penalty caused by mismatch binding. The intermediate step shown possesses a much higher backward reaction rate constant. Consequently, there should be much fewer products at equilibrium.
“FIG. 11 shows the results of a fluorescence assay. (A) shows sequences of correct and single-base-changed targets, and a corresponding probe. The probe is functionalized with the ROX fluorophore and the Iowa Black Red Quencher. (B) shows the kinetic traces of the reaction between the probe and the correct target (top) or spurious insertion target (bottom) with various concentrations of target. In all traces, [PtPb]=10 nM. (C) shows a log-log plot of hybridization yield X as a function of the concentration of the target. Dots represent experimental values of X, and lines represent the analytic relationship between X and [Target], using a least-squares fit for the y-intercept (X at equal stoichiometry). Discrimination factor (Q) is defined as $Q=(X_{\text{sub.correct}})/(X_{\text{sub.mutated}})$, and concentration tolerance $\delta$ is defined as $R=(TtTb)_{\text{sub.X=0.5}}/([StSb])_{\text{sub.X=0.5}}$, the ratio of concentrations needed to achieve 50% yield at equilibrium.

“FIG. 12 shows robustness over mutation position identities, as well as temperature and salinity. (A) shows tested mutation position and identities. (B) shows a kinetics trace for all correct targets (Correct) and mutated targets (All SNPs). The mutated targets give little to no signal. (C) shows the discrimination factor (Q) as measured for the targets shown. The discrimination factor is defined as $Q=(X_{\text{sub.correct}})/(X_{\text{sub.mutated}})$, and has a median of 43. (D) shows that mutated target m8G-C was tested under different temperature and salinity.

“FIG. 13 shows the detection of a mutation in the RpoB gene from M. tuberculosis (TB). (A) shows the subsequence of TB (SEQ ID NO:9). Two systems of different length and sources were tested. The short 50 nt target was made synthetically, and the 100 nt target was made from a plasmid containing the subsequence of TB using PCR. (B) shows testing of one mutation at position 526 with a s50 nt TB subsequence under various concentrations as shown. (C) shows single strands with a desired toehold end could be generated from unbalanced PCR, wherein one primer has 100 times lower concentration than ordinary PCR. Annealing the two single strands, the double strand with toeholds may be generated. (D) shows the results of testing the purified annealing product.

“FIG. 14 shows various methods for diagnosing TB antibiotic resistance according to some embodiments. (A) An example of TB targets and interpretation algorithm (partial set) for identification of resistance (RMP: rifampin, INH: isoniazid). Adapted from the Genotype MTBDR+ line probe assay (Niemz et al., 2011). (B) A logic circuit diagram for a diagnostic circuit for detection of different markers associated with TB antibiotic resistance. The circuit combines an embedded analysis with a simplified readout.

“FIG. 15 shows a schematic of a two-stage strip for sequencing DNA circuit reactions and visually detecting output DNA according to some
embodiments. Labeled outputs that are prebound with immobilized DNA circuit elements are only released when the DNA circuit is completed by input DNA. These labeled outputs are released by a fluidic timer to be captured by hybridization for visual detection. Fluidic timers are made from dried sugar; time delays are adjustable from seconds to an hour.

“FIG. 16 shows the length of paper-based fluidic delays as a function of percentage of dried sugar according to some embodiments. (A) Delays are created by dipping strips into sugar solutions with different concentrations, followed by drying; delays from minutes to over an hour are possible. A relative delay of 10 equates to approximately 300 seconds for the strips used here. (B) Sugar solutions pipetted onto a paper strip create delays used to stage fluids in different reaction zones.”


**Patent Issued for Bipartite Inhibitors of Bacterial RNA Polymerase**

By a News Reporter-Staff News Editor at Life Science Weekly – Rutgers, The State University of New Jersey (New Brunswick, NJ) has been issued patent number 8372839, according to news reporting originating out of Alexandria, Virginia, by NewsRx editors.

The patent’s inventors are Ebright, Richard H. (North Brunswick, NJ); Wang, Dongye (Edison, NJ).

This patent was filed on November 4, 2006 and was cleared and issued on February 12, 2013.

New approaches to drug development are necessary to combat the ever-increasing number of antibiotic-resistant pathogens.


"The structures reveal that RNAP-bacterial or eukaryotic-has a shape reminiscent of a crab claw. The two ‘pincers’ of the ‘claw’ define the active-center cleft that can accommodate a double-stranded nucleic acid–and which has the active-center Mg.sup.2+ at its base. The largest subunit (.beta.’ in bacterial RNAP) makes up one pincer, termed the ‘clamp,’ and part of the base of the active-center cleft. The second-largest subunit (.beta. in bacterial RNAP) makes up the other pincer and part of the base of the active-center cleft.


"Bacterial RNAP is a proven target for antibacterial therapy (Chopra, et al. (2002) J. Appl. Microbiol. 92, 4S-15S; Darst, S. (2004) Trends Biochem. Sci. 29, 159-162). The suitability of bacterial RNAP as a target for antibacterial therapy follows from the fact that bacterial RNAP is an essential enzyme (permitting efficacy), the fact that bacterial RNAP subunit sequences are conserved (providing a basis for
broad-spectrum activity), and the fact that bacterial RNAP subunit sequences are only weakly conserved in eukaryotic RNAP I, RNAP II, and RNAP III (providing a basis for therapeutic selectivity).


Supplementing the background information on this patent, NewsRx reporters also obtained the inventors’ summary information for this patent: “The invention provides a new class of inhibitors of bacterial RNAP. Importantly, the invention provides inhibitors that can exhibit potencies higher than those of known inhibitors. Especially importantly, the invention provides inhibitors that can inhibit bacterial RNAP derivatives resistant to known inhibitors.

“The invention provides bipartite inhibitors of bacterial RNAP that contain: (1) a first moiety that binds to the rifamycin binding site (‘Rif pocket’) of bacterial RNAP; (2) a second moiety that binds to the secondary channel of bacterial RNAP; and (3) a linker connecting said first and second moieties.

“The bipartite inhibitors can interact with bacterial RNAP both through the first moiety and through the second moiety. Their ability to interact with bacterial RNAP through two moieties (both the first moiety and the second moiety) can confer an affinity for interaction with bacterial RNAP that is higher than the affinity of the first moiety and the affinity of the second moiety. Their ability to interact to interact with bacterial RNAP through two moieties (both the first moiety and the second moiety) also can confer an ability to interact with a bacterial RNAP derivative resistant to at least one of the first moiety and the second moiety.

“The bipartite inhibitors have applications in control of bacterial gene expression, control of bacterial growth, antibacterial chemistry, and antibacterial therapy.

“The invention also provides a method for preparing a compound that contains: (1) a first moiety that binds to the rifamycin binding site (‘Rif pocket’) of bacterial RNAP; (2) a second moiety that binds to the secondary channel of bacterial RNAP; and (3) a linker connecting said first and second moieties. The method includes providing precursors.
X-.alpha.' and '.alpha.-Y, and reacting moieties .alpha.' and '.alpha. to form .alpha..

“For example, one precursor may contain an activated ester and the other precursor contain an amine. One precursor may contain a haloacetyl moiety and the other precursor contain an amine. One precursor may contain a haloacetyl moiety and the other precursor contain a sulfhydryl. One precursor may contain an azide and the other precursor contain an alkyne. One precursor may contain an azide and the other precursor contain a phosphine. One precursor may contain a boronic acid and the other precursor contain a substituted phenol. One precursor may contain a phenylboronic acid and the other precursor contain salicylhydroxamic acid.

“These and other aspects of the present invention will be better appreciated by reference to the following drawings and Detailed Description.”

Chapter 4

Immunology

National Autonomous University, Mexico City: Monocytes from tuberculosis patients that exhibit cleaved caspase 9 and denaturalized cytochrome c are more susceptible to death mediated by Toll-like receptor 2

By a News Reporter-Staff News Editor at Life Science Weekly – Current study results on Mycobacterium Infections have been published. According to news reporting originating in Mexico City, Mexico, by NewsRx journalists, research stated, “Experimental models have shown that lipoproteins from Mycobacterium tuberculosis induce apoptosis via Toll-like receptor 2 (TLR2) in the THP-1 cell line and in monocyte-derived macrophages from healthy volunteers. We found an increased percentage of circulating monocytes in patients with tuberculosis (TB) in comparison to healthy controls.”

The news reporters obtained a quote from the research from National Autonomous University, “Patients with TB showed a higher TLR2 and TLR4 expression density on monocytes, and a higher proportion of TLR2(+) monocytes, as well as increased serum tumor necrosis factor-a level. In culture, monocytes from TB patients were more susceptible to death than monocytes from healthy controls. Moreover, death-susceptible monocytes were positive to both TLR2 and TLR4 at the start of culture. Freshly obtained monocytes from TB patients exhibited cleaved caspase 9 and denaturalized cytochrome c. For levels of caspase 8, apoptosis-regulating signal kinase 1, and phospho-p38 mitogen-activated protein kinase there was no difference between samples from TB patients and from healthy controls. The culture filtrate antigen extract from M. tuberculosis H37Rv strain induced the death of monocytes from patient with TB after a 4-hr incubation, which was abrogated by neutralizing antibodies for TLR2 but not TLR4. Similarly, Pam3CSK4, a synthetic agonist triacylated ligand to TLR2, also
induced the death of monocytes, although it did not increase levels of cleaved caspase 9."

According to the news reporters, the research concluded: "Our findings suggest that monocytes from TB patients are more susceptible to death, probably through mitochondrial damage, and that cell death increases in the presence of mycobacterial antigen by a TLR2-dependent pathway."


Our news correspondents report that additional information may be obtained by contacting L. Chavez-Galan, Laboratorio de Inmunologia Integrativa, Universidad Nacional Autonoma de Mexico, Mexico City, Mexico. (2013 Apr 23)

**University of Barcelona: Interferon-gamma release assays versus tuberculin skin test for targeting people for tuberculosis preventive treatment: An evidence-based review**

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators publish new report on Infection Research. According to news originating from Barcelona, Spain, by NewsRx correspondents, research stated, “To assess whether Interferon-gamma release assays (IGRAs) reduce the number of people considered for tuberculosis (TB) preventive treatment without increasing subsequent active disease. Longitudinal studies with both tuberculin skin test (TST) and IGRAs were identified through a PubMed search.”

Our news journalists obtained a quote from the research from the University of Barcelona, “Reductions in diagnosis of TB infection and increases in incident TB in people considered not infected, using IGRAs either instead of TST or as a confirmatory test (two-step approach), were assessed. In comparison with TST alone, the pooled reductions in diagnosis of TB infection obtained with IGRAs were 16.7% and 5.8% at 5 and 10 mm cut-offs respectively, and 24.5% and 12.4% at 5 and 10 mm respectively with the two-step approach. Compared with TST alone, incident TB among people considered not infected increased with the two-step approach (0.94% with T-SPOT®.TB and 1.1% with QuantiFERON®-TB Gold In-Tube) in one of seven studies in high-income countries. In middle-and low-income countries, two of four studies presented increases (0.08 and 0.03 per 100 patient-years respectively) with the two-step approach.”
According to the news editors, the research concluded: “In high-income countries, the use of IGRAs, either instead of TST or as confirmatory test reduces the number of people considered for preventive treatment, without a significant risk of subsequent active disease.”


The news correspondents report that additional information may be obtained from L. Munoz, University of Barcelona, Dept. of Clin Sci, Barcelona 08907, Spain. (2013 Apr 23)

**University of Stellenbosch, Tygerberg: Plasma cytokines and chemokines differentiate between active disease and non-active tuberculosis infection**

By a News Reporter-Staff News Editor at AIDS Weekly – Investigators discuss new findings in Infection Research. According to news reporting originating in Tygerberg, South Africa, by NewsRx journalists, research stated, “To analyse cytokines and chemokines from unstimulated plasma samples for detection of active TB disease, latent TB, discriminating active TB cases from latently infected contacts and for monitoring anti TB treatment. We analysed ex vivo plasma samples from 33 TB patients (17 HIV negative and 16 HIV positive) and 30 healthy household contacts with Luminex.”

The news reporters obtained a quote from the research from the University of Stellenbosch, “We found statistically significant differences (p \textless 0.05) in median plasma concentrations of EGF, fractalkine, IFN-gamma, IL-4, MCP-3 and IP-10 between contacts and TB patients. Single cytokines or chemokines predict with an area under the Receiver Operating Characteristic (ROC) curve of 0.59 for VEGF to 0.98 for IP 10 while a combination of fractalkine, IFN-g, IL-4, IP-10 and TNF identified 96.87% of TB cases and 100% of household contacts. However, none of the cytokines were significantly different in QFT positive and QFT negative contacts (p \textgreater 0.05). HIV does not affect the median plasma level of any of the cytokines or chemokines and there was not significant difference between HIV positive and HIV negative TB patients (p \textgreater 0.05) in any of the cytokines or chemokines. The median plasma concentrations of IFN-gamma, IL-4, MCP-3, MIP-1 beta and IP-10 were significantly different (p \textless 0.05) before treatment and after treatment.”
According to the news reporters, the research concluded: “Plasma cytokines and chemokines could be used as immunological markers for diagnosing active TB disease and for monitoring effective antituberculosis therapy.”


Our news correspondents report that additional information may be obtained by contacting A. Mihret, University of Stellenbosch, Fac Sci, Dept. of Stat & Actuarial Sci, Center Stat Consultat, ZA-7505 Tygerberg, South Africa. (2013 Apr 22)

**Yonsei University, Seoul: Comparison of the tuberculin skin test and interferon-gamma release assay for the diagnosis of latent tuberculosis infection before kidney transplantation**

By a News Reporter-Staff News Editor at Life Science Weekly – Data detailed on Infection Research have been presented. According to news reporting from Seoul, South Korea, by NewsRx journalists, research stated, “The evaluation of latent tuberculosis infection (LTBI) is recommended before kidney transplantation. The interferon-gamma release assay has been reported to be more specific than the tuberculin skin test (TST) for detecting LTBI.”

The news correspondents obtained a quote from the research from Yonsei University, “We compared the TST and QuantiPERON-TB Gold In-Tube test (QFT-GIT) for the screening for LTBI and determined the agreement between the two tests in renal transplant recipients before transplantation. Adult patients who were evaluated for renal transplantation between May 2010 and February 2012 at Severance Hospital in South Korea were prospectively enrolled. We performed TST and QFT-GIT. Of the 126 patients, 23 (19.3 %) had positive TST results and 53 (42.1 %) had positive QFT-GIT results. Agreement between the TST and QFT-GIT was fair (kappa = 0.26, P<0.001). The induration size of TST was significantly correlated with a positive rate of QFT-GIT (P = 0.015). Age (odds ratio [OR] 1.08, 95 % confidence interval [CI] 1.03-1.13, P = 0.003), male sex (OR 2.73, 95 % CI 1.17-6.38, P = 0.021), and risk for LTBI (OR 4.62, 95 % CI 1.15-18.64, P = 0.031) were significantly associated with positive QFT-GIT results. For positive TST results, only male sex was associated (OR 4.29, 95 % CI 1.40-13.20, P
The positivity for QFT-GIT was higher than the positivity for TST, and QFT-GIT more accurately reflected the risk for LTBI."

According to the news reporters, the research concluded: “However, a further longitudinal study is needed in order to confirm that the QFT-GIT test can truly predict the development of TB after renal transplantation.”

For more information on this research see: Comparison of the tuberculin skin test and interferon-gamma release assay for the diagnosis of latent tuberculosis infection before kidney transplantation. *Infection*, 2013;41(1):103-110. *Infection* can be contacted at: Springer Heidelberg, Tiergartenstrasse 17, D-69121 Heidelberg, Germany. (Springer - www.springer.com; Infection - http://www.springerlink.com/content/0300-8126/)

Our news journalists report that additional information may be obtained by contacting S.Y. Kim, Yonsei University, Coll Med, Res Inst Transplantat, Dept. of Surg, Seoul 120752, South Korea. (2013 Apr 09)

**Department of ENT, Maharashtra: Primary tuberculosis of nasopharynx (adenoid)- a rare presentation**

By a News Reporter-Staff News Editor at Tuberculosis Week – New research on Tuberculosis is the subject of a report. According to news originating from Maharashtra, India, by NewsRx correspondents, research stated, “Tuberculosis has global presence and no part of human body is immune to it, most frequent site beings lungs. Nasopharyngeal tuberculosis is a rare type of extrapulmonary tuberculosis comprising only less than 1% of tuberculosis found in the upper respiratory tract.”

Our news journalists obtained a quote from the research from the Department of ENT, “The authors are presenting here a case of primary tuberculousis affecting the nasopharynx (adenoids) which is one of the rare differential diagnosis of nasopharyngeal mass. Isolated nasopharyngeal tuberculosis is a rare condition even in the endemic areas. In literature there are varied clinical presentations of nasopharyngeal tuberculosis. Tuberculosis should be one of the differential diagnosis of nasopharyngeal lesion. Biopsy and histologic study should be performed in every patient to avoid misdiagnosis.”

According to the news editors, the research concluded: “When treated properly, nasopharyngeal tuberculosis carries a excellent prognosis, and complete resolution of disease is the rule.”

University of Toulouse: Dressed not to kill: CD16(+) monocytes impair immune defence against tuberculosis

By a News Reporter-Staff News Editor at Tuberculosis Week – Current study results on Immunology have been published. According to news reporting from Toulouse, France, by NewsRx journalists, research stated, “Monocytes are blood leukocytes that can differentiate into several phagocytic cell types, including DCs, which are instrumental to the inflammatory response and host defence against microbes.”

The news correspondents obtained a quote from the research from the University of Toulouse, “A study published in this issue of the European Journal of Immunology by Balboa et al. [Eur. J. Immunol. 2013. 43: 335-347] suggests that a shift of the CD16 monocyte population toward a CD16+ subpopulation may represent an immune evasion strategy that ultimately favors persistence of Mycobacterium tuberculosis.”

According to the news reporters, the research concluded: “Together with other recent reports, the article by Balboa et al. sheds new light on the function of CD16+ monocytes in health and disease; in this commentary, we discuss the implications stemming from these findings.”


Our news journalists report that additional information may be obtained by contacting G. Lugo-Villarino, University of Toulouse, Inst Pharmacol & Biol Struct, Univ Toulouse, F-31062 Toulouse, France. (2013 Mar 25)
National Center for Scientific Research (CNRS), Toulouse: TAC from Mycobacterium tuberculosis: a paradigm for stress-responsive toxin-antitoxin systems controlled by SecB-like chaperones

By a News Reporter-Staff News Editor at Life Science Weekly – Current study results on Cell Stress and Chaperones have been published. According to news reporting originating in Toulouse, France, by NewsRx journalists, research stated, “Bacterial type II toxin-antitoxins (TAs) are two-component systems that modulate growth in response to specific stress conditions, thus promoting adaptation and persistence. The major human pathogen Mycobacterium tuberculosis potentially encodes 75 TAs and it has been proposed that persistence induced by active toxins might be relevant for its pathogenesis.”

The news reporters obtained a quote from the research from National Center for Scientific Research (CNRS), “In this work, we focus on the newly discovered toxin-antitoxin-chaperone (TAC) system of M. tuberculosis, an atypical stress-responsive TA system tightly controlled by a molecular chaperone that shows similarity to the canonical SecB chaperone involved in Sec-dependent protein export in Gram-negative bacteria. We performed a large-scale genome screening to reconstruct the evolutionary history of TAC systems and found that TAC is not restricted to mycobacteria and seems to have disseminated in diverse taxonomic groups by horizontal gene transfer.”

According to the news reporters, the research concluded: “Our results suggest that TAC chaperones are evolutionary related to the solitary chaperone SecB and have diverged to become specialized toward their cognate antitoxins.”


Our news correspondents report that additional information may be obtained by contacting A. Sala, Laboratoire de Microbiologie et Génétique Moléculaires, Centre National de la Recherche Scientifique and Université Paul Sabatier, 31000, Toulouse, France. (2013 Mar 19)
McMaster University, Hamilton: Immunotherapeutic effects of recombinant adenovirus encoding granulocytemacrophage colony-stimulating factor in experimental pulmonary tuberculosis

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – Researchers detail new data in Immunology. According to news originating from Hamilton, Canada, by NewsRx correspondents, research stated, “BALB/c mice with pulmonary tuberculosis (TB) develop a T helper cell type 1 that temporarily controls bacterial growth. Bacterial proliferation increases, accompanied by decreasing expression of interferon (IFN)-, tumour necrosis factor (TNF)- and inducible nitric oxide synthase (iNOS).”

Our news journalists obtained a quote from the research from McMaster University, “Activation of dendritic cells (DCs) is delayed. Intratracheal administration of only one dose of recombinant adenoviruses encoding granulocytemacrophage colony-stimulating factor (AdGM-CSF) 1 day before Mycobacterium tuberculosis (Mtb) infection produced a significant decrease of pulmonary bacterial loads, higher activated DCs and increased expression of TNF-, IFN- and iNOS. When AdGM-CSF was given in female mice B6D2F1 (C57BL/6J X DBA/2J) infected with a low Mtb dose to induce chronic infection similar to latent infection and corticosterone was used to induce reactivation, a very low bacilli burden in lungs was detected, and the same effect was observed in healthy mice co-housed with mice infected with mild and highly virulent bacteria in a model of transmissibility.”

According to the news editors, the research concluded: “Thus, GM-CSF is a significant cytokine in the immune protection against Mtb and gene therapy with AdGM-CSF increased protective immunity when administered in a single dose 1 day before Mtb infection in a model of progressive disease, and when used to prevent reactivation of latent infection or transmission.”


The news correspondents report that additional information may be obtained from A. Francisco-Cruz, McMaster University, Dept. of Pathol & Mol Med, Hamilton, ON, Canada. (2013 Mar 18)
CONICET, Buenos Aires: Impaired dendritic cell differentiation of CD16-positive monocytes in tuberculosis: Role of p38 MAPK

By a News Reporter-Staff News Editor at Tuberculosis Week – Investigators publish new report on Immunology. According to news originating from Buenos Aires, Argentina, by NewsRx correspondents, research stated, “Tuberculosis (TB) is one of the world’s most pernicious diseases mainly due to immune evasion strategies displayed by its causative agent Mycobacterium tuberculosis (Mtb). Blood monocytes (Mos) represent an important source of DCs during chronic infections; consequently, the alteration of their differentiation constitutes an escape mechanism leading to mycobacterial persistence.”

Our news journalists obtained a quote from the research from CONICET, “We evaluated whether the CD16(+) /CD16(-) Mo ratio could be associated with the impaired Mo differentiation into DCs found in TB patients. The phenotype and ability to stimulate Mtb-specific memory clones DCs from isolated Mo subsets were assessed. We found that CD16(-) Mos differentiated into CD1a(+) DC-SIGN(high) cells achieving an efficient recall response, while CD16(+) Mos differentiated into a CD1a(-) DC-SIGN(low) population characterized by a poor mycobacterial Ag-presenting capacity. The high and sustained phosphorylated p38 expression observed in CD16(+) Mos was involved in the altered DC profile given that its blockage restored DC phenotype and its activation impaired CD16(-) Mo differentiation. Furthermore, depletion of CD16(+) Mos indeed improved the differentiation of Mos from TB patients toward CD1a(+) DC-SIGN(high) DCs.”

According to the news editors, the research concluded: “Therefore, Mos from TB patients are less prone to differentiate into DCs due to their increased proportion of CD16(+) Mos, suggesting that during Mtb infection Mo subsets may have different fates after entering the lungs.”


The news correspondents report that additional information may be obtained from L. Balboa, IMEX-CONICET, Academia Nacional de Medicina, Buenos Aires, Argentina. (2013 Mar 04)
LIONEX Diagnostics and Therapeutics, Braunschweig: Monocytes and the 38kDa-antigen of mycobacterium tuberculosis modulate natural killer cell activity and their cytolysis directed against ovarian cancer cell lines

By a News Reporter-Staff News Editor at Biotech Week – Data detailed on Mycobacterium Infections have been presented. According to news originating from Braunschweig, Germany, by NewsRx correspondents, research stated, “Despite strong efforts to improve clinical outcome of ovarian cancer patients by conventional and targeted immuno-based therapies, the prognosis of advanced ovarian cancer is still poor. Natural killer (NK) cells mediate antibody-dependent cellular cytotoxicity (ADCC), release immunostimulatory cytokines and thus function as potent anti-tumour effector cells.”

Our news journalists obtained a quote from the research from LIONEX Diagnostics and Therapeutics, “However, tumour cells developed mechanisms to escape from an effective immune response. So highly immunogenic substances, like the 38 kDa-preparation of M. tuberculosis, PstS-1, are explored for their potential to enhance cancer-targeted immune responses. In this study we examined the modulation of different NK cell functions by accessory monocytes and PstS-1. We focussed on NK cell activation as well as natural and antibody-dependent cellular cytotoxicity directed against epidermal-growth-factor-receptor (EGFR)-positive ovarian cancer cell lines. Activation, cytokine release and cytotoxicity of NK cells stimulated by monocytes and PstS-1 were determined by FACS-analysis, ELISA, Bioplex assay and quantitative polymerase-chain reaction (qPCR). Transwell assays were used to discriminate cell-cell contact-dependent from contact-independent mechanisms. Five ovarian cancer cell lines (A2780, IGROV-1, OVCAR-3, OVCAR-4 and SKOV-3) with different EGFR-expression were used as target cells for natural and antibody-dependent cellular cytotoxicity assays. Cetuximab (anti-EGFR-antibody) was used for ADCC studies. Our data show that monocytes effectively enhance activation as well natural and antibody-dependent cytolytic activity of NK cells. PstS-1 directly stimulated monocytes and further activated monocyte-NK-cocultures. However, PstS-1 did not directly influence purified NK cells and did also not affect natural and antibody-dependent cellular cytotoxicity directed against EGFR-positive ovarian cancer cells, even in presence of monocytes. Direct cell-cell contact between NK cells and monocytes was required for NK activation, while released cytokines seemed to play a minor role. Our data suggest that monocytes enhance natural and antibody-dependent cytotoxic activity of NK cells in a cell-cell contact dependent manner. The TLR-agonist PstS-1 provides additional monocyte activation and induces NK activation markers, while NK cytotoxicity remains unaffected.”
According to the news editors, the research concluded: “We conclude that monocytes provide accessory function for ADCC exerted by NK during antibody-based cancer immunotherapy directed against EGFR-positive ovarian cancer cells.”


The news correspondents report that additional information may be obtained from N. Gottschalk, LIONEX Diagnost & Therapeut GmbH, D-38126 Braunschweig, Germany. (2013 Jan 23)

**KIIT University, Bhubaneswar:** Azurophil granule proteins constitute the major mycobactericidal proteins in human neutrophils and enhance the killing of mycobacteria in macrophages

By a News Reporter-Staff News Editor at Tuberculosis Week – Data detailed on Life Science Research have been presented. According to news reporting originating from Bhubaneswar, India, by NewsRx correspondents, research stated, “Pathogenic mycobacteria reside in, and are in turn controlled by, macrophages. However, emerging data suggest that neutrophils also play a critical role in innate immunity to tuberculosis, presumably by their different antibacterial granule proteins.”

Our news editors obtained a quote from the research from KIIT University, “In this study, we purified neutrophil azurophil and specific granules and systematically analyzed the antimycobacterial activity of some purified azurophil and specific granule proteins against *M. smegmatis*, *M. bovis*-BCG and *M. tuberculosis* H37Rv. Using gel overlay and colony forming unit assays we showed that the defensin-depleted azurophil granule proteins (AZP) were more active against mycobacteria compared to other granule proteins and cytosolic proteins. The proteins showing antimycobacterial activity were identified by MALDI-TOF mass spectrometry. Electron microscopic studies demonstrate that the AZP disintegrate bacterial cell membrane resulting in killing of mycobacteria. Exogenous addition of AZP to murine macrophage RAW 264.7, THP-1 and peripheral blood monocyte-derived macrophages significantly reduced the intracellular survival of mycobacteria without exhibiting cytotoxic activity on macrophages. Immunofluorescence studies showed that macrophages actively endocytose neutrophil granular proteins. Treatment with AZP resulted in increase in co-localization
of BCG containing phagosomes with lysosomes but not in increase of autophagy.”

According to the news editors, the research concluded: “These data demonstrate that neutrophil azurophil proteins may play an important role in controlling intracellular survival of mycobacteria in macrophages.”

For more information on this research see: Azurophil granule proteins constitute the major mycobactericidal proteins in human neutrophils and enhance the killing of mycobacteria in macrophages. Plos One, 2012;7(12):e50345. (Public Library of Science - www.plos.org; Plos One - www.plosone.org)

The news editors report that additional information may be obtained by contacting P. Jena, School of Biotechnology, Campus-11, KIIT University, Bhubaneswar, Orissa, India. (2013 Jan 07)

Vanderbilt University, Nashville: Real-time recognition of Mycobacterium tuberculosis and lipoarabinomannan using the quartz crystal microbalance

By a News Reporter-Staff News Editor at Tuberculosis Week – Fresh data on Chemical Sensors and Actuators are presented in a new report. According to news reporting out of Nashville, Tennessee, by NewsRx editors, research stated, “A quartz crystal microbalance (QCM) immunosensor has been successfully employed to screen for both whole Mycobacteria tuberculosis (Mtb) bacilli and a Mtb surface antigen, lipoarabinomannan (LAM). One of the most abundant components of the Mtb cell surface.”

Our news journalists obtained a quote from the research from Vanderbilt University, “LAM, may be detected without the presence of the entire bacterium. Using available antibodies with proven utility in enzyme-linked immunoassays (ELISAs), a sensor was designed to measure Mtb bacilli and LAM. Equilibrium association constants (K-a) were determined for the interaction of Mtb with immobilized alpha-LAM and anti-H37Rv antibodies, where avidity was seen to strengthen this interaction and provide for greater binding than might have otherwise been achieved. The binding of LAM to immobilized alpha-LAM had a high associate rate constant (k(a)) allowing for rapid detection. Evaluating these binding constants helped to compare the sensitivity of these immunosensors to conventional ELISAs.”

According to the news editors, the research concluded: “The use of these assays with better antibodies may allow for immunosensor use in determining LAM as a point-of-care (POC) diagnostic for Mtb.”

For more information on this research see: Real-time recognition of Mycobacterium tuberculosis and lipoarabinomannan using the quartz crystal microbalance. Sensors and Actuators B-Chemical,
Albert Einstein College of Medicine, Bronx: Antibody responses to mycobacterial antigens in children with tuberculosis: challenges and potential diagnostic value

By a News Reporter-Staff News Editor at Tuberculosis Week – Current study results on Tuberculosis have been published. According to news reporting out of Bronx, New York, by NewsRx editors, research stated, “The identification of easily detectable biomarkers for active tuberculosis (TB) is a global health priority. Such biomarkers would be of particular value in childhood TB, which poses greater diagnostic challenges than adult TB.”

Our news journalists obtained a quote from the research from the Albert Einstein College of Medicine, “Serum antibodies can be detected by simple formats that provide extremely rapid results. However, attempts to develop accurate serodiagnostic tests for TB have been unsuccessful. Whereas antibody responses to mycobacterial antigens in adult TB have been studied extensively and reviewed, the same cannot be said for serologic data in pediatric populations. Here we appraise studies on serological responses in childhood TB and discuss findings and limitations in the context of the developing immune system, the age range, and the spectrum of TB manifestations. We found that the antibody responses to mycobacterial antigens in childhood TB can vary widely, with sensitivities and specificities ranging from 14% to 85% and from 86% to 100%, respectively. We conclude that the limitations in serodiagnostic studies of childhood TB are manifold, thereby restricting the interpretation of currently available data. Concerns about the methodology used in published studies suggest that conclusions about the eventual value of serodiagnosis cannot be made at this time. However, the available data suggest a potential adjunctive value for serology in the diagnosis of childhood TB.”

According to the news editors, the research concluded: “Despite the difficulties noted in this field, there is optimism that the application of novel antigens and the integration of those factors which contribute to the serological responses in childhood TB can lead to useful future diagnostics.”

For more information on this research see: Antibody responses to mycobacterial antigens in children with tuberculosis: challenges
and potential diagnostic value. *Clinical and Vaccine Immunology*, 2012;19(12):1898-906. (American Society for Microbiology - www.asm.org; Clinical and Vaccine Immunology - cdli.asm.org)

Our news journalists report that additional information may be obtained by contacting J.M. Achkar, Dept. of Medicine, Albert Einstein College of Medicine, Bronx, New York, United States. (2012 Dec 24)

**University of California, Berkeley: The crystal structure of the Rv0301-Rv0300 VapBC-3 toxin-antitoxin complex from M. tuberculosis reveals a Mg2+ ion in the active site and a putative RNA-binding site**

By a News Reporter-Staff News Editor at Tuberculosis Week – Researchers detail new data in Proteomics. According to news reporting from Berkeley, California, by NewsRx journalists, research stated, “VapBC pairs account for 45 out of 88 identified toxin-antitoxin (TA) pairs in the Mycobacterium tuberculosis (Mtbc) H37Rv genome. A working model suggests that under times of stress, antitoxin molecules are degraded, releasing the toxins to slow the metabolism of the cell, which in the case of VapC toxins is via their RNase activity.”

The news correspondents obtained a quote from the research from the University of California, “Otherwise the TA pairs remain bound to their promoters, autoinhibiting transcription. The crystal structure of Rv0301-Rv0300, an Mtbc VapBC TA complex determined at 1.49 angstrom resolution, suggests a mechanism for these three functions: RNase activity, its inhibition by antitoxin, and its ability to bind promoter DNA. The Rv0301 toxin consists of a core of five parallel beta strands flanked by alpha helices. Three proximal aspartates coordinate a Mg2+ ion forming the putative RNase active site. The Rv0300 antitoxin monomer is extended in structure, consisting of an N-terminal beta strand followed by four helices. The last two helices wrap around the toxin and terminate near the putative RNase active site, but with different conformations. In one conformation, the C-terminal arginine interferes with Mg2+ ion coordination, suggesting a mechanism by which the antitoxin can inhibit toxin activity. At the N-terminus of the antitoxin, two pairs of Ribbon-Helix-Helix (RHH) motifs are related by crystallographic twofold symmetry.”

According to the news reporters, the research concluded: “The resulting hetero-octameric complex is similar to the FitAB system, but the two RHH motifs are about 30 angstrom closer together in the Rv0301-Rv0300 complex, suggesting either a different span of the DNA recognition sequence or a conformational change.”

For more information on this research see: The crystal structure of the Rv0301-Rv0300 VapBC-3 toxin-antitoxin complex from M. tuberculosis reveals a Mg2+ ion in the active site and a putative RNA-binding
University of Maryland, Baltimore: R753Q Polymorphism Inhibits Toll-like Receptor (TLR) 2 Tyrosine Phosphorylation, Dimerization with TLR6, and Recruitment of Myeloid Differentiation Primary Response Protein 88

By a News Reporter-Staff News Editor at Tuberculosis Week – Current study results on Mycobacterium Infections have been published. According to news reporting originating from Baltimore, Maryland, by NewsRx correspondents, research stated, “The R753Q polymorphism in the Toll-IL-1 receptor domain of Toll-like receptor 2 (TLR2) has been linked to increased incidence of tuberculosis and other infectious diseases, but the mechanisms by which it affects TLR2 functions are unclear. Here, we studied the impact of the R753Q polymorphism on TLR2 expression, hetero-dimerization with TLR6, tyrosine phosphorylation, and recruitment of myeloid differentiation primary response protein (MyD) 88 and MyD88 adapter-like (Mal).”

Our news editors obtained a quote from the research from the University of Maryland, “Complementation of HEK293 cells with transfected WT or R753Q TLR2 revealed their comparable total levels and only minimal changes in cell surface expression of the mutant species. Notably, even a 100-fold increase in amounts of transfected R753Q TLR2 versus WT variant did not overcome the compromised ability of the mutant TLR2 to activate nuclear factor kappa B (NF-kappa B), indicating that a minimal decrease in cell surface levels of the R753Q TLR2 cannot account for the signaling deficiency. Molecular modeling studies suggested that the R753Q mutation changes the electrostatic potential of the DD loop and results in a discrete movement of the residues critical for protein-protein interactions. Confirming these predictions, biochemical assays demonstrated that R753Q TLR2 exhibits deficient agonist-induced tyrosine phosphorylation, hetero-dimerization with TLR6, and recruitment of Mal and MyD88. These proximal signaling deficiencies correlated with impaired capacities of
the R753Q TLR2 to mediate p38 phosphorylation, NF-kappa B activation, and induction of IL-8 mRNA in transfected HEK293 cells challenged with inactivated Mycobacterium tuberculosis or mycobacterial components.”

According to the news editors, the research concluded: “Thus, the R753Q polymorphism renders TLR2 signaling-incompetent by impairing its tyrosine phosphorylation, dimerization with TLR6, and recruitment of Mal and MyD88.”


The news editors report that additional information may be obtained by contacting Y.B. Xiong, University of Maryland, Sch Med, Dept. of Med, Baltimore, MD 21201, United States. (2012 Dec 10)

Northeastern University, Boston: Efferocytosis Is an Innate Antibacterial Mechanism

By a News Reporter-Staff News Editor at Tuberculosis Week – A new study on Cell Biology is now available. According to news reporting originating from Boston, Massachusetts, by NewsRx correspondents, research stated, “Mycobacterium tuberculosis persists within macrophages in an arrested phagosome and depends upon necrosis to elude immunity and disseminate.”

Our news editors obtained a quote from the research from Northeastern University, “Although apoptosis of M. tuberculosis-infected macrophages is associated with reduced bacterial growth, the bacteria are relatively resistant to other forms of death, leaving the mechanism underlying this observation unresolved. We find that after apoptosis, M. tuberculosis-infected macrophages are rapidly taken up by uninfected macrophages through efferocytosis, a dedicated apoptotic cell engulfment process. Efferocytosis of M. tuberculosis sequestered within an apoptotic macrophage further compartmentalizes the bacterium and delivers it along with the apoptotic cell debris to the lysosomal compartment. M. tuberculosis is killed only after efferocytosis, indicating that apoptosis itself is not intrinsically bactericidal but requires subsequent phagocytic uptake and lysosomal fusion of the apoptotic body harboring the bacterium.”
CHAPTER 4 IMMUNOLOGY

According to the news editors, the research concluded: “While efferocytosis is recognized as a constitutive housekeeping function of macrophages, these data indicate that it can also function as an antimicrobial effector mechanism.”


The news editors report that additional information may be obtained by contacting C.J. Martin, Northeastern Univ, Antimicrobial Discovery Center, Boston, MA 02115, United States. (2012 Dec 03)

Third Military Medical University, Chongqing: Association of tuberculosis and polymorphisms in the promotor region of macrophage migration inhibitory factor (MIF) in a Southwestern China Han population

By a News Reporter-Staff News Editor at China Weekly News – Research findings on Mycobacterium Infections are discussed in a new report. According to news originating from Chongqing, People’s Republic of China, by VerticalNews correspondents, research stated, “The macrophage migration inhibitory factor (MIF) is a pro-inflammatory cytokine that plays an important role in the pathogenesis of immune diseases. High levels of MIF have been detected in the sera of patients with tuberculosis (TB), and it has been proposed that MIF gene polymorphisms may influence the risk of developing TB.”

Our news journalists obtained a quote from the research from Third Military Medical University, “The aim of this study was to evaluate the potential relationship between functional polymorphisms of MIF and TB in a Han population from Southwestern China. TB patients (n=215) and healthy unrelated controls (n=245) were recruited for this study. Genomic DNA was isolated from all the participants. The MIF-173 G/C SNP was genotyped using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP). The MIF-794 CATT(5-8) microsatellite was evaluated by direct sequencing of the subsequent PCR products. Association analysis of the two polymorphisms showed that the frequency of -173 (GC+CC) in TB patients and controls was 49.3% and 31.4%, respectively, which was statistically significant (OR=2.12, 95% CI=1.45-3.10, p<0.001); the frequencies of -794 (7/X+8/X) were 56.7% and 45.3%, respectively, also statistically significant between the TB and healthy controls (OR=1.58, 95% CI=1.10-2.29, p=0.015). In summary, Genetic variation in the MIF gene is closely associated with tuberculosis.”
According to the news editors, the research concluded: “Both the 173 (GC+CC) SNP and -794 (7/X+8/X) microsatellite increased the risk of Chinese Han developing TB.”

For more information on this research see: Association of tuberculosis and polymorphisms in the promoter region of macrophage migration inhibitory factor (MIF) in a Southwestern China Han population. *Cytokine*, 2012;60(1):64-7. (Elsevier - www.elsevier.com; Cytokine - http://www.elsevier.com/wps/product/cws_home/622815)

The news correspondents report that additional information may be obtained from Y. Li, Dept. of Clinical Laboratory, Institute of Surgery Research, Daping Hospital, Third Military Medical University, Chongqing 400042, People’s Taiwan. (2012 Nov 13)

**Brigham and Women’s Hospital, Boston:**

**Community-Based Rapid Oral Human Immunodeficiency Virus Testing for Tuberculosis Patients in Lima, Peru**

By a News Reporter-Staff News Editor at AIDS Weekly – Current study results on Mycobacterium Infections have been published. According to news reporting from Boston, Massachusetts, by NewsRx journalists, research stated, “Among tuberculosis patients, timely diagnosis of human immunodeficiency virus (HIV) co-infection and early antiretroviral treatment are crucial, but are hampered by a myriad of individual and structural barriers. Community-based models to provide counseling and rapid HIV testing are few but offer promise.”

The news correspondents obtained a quote from the research from Brigham and Women’s Hospital, “During November 2009 April 2010, community health workers offered and performed HIV counseling and testing by using the OraQuick Rapid HIV-1/2 Antibody Test to new tuberculosis cases in 22 Ministry of Health establishments and their household contacts (n = 130) in Lima, Peru. Refusal of HIV testing or study participation was low (4.7%). Intervention strengths included community-based approach with participant preference for testing site, use of a rapid, non-invasive test, and accompaniment to facilitate HIV care and family disclosure. We will expand the intervention under programmatic auspices for rapid community-based testing for new tuberculosis cases in high incidence establishments.”

According to the news reporters, the research concluded: “Other potential target populations include contacts of HIV-positive persons and pregnant women.”

For more information on this research see: Community-Based Rapid Oral Human Immunodeficiency Virus Testing for Tuberculosis Patients in Lima, Peru. *American Journal of Tropical Medicine and Hygiene*, 2012;60(1):64-7.
Research Institute, Novosibirsk: Cytotoxic activity of dendritic cells as a possible mechanism of negative regulation of T lymphocytes in pulmonary tuberculosis

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – Investigators publish new report on Immunology. According to news reporting originating in Novosibirsk, Russia, by NewsRx journalists, research stated, “The PD-1/B7-H1-mediated induction of T cell apoptosis/anergy as a possible mechanism of immune response failure was studied in 76 patients with pulmonary tuberculosis (TB) with normal and low-proliferative response to antigens of M. tuberculosis (purified protein derivative (PPD)). It was revealed that dendritic cells (DCs), generated in vitro from patient blood monocytes with GM-CSF + IFN-α, were characterized by increased B7-H1 expression, upproduction of IL-10, and reducing of allostimulatory activity in mixed lymphocyte culture (MLC).”

The news reporters obtained a quote from the research from Research Institute, “Moreover, DCs of patients with TB were able to enhance T cell apoptosis and to block T-cell division in MLC. It was shown that neutralizing anti-PD1 antibodies significantly decreased the proapoptogenic/tolerogenic effect of DCs. Correlation analysis revealed a direct relationship between IL-10 production and level of B7-H1 expression in the general group of investigated patients. It was demonstrated that generation of healthy donor DCs in the presence of IL-10 led to an increase in the number of DCs-expressed B7-H1 molecule, DC proapoptogenic activity, and a decrease in their allostimulatory activity.”

According to the news reporters, the research concluded: “Obviously, the revealed phenomenon of the PD-1/B7-H1-mediated pro-apoptogenic activity of DCs is clinically significant since the cytotoxic/tolerogenic potential of DCs is more pronounced in patients with PPD anergy.”

For more information on this research see: Cytotoxic activity of dendritic cells as a possible mechanism of negative regulation of T lymphocytes in pulmonary tuberculosis. Clinical and Developmental Immunology, 2012;2012():628635. (Hindawi Publishing - www.hindawi.com; Clinical and Developmental Immunology - http://www.hindawi.com/journals/cdi/)
Bose Institute, Kolkata: Identification of a novel role of ESAT-6-dependent miR-155 induction during infection of macrophages with Mycobacterium tuberculosis

By a News Reporter-Staff News Editor at Tuberculosis Week – A new study on Cellular Microbiology is now available. According to news reporting originating in Kolkata, India, by NewsRx journalists, research stated, "Mycobacterium tuberculosis (M.tb.) replicates in host macrophages to cause tuberculosis. We have investigated the role of miRNAs in M.tb.-infected murine RAW264.7 cells and bone marrow-derived macrophages (BMDMs), focusing on miR-155, the most highly upregulated miRNA."

The news reporters obtained a quote from the research from Bose Institute, "We observed that miR-155 upregulation is directly linked to the attenuation of expression of BTB and CNC homology 1 (Bach1) and SH2-containing inositol 5'-phosphatase (SHIP1). Bach1 is a transcriptional repressor of haem oxygenase-1 (HO-1), whereas SHIP1 inhibits the activation of the serine/threonine kinase AKT. We hypothesize that M.tb.-induced miR-155 induction leads to repression of Bach1, which augments the expression of HO-1, a documented activator of the M.tb. dormancy regulon. SHIP1 repression facilitates AKT activation, which is required for M.tb. survival. In addition, M.tb.-induced miR-155 inhibits expression of cyclooxygenase-2 (Cox-2) and interleukin-6 (IL-6), two modulators of the innate immune response. Importantly, we observed that the virulence-associated secreted protein ESAT-6 plays a key role in miR-155 induction and its subsequent effects on Bach1 and SHIP1 repression. Inhibition of miR-155 hindered survival of M.tb. in RAW264.7 and in murine BMDMs."

According to the news reporters, the researchers concluded: "Thus, our results offer new insights into the role of miRNAs in modulation of the host innate immune response by M.tb. for its own benefit."


Our news correspondents report that additional information may be obtained by contacting R. Kumar, Dept. of Chemistry, Bose Institute,
Pulmonary Tuberculosis in Humans

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – Fresh data on Life Science Research are presented in a new report. According to news reporting originating in Moscow, Russia, by NewsRx journalists, research stated, “Effector CD4 T cells represent a key component of the host’s anti-tuberculosis immune defense. Successful differentiation and functioning of effector lymphocytes protects the host against severe M. tuberculosis (Mtb) infection.”

The news reporters obtained a quote from the research from Research Institute, “On the other hand, effector T cell differentiation depends on disease severity/activity, as T cell responses are driven by antigenic and inflammatory stimuli released during infection. Thus, tuberculosis (TB) progression and the degree of effector CD4 T cell differentiation are interrelated, but the relationships are complex and not well understood.”

According to the news reporters, the researchers concluded: “We have analyzed an association between the degree of Mtb-specific CD4 T cell differentiation and severity/activity of pulmonary TB infection.”

For more information on this research see: Mtb-Specific CD27(low) CD4 T Cells as Markers of Lung Tissue Destruction during Pulmonary Tuberculosis in Humans. Plos One, 2012;7(8):e43733. (Public Library of Science - www.plos.org; Plos One - www.plosone.org)

Our news correspondents report that additional information may be obtained by contacting I.Y. Nikitina, Dept. of Immunology, Central Tuberculosis Research Institute, Moscow, Russia. (2012 Sep 24)

Center for Biotechnology, Trivandrum: Comparative Analysis of Mycobacterial Truncated Hemoglobin Promoters and the groEL2 Promoter in Free-Living and Intracellular Mycobacteria

By a News Reporter-Staff News Editor at Health & Medicine Week – Research findings on Mycobacterium Infections are discussed in a new report. According to news originating from Trivandrum, India, by NewsRx correspondents, research stated, “The success of Mycobacterium tuberculosis depends on its ability to withstand and survive the hazardous environment inside the macrophages that are created by reactive oxygen intermediates, reactive nitrogen intermediates, severe
hypoxia, low pH, and high CO(2) levels. Therefore, an effective detoxification system is required for the pathogen to persist in vivo.”

Our news journalists obtained a quote from the research from Center for Biotechnology, “The genome of *M. tuberculosis* contains a new family of hemoproteins named truncated hemoglobin O (trHbO) and truncated hemoglobin N (trHbN), encoded by the glbO and glbN genes, respectively, important in the survival of *M. tuberculosis* in macrophages. Mycobacterial heat shock proteins are known to undergo rapid upregulation under stress conditions. The expression profiles of the promoters of these genes were studied by constructing transcriptional fusions with green fluorescent protein and monitoring the promoter activity in both free-living and intracellular milieus at different time points. Whereas glbN showed an early response to the oxidative and nitrosative stresses tested, glbO gave a lasting response to lower concentrations of both stresses. At all time points and under all stress conditions tested, groEL2 showed higher expression than both trHb promoters and expression of both promoters showed an increase while inside the macrophages. Real-time PCR analysis of trHb and groEL2 mRNAs showed an initial upregulation at 24 h postinfection. The presence of the glbO protein imparted an increased survival to *M. smegmatis* in THP-1 differentiated macrophages compared to that imparted by the glbN and hsp65 proteins.”

According to the news editors, the researchers concluded: “The comparative upregulation shown by both trHb promoters while grown inside macrophages indicates the importance of these promoters for the survival of *M. tuberculosis* in the hostile environment of the host.”

For more information on this research see: Comparative Analysis of Mycobacterial Truncated Hemoglobin Promoters and the groEL2 Promoter in Free-Living and Intracellular Mycobacteria. *Applied and Environmental Microbiology*, 2012;78(18):6499-506. (American Society for Microbiology - www.asm.org; Applied and Environmental Microbiology - aem.asm.org)

The news correspondents report that additional information may be obtained from S.V. Joseph, Dept. of Molecular Microbiology, Rajiv Gandhi Centre for Biotechnology, Trivandrum, India. (2012 Sep 21)

**Ludwik Hirszfeld Institute of Immunology and Experimental Therapy, Wroclaw: A Novel Role of the PrpR as a Transcription Factor Involved in the Regulation of Methylcitrate Pathway in Mycobacterium tuberculosis**

By a News Reporter-Staff News Editor at Chemicals & Chemistry – Current study results on Gram-Positive Bacteria have been published. According to news originating from Wroclaw, Poland, by VerticalNews correspondents, research stated, “*Mycobacterium tuberculosis*,

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the pathogen that causes tuberculosis, presumably utilizes fatty acids as a major carbon source during infection within the host. Metabolism of even-chain-length fatty acids yields acetyl-CoA, whereas metabolism of odd-chain-length fatty acids additionally yields propionyl-CoA.”

Our news journalists obtained a quote from the research from the Ludwik Hirszfeld Institute of Immunology and Experimental Therapy, “Utilization of these compounds by tubercle bacilli requires functional glyoxylate and methylcitrate cycles, respectively. Enzymes involved in both pathways are essential for *M. tuberculosis* viability and persistence during growth on fatty acids. However, little is known about regulatory factors responsible for adjusting the expression of genes encoding these enzymes to particular growth conditions. Here, we characterized the novel role of PrpR as a transcription factor that is directly involved in regulating genes encoding the key enzymes of methylcitrate (methylcitrate dehydratase [PrpD] and methylcitrate synthase [PrpC]) and glyoxylate (isocitrate lyase [Icl1]) cycles. Using cell-free systems and intact cells, we demonstrated an interaction of PrpR protein with prpDC and icl1 promoter regions and identified a consensus sequence recognized by PrpR. Moreover, we showed that an *M. tuberculosis* prpR-deletion strain exhibits impaired growth in vitro on propionate as the sole carbon source. Real-time quantitative reverse transcription-polymerase chain reaction confirmed that PrpR acts as a transcriptional activator of prpDC and icl1 genes when propionate is the main carbon source. Similar results were also obtained for a non-pathogenic *Mycobacterium smegmatis* strain. Additionally, we found that ramB, a prpR paralog that controls the glyoxylate cycle, is negatively regulated by PrpR. Our data demonstrate that PrpR is essential for the utilization of odd-chain-length fatty acids by tubercle bacilli.”

According to the news editors, the researchers concluded: “Since PrpR also acts as a ramB repressor, our findings suggest that it plays a key role in regulating expression of enzymes involved in both glyoxylate and methylcitrate pathways.”

For more information on this research see: A Novel Role of the PrpR as a Transcription Factor Involved in the Regulation of Methylcitrate Pathway in Mycobacterium tuberculosis. *Plos One*, 2012;7(8):e43651. (Public Library of Science - www.plos.org; Plos One - www.plosone.org)

The news correspondents report that additional information may be obtained from P. Masiewicz, Dept. of Microbiology, Ludwik Hirszfeld Institute of Immunology and Experimental Therapy, Polish Academy of Sciences, Wroclaw, Poland. (*2012 Sep 14*)
National Taiwan University Hospital, Taipei: Expression of toll-like receptor 2 and plasma level of interleukin-10 are associated with outcome in tuberculosis

By a News Reporter-Staff News Editor at Blood Weekly – Research findings on Mycobacterium Infections are discussed in a new report. According to news reporting from Taipei, Taiwan, by NewsRx journalists, research stated, “Toll-like receptor (TLR) 2-mediated innate immunity is an important defense system against Mycobacterium tuberculosis infection. Studies on TLR2 protein expression and downstream cytokines in tuberculosis patients are lacking.”

The news correspondents obtained a quote from the research from National Taiwan University Hospital, “TLR2 expression in the peripheral blood monocytes of 87 tuberculosis patients and 94 healthy subjects was evaluated using flow cytometry. TLR2 expression and its downstream cytokines, including interleukin (IL)-6, IL-10, tumor necrosis factor (TNF)-alpha, and interferon-gamma, were correlated with the clinical manifestations and outcomes of tuberculosis. The TLR2 expression in peripheral blood monocytes was higher in tuberculosis patients than in healthy subjects. Among the tuberculosis patients, those aged=70 years with disseminated tuberculosis or aged &lt;70 years with symptom duration=14 days had lower initial TLR2 expression. After two months of treatment, TLR2 expression decreased in most patients, except in those whose sputum samples remained culture-positive for M. tuberculosis. Proportional hazards regression analyses revealed that high initial TLR2 expression and IL-10 plasma level were associated with shorter survival. TLR2 may play an important role in the course of tuberculosis.”

According to the news reporters, the researchers concluded: “It's expression on peripheral blood monocytes and the plasma level of the downstream anti-inflammatory cytokine IL-10 may be important outcome predictors and have potential use in the management of tuberculosis.”

For more information on this research see: Expression of toll-like receptor 2 and plasma level of interleukin-10 are associated with outcome in tuberculosis. European Journal of Clinical Microbiology & Infectious Diseases, 2012;31(9):2327-33. (Springer - www.springer.com; European Journal of Clinical Microbiology & Infectious Diseases - http://www.springerlink.com/content/0934-9723/)

Our news journalists report that additional information may be obtained by contacting J.Y. Wang, Dept. of Internal Medicine, National Taiwan University Hospital, No 7, Chung-Shan South Road, Taipei, 10002, Taiwan. (2012 Sep 06)
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Detection of antibodies to tuberculosis antigens in free-ranging lions (Panthera leo) infected with mycobacterium bovis in Kruger National Park, South Africa

By a News Reporter-Staff News Editor at Agriculture Week – Investigators publish new report on Mycobacterium Infections. According to news reporting originating from West Palm Beach, Florida, by VerticalNews correspondents, research stated, “Bovine tuberculosis (TB), caused by Mycobacterium bovis, has become established in Kruger National Park, South Africa, in the cape buffalo (Syncerus caffer) population and in other species. TB in prey species has resulted in infection and morbidity in the resident lion (Panthera leo) prides.”

Our news editors obtained a quote from the research, “The only validated live animal test currently available for lions is the intradermal tuberculin test. Because this test requires capture twice, 72 hr apart, of free-ranging lions to read results, it is logistically difficult to administer in a large ecosystem. Therefore, development of a rapid animal-side screening assay would be ideal in providing information for wildlife managers, veterinarians, and researchers working with free-living lion prides. This study reports preliminary descriptive results from an ongoing project evaluating two serologic tests for M. bovis (ElephantTB Stat-Pak and dual path platform VetTB). Disease status was determined by postmortem culture and presence of pathologic lesions in 14 free-ranging lions. Seropositivity was found to be associated with M. bovis infection.”

According to the news editors, the researchers concluded: “Extended field studies are underway to validate these rapid animal-side immunoassays for antemortem screening tests for TB in lions.”

For more information on this research see: Detection of antibodies to tuberculosis antigens in free-ranging lions (Panthera leo) infected with mycobacterium bovis in Kruger National Park, South Africa. Journal of Zoo and Wildlife Medicine, 2012;43(2):317-23. Journal of Zoo and Wildlife Medicine can be contacted at: Amer Assoc Zoo Veterinarians, 6 North Pennell Road, Media, PA 19063, USA.

The news editors report that additional information may be obtained by contacting M. Miller, Palm Beach Zoo, 1301 Summit Boulevard, West Palm Beach, Florida 33405, United States.

Publisher contact information for the Journal of Zoo and Wildlife Medicine is: Amer Assoc Zoo Veterinarians, 6 North Pennell Road, Media, PA 19063, USA. (2012 Aug 09)
Colorado State University, Fort Collins: T lymphocyte surface expression of exhaustion markers as biomarkers of the efficacy of chemotherapy for tuberculosis

By a News Reporter-Staff News Editor at Tuberculosis Week – Investigators discuss new findings in Mycobacterium Infections. According to news reporting out of Fort Collins, Colorado, by NewsRx editors, researchers stated “Predictive biomarkers illustrating the effectiveness of chemotherapeutic regimens for tuberculosis still remain elusive. To date, most are predicated on assays using sputum or serum; as a result, if not predictive, treatment failure in patients may not be evident for some time.”

Our news journalists obtained a quote from the research from Colorado State University, “We report here the results of a simple screening study in which T cell surface markers were examined in mice infected with Mycobacterium tuberculosis and then treated with drugs. These studies identified certain markers, the exhaustion markers PD-1 and TIM-3, as well as the marker KLRG-1, particularly on CD8 T cells, that changed in concert with reduction of the bacterial load in the lungs.”

According to the news editors, the researchers concluded: “While there is no guarantee these changes would also be seen on T cells in the blood, this approach should be further investigated.”


Our news journalists report that additional information may be obtained by contacting M. Henao-Tamayo, Mycobacteria Research Laboratories, Dept. of Microbiology, Immunology and Pathology, Colorado State University, Fort Collins CO 80523, United States. (2012 Jul 30)

Sacred Heart Catholic University, Rome: Microbiological and immunological diagnosis of tuberculous spondylodiscitis

By a News Reporter-Staff News Editor at Biotech Week – New research on Tuberculosis is the subject of a report. According to news reporting out of Rome, Italy, by NewsRx editors, researchers stated “Tuberculous spondylodiscitis is one the many manifestations of active tuberculosis (TB) and can result following primary infection or, more frequently, from reactivation of active TB in subjects with latent TB. Definitive diagnosis of tuberculous spondylodiscitis requires the identification of Mycobacterium tuberculosis in the biological sample following microbiological analysis.”
Our news journalists obtained a quote from the research by the authors from Sacred Heart Catholic University, “To summarize the recent advancement in the diagnosis of TB, focusing on classical and molecular microbiological procedures, providing an overview on the recent advancements in the understanding of TB pathogenesis and their implications for the immunological diagnosis Materials and Methods: Isolation in culture of the bacilli and detection using molecular tools are the gold standards, though sensitivity of these assays is significantly lower compared to what observed for pulmonary TB, making diagnosis of spinal TB challenging. The use of the interferon-gamma release assays (IGRAs) for the immunological diagnosis of TB infection could be of help and shall precede the invasive techniques, such as biopsy or surgery, required to obtain the biological sample. IGRAs measure the presence of effector T cells in the blood that can readily respond to an antigenic stimuli by secreting cytokines, and that are an indication of the presence of the bacilli in vivo. IGRAs are more sensitive and specific than the intradermic reaction of Mantoux, though both these immunological tests cannot distinguish between latent TB infection and active TB.”

According to the news editors, the researchers concluded: “A modern diagnosis of TB spondylodiscitis should rely on the use of microbiological and immunological assays and the latter could potentially be of great help in monitoring therapy effectiveness.”

For more information on this research see: Microbiological and immunological diagnosis of tuberculous spondylodiscitis. European Review for Medical and Pharmacological Sciences, 2012;16():73-78. European Review for Medical and Pharmacological Sciences can be contacted at: Verduci Publisher, Via Gregorio Vii, Rome, 186-00165, Italy.

Our news journalists report that additional information may be obtained by contacting G. Delogu, Sacred Heart Catholic University, Sch Med, Inst Microbiol, I-00168 Rome, Italy. (2012 Jun 20)

University of California, San Francisco: Sulfolipid-1 Biosynthesis Restricts Mycobacterium tuberculosis Growth in Human Macrophages

By a News Reporter-Staff News Editor at Tuberculosis Week – A new study on Tuberculosis is now available. According to news reporting out of San Francisco, California, by NewsRx editors, researchers stated “Mycobacterium tuberculosis (Mtb), the causative agent of tuberculosis, is a highly evolved human pathogen characterized by its formidable cell wall. Many unique lipids and glycolipids from the Mtb cell wall are thought to be virulence factors that mediate host-pathogen interactions.”
Our news journalists obtained a quote from the research by the authors from the University of California, “An intriguing example is Sulfolipid-1 (SL-1), a sulfated glycolipid that has been implicated in Mtb pathogenesis, although no direct role for SL-1 in virulence has been established. Previously, we described the biochemical activity of the sulfotransferase Stf0 that initiates SL-1 biosynthesis. Here we show that a stf0-deletion mutant exhibits augmented survival in human but not murine macrophages, suggesting that SL-1 negatively regulates the intracellular growth of Mtb in a species-specific manner. Furthermore, we demonstrate that SL-1 plays a role in mediating the susceptibility of Mtb to a human cationic antimicrobial peptide in vitro, despite being dispensable for maintaining overall cell envelope integrity.”

According to the news editors, the researchers concluded: “Thus, we hypothesize that the species-specific phenotype of the stf0 mutant is reflective of differences in antimycobacterial effector mechanisms of macrophages.”

For more information on this research see: Sulfolipid-1 Biosynthesis Restricts Mycobacterium tuberculosis Growth in Human Macrophages. ACS Chemical Biology, 2012;7(5):863-870. ACS Chemical Biology can be contacted at: Amer Chemical Soc, 1155 16TH St, NW, Washington, DC 20036, USA. (American Chemical Society - www.acs.org; ACS Chemical Biology - http://www.pubs.acs.org/journal/acbcct)

Institute for Microbiology and Immunology, Berlin:
Successful oral desensitization to i.v. para-aminosalicylic acid (PAS) using encapsulated PAS dry substance

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators discuss new findings in Tuberculosis. According to news originating from Berlin, Germany, by NewsRx correspondents, researchers stated “Para-Aminosalicylic acid (PAS) is commonly used in the treatment of drug-resistant tuberculosis, including multidrug-resistant tuberculosis. Since its first use in the 1940s, hypersensitivity reactions frequently limit its use in clinical practice.”

Our news journalists obtained a quote from the research by the authors from Institute for Microbiology and Immunology, “Cases of successful desensitization against PAS using orally administered ascending doses are described in the literature. A 25-year-old patient with severe pulmonary multidrug-resistant tuberculosis developed drug fever with rash, acral cyanosis, and shivering immediately after the intravenous application of PAS. Hard gelatine capsules containing PAS dry
substance were prepared in order to desensitize this patient. Encapsulated PAS was applied orally in rising doses starting with 10 mg/day and doubling the dose every 2 days until the half-maximal dose of 5,120 mg was reached. Desensitization covers a period of 21 days. Subsequent intravenous application of PAS at the full dose was well tolerated. In a 12-month follow-up period, no more allergic reactions appeared.”

According to the news editors, the researchers concluded: “PAS dry substance encapsulated in hard gelatine capsules and administered orally in rising concentrations may be useful to archive a successful desensitization for subsequent intravenous applications.”

For more information on this research see: Successful oral desensitization to i.v. para-aminosalicylic acid (PAS) using encapsulated PAS dry substance. *Infection*, 2012;40(2):199-202. *Infection* can be contacted at: Springer Heidelberg, Tiergartenstrasse 17, D-69121 Heidelberg, Germany. (Springer - www.springer.com; Infection - [http://www.springerlink.com/content/0300-8126/](http://www.springerlink.com/content/0300-8126/))

The news correspondents report that additional information may be obtained from S.M. Vesenbeckh, HELIOS Klinikum Emil von Behring, Inst Microbiol Immunol & Lab Med, Berlin, Germany. (2012 Jun 12)

**University of Antioquia, Medellin: Evaluation of Toll-like receptor and adaptor molecule polymorphisms for susceptibility to tuberculosis in a Colombian population**

By a News Reporter-Staff News Editor at Life Science Weekly – Fresh data on Tuberculosis are presented in a new report. According to news reporting from Medellin, Colombia, by NewsRx journalists, researchers stated “Immunological studies have supported the idea that innate immunity is critical for the control of *Mycobacterium tuberculosis* (Mtb) infection in humans. Despite the overwhelming evidence showing the critical role of Toll-like receptors (TLRs) in the in vitro recognition of Mtb, the in vivo significance of individual TLRs has been more difficult to demonstrate consistently.”

The news correspondents obtained a quote from the research by the authors from the University of Antioquia, “We were interested in examining the role of genes of TLRs and molecules involved in their signalling cascades, and a case-control study was designed to test the association of polymorphisms of these innate immune genes with pulmonary tuberculosis (TB) in a Colombian population. In this study, we did not find an association with TLR2, TLR4, TLR9, MyD88 or MAL/TIRAP polymorphic variants.”

According to the news reporters, the researchers concluded: “These findings suggest that those genes are not involved as risk factors for pulmonary TB in our population.”

Our news journalists report that additional information may be obtained by contacting D. Sanchez, Grupo de Inmunologia Celular e Inmunogenetica, Instituto de Investigaciones Medicas, Facultad de Medicina, Universidad de Antioquia, Medellin, Colombia Centro Colombiano de Investigacion en Tuberculosis (CCITB) Medellin, Colombia. *(2012 Jun 12)*

**University of California, San Diego: Dissecting Mechanisms of Immunodominance to the Common Tuberculosis Antigens ESAT-6, CFP10, Rv2031c (hspX), Rv2654c (TB7.7), and Rv1038c (EsxJ)**

By a News Reporter-Staff News Editor at Life Science Weekly – Research findings on Tuberculosis are discussed in a new report. According to news reporting from San Diego, California, by NewsRx journalists, researchers stated “Diagnosis of tuberculosis often relies on the ex vivo IFN-gamma release assays QuantiFERON-TB Gold In-Tube and T-SPOT. TB. However, understanding of the immunological mechanisms underlying their diagnostic use is still incomplete.”

The news correspondents obtained a quote from the research by the authors from the University of California, “Accordingly, we investigated T cell responses for the TB Ags included in the these assays and other commonly studied Ags: early secreted antigenic target 6 kDa, culture filtrate protein 10 kDa, Rv2031c, Rv2654c, and Ry1038c. PBMC from latently infected individuals were tested in ex vivo ELISPOT assays with overlapping peptides spanning the entirety of these Ags. We found striking variations in prevalence and magnitude of ex vivo reactivity, with culture filtrate protein 10 kDa being most dominant, followed by early secreted antigenic target 6 kDa and Rv2654c being virtually inactive. Ry2031c and Ry1038c were associated with intermediate patterns of reactivity. Further studies showed that low reactivity was not due to lack of HLA binding peptides, and high reactivity was associated with recognition of a few discrete dominant antigenic regions. Different donors recognized the same core sequence in a given epitope. In some cases, the identified epitopes were restricted by a single specific common HLA molecule (selective restriction), whereas in other cases, promiscuous restriction of the same epitope by multiple HLA molecules.
was apparent. Definition of the specific restricting HLA allowed to produce tetrameric reagents and showed that epitope-specific T cells recognizing either selectively or promiscuously restricted epitopes were predominantly T effector memory.”

According to the news reporters, the researchers concluded: “These results highlight the feasibility of more clearly defined TB diagnostic reagent. The Journal of Immunology, 2012, 188:5020-5031.”

For more information on this research see: Dissecting Mechanisms of Immunodominance to the Common Tuberculosis Antigens ESAT-6, CFP10, Rv2031c (hspX), Rv2654c (TB7.7), and Rv1038c (EsxJ). Journal of Immunology, 2012;188(10):5020-5031. Journal of Immunology can be contacted at: Amer Assoc Immunologists, 9650 Rockville Pike, Bethesda, MD 20814, USA. (The American Association of Immunologists - www.aai.org; Journal of Immunology - www.jimmunol.org)

Our news journalists report that additional information may be obtained by contacting C.S.L. Arlehamn, University of California, Antiviral Res Center, San Diego, CA 92103, United States. (2012 Jun 12)

Chonnam National University School of Medicine, Gwangju: Dysfunction of Natural Killer T Cells in Patients with Active Mycobacterium tuberculosis Infection

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – New research on Tuberculosis is the subject of a report. According to news reporting originating in Gwangju, South Korea, by NewsRx journalists, researchers stated “Natural killer T (NKT) cells are known to play a protective role in the immune responses of mice against a variety of infectious pathogens. However, little is known about the detailed information of NKT cells in patients with Mycobacterium tuberculosis infection.”

The news reporters obtained a quote from the research by the authors from the Chonnam National University School of Medicine, “The aims of this study were to examine NKT cell levels and functions in patients with active M. tuberculosis infection, to investigate relationships between NKT cell levels and clinical parameters, and to determine the mechanism responsible for the poor response to a-galactosylceramide (a-GalCer). NKT cell levels were significantly lower in the peripheral blood of pulmonary tuberculosis and extrapulmonary tuberculosis patients, and the proliferative responses of NKT cells to a-GalCer were also lower in patients, whereas NKT cell levels and responses were comparable in latent tuberculosis infection subjects and healthy controls. Furthermore, this NKT cell deficiency was found to be correlated with serum C-reactive protein levels. In addition, the poor response to a-GalCer in M. tuberculosis-infected patients was found to be due to increased NKT cell apoptosis, reduced CD1d expression, and a defect
in NKT cells. Notably, *M. tuberculosis* infection was associated with an elevated expression of the inhibitory programmed death-1 (PD-1) receptor on NKT cells, and blockade of PD-1 signaling enhanced the response to a-GalCer.

According to the news reporters, the researchers concluded: “This study shows that NKT cell levels and functions are reduced in *M. tuberculosis*-infected patients and these deficiencies were found to reflect the presence of active tuberculosis.”

For more information on this research see: Dysfunction of Natural Killer T Cells in Patients with Active Mycobacterium tuberculosis Infection. *Infection and Immunity*, 2012;80(6):2100-8. (American Society for Microbiology - www.asm.org; Infection and Immunity - iai.asm.org)

Our news correspondents report that additional information may be obtained by contacting S.J. Kee, Dept. of Laboratory Medicine, Chonnam National University Medical School and Hospital, Gwangju, South Korea. (2012 Jun 11)

**MRC National Institute for Medical Research, London:**

**Programmed death ligand 1 is over-expressed by neutrophils in the blood of patients with active tuberculosis**

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators discuss new findings in Tuberculosis. According to news reporting out of London, United Kingdom, by NewsRx editors, researchers stated “Tuberculosis (TB), caused by *Mycobacterium tuberculosis* (Mtb), remains one of the world’s largest infectious disease problems. Despite decades of intensive study, the immune response to Mtb is incompletely characterised, reflecting the extremely complex interaction between pathogen and host.”

Our news journalists obtained a quote from the research by the authors from MRC National Institute for Medical Research, “Pathways that may alter the balance between host protection and pathogenesis are therefore of great interest. One pathway shown to play a role in the pathogenesis of chronic infections, including TB, is the programmed death-1 (PD-1) pathway.”

According to the news editors, the researchers concluded: “We show here that the expression of the programmed death ligand 1 (PD-L1), which interacts with PD-1, is increased in whole blood from active TB patients compared with whole blood from healthy controls or Mtb-exposed individuals, and that expression by neutrophils is largely responsible for this increase.”

Case Western Reserve University, Cleveland: Mycobacterium tuberculosis ManLAM inhibits T-cell-receptor signaling by interference with ZAP-70, Lck and LAT phosphorylation

By a News Reporter-Staff News Editor at Proteomics Weekly – A new study on Tuberculosis is now available. According to news originating from Cleveland, Ohio, by NewsRx correspondents, researchers stated “Immune evasion is required for Mycobacterium tuberculosis to survive in the face of robust CD4(+) T cell responses. We have shown previously that M. tuberculosis cell wall glycolipids, including mannose capped lipoarabinomannan (ManLAM), directly inhibit polyclonal murine CD4(+) T cell activation by blocking ZAP-70 phosphorylation.”

Our news journalists obtained a quote from the research by the authors from Case Western Reserve University, “We extended these studies to antigen-specific murine CD4(+) T cells and primary human T cells and found that ManLAM inhibited them as well. Lck and LAT phosphorylation also were inhibited by ManLAM without affecting their localization to lipid rafts.”

According to the news editors, the researchers concluded: “Inhibition of proximal TCR signaling was temperature sensitive, suggesting that ManLAM insertion into T cell membranes was required. Thus, M. tuberculosis ManLAM inhibits antigen-specific CD4(+) T cell activation by interfering with very early events in TCR signaling through ManLAM’s insertion in T cell membranes.”


The news correspondents report that additional information may be obtained from R.N. Mahon, Dept. of Pathology, Case Western Reserve University and University Hospitals Case Medical Center, Cleveland OH 44106, United States. (2012 Jun 04)
Patent Issued for Immunostimulatory Recombinant Intracellular Pathogen Immunogenic Compositions and Methods of Use

By a News Reporter-Staff News Editor at Biotech Week – A patent by the inventors Horwitz, Marcus A. (Los Angeles, CA); Harth, Gunter (Los Angeles, CA), filed on April 10, 2007, was cleared and issued on October 16, 2012, according to news reporting originating from Alexandria, Virginia, by NewsRx correspondents.

Patent number 8287879 is assigned to The Regents of the University of California (Oakland, CA).

The following quote was obtained by the news editors from the background information supplied by the inventors: “It has long been recognized that parasitic microorganisms possess the ability to infect animals thereby causing disease and often death. Pathogenic agents have been a leading cause of death throughout history and continue to inflict immense suffering. Though the last hundred years have seen dramatic advances in the prevention and treatment of many infectious diseases, complicated host-parasite interactions still limit the universal effectiveness of therapeutic measures. Difficulties in countering the sophisticated invasive mechanisms displayed by many pathogenic organisms are evidenced by the resurgence of various diseases such as tuberculosis, as well as the appearance of numerous drug resistant strains of bacteria and viruses.

“Among those pathogenic agents of major epidemiological concern, intracellular bacteria have proven to be particularly intractable in the face of therapeutic or prophylactic measures. Intracellular bacteria, including the genus Mycobacterium, complete all or part of their lifecycle within the cells of the infected host organism rather than extracellularly. Around the world, intracellular bacteria are responsible for untold suffering and millions of deaths each year. Tuberculosis is the leading cause of death from a single disease agent worldwide, with 8 million new cases and 2 million deaths annually. In addition, intracellular bacteria are responsible for millions of cases of leprosy. Other debilitating diseases transmitted by intracellular agents include cutaneous and visceral leishmaniasis, American trypanosomiasis (Chagas disease), listeriosis, toxoplasmosis, histoplasmosis, trachoma, psittacosis, Q-fever, legionellosis, anthrax and tularemia.

“Currently it is believed that approximately one-third of the world’s population is infected by Mycobacterium tuberculosis resulting in millions of cases of pulmonary tuberculosis annually. More specifically, human pulmonary tuberculosis primarily caused by M. tuberculosis is a major cause of death in developing countries. Mycobacterium tuberculosis is capable of surviving inside macrophages and monocytes, and therefore may produce a chronic intracellular infection. Mycobacterium
tuberculosis is relatively successful in evading the normal defenses of the host organism by concealing itself within the cells primarily responsible for the detection of foreign elements and subsequent activation of the immune system. Moreover, many of the front-line chemotherapeutic agents used to treat tuberculosis have relatively low activity against intracellular organisms as compared to extracellular forms. These same pathogenic characteristics have heretofore limited the effectiveness of immunotherapeutic agents or immunogenic compositions against tubercular infections.

"Recently, tuberculosis resistance to one or more drugs was reported in 36 of the 50 United States. In New York City, one-third of all cases tested was resistant to one or more major drugs. Though non-resistant tuberculosis can be cured with a long course of antibiotics, the outlook regarding drug resistant strains is bleak. Patients infected with strains resistant to two or more major antibiotics have a fatality rate of around 50%. Accordingly, safe and effective immunogenic compositions against multi-drug resistant strains of M. tuberculosis are sorely needed.

"Initial infections of M. tuberculosis almost always occur through the inhalation of aerosolized particles as the pathogen can remain viable for weeks or months in moist or dry sputum. Although the primary site of the infection is in the lungs, the organism can also cause infection of nearly any organ including, but not limited to, the bones, spleen, kidney, meninges and skin. Depending on the virulence of the particular strain and the resistance of the host, the infection and corresponding damage to the tissue may be minor or extensive. In the case of humans, the initial infection is controlled in the majority of individuals exposed to virulent strains of the bacteria. The development of acquired immunity following the initial challenge reduces bacterial proliferation thereby allowing lesions to heal and leaving the subject largely asymptomatic.

"When M. tuberculosis is not controlled by the infected subject it often results in the extensive degradation of lung tissue. In susceptible individuals, lesions are usually formed in the lung as the tubercle bacilli reproduce within alveolar or pulmonary macrophages. As the organisms multiply, they may spread through the lymphatic system to distal lymph nodes and through the blood stream to the lung apices, bone marrow, kidney and meninges surrounding the brain. Primarily as the result of cell-mediated hypersensitivity responses, characteristic granulomatous lesions or tubercles are produced in proportion to the severity of the infection. These lesions consist of epithelioid cells bordered by monocytes, lymphocytes and fibroblasts. In most instances a lesion or tubercle eventually becomes necrotic and undergoes caseation (conversion of affected tissues into a soft cheesy substance).

"While M. tuberculosis is a significant pathogen, other species of the genus Mycobacterium also cause disease in animals including man
and are clearly within the scope of the present invention. For example, *M. bovis* is closely related to *M. tuberculosis* and is responsible for tubercular infections in domestic animals such as cattle, pigs, sheep, horses, dogs and cats. Further, *M. bovis* may infect humans via the intestinal tract, typically from the ingestion of raw milk. The localized intestinal infection eventually spreads to the respiratory tract and is followed shortly by the classic symptoms of tuberculosis. Another important pathogenic species of the genus *Mycobacterium* is *M. leprae* that causes millions of cases of the ancient disease leprosy. Other species of this genus which cause disease in animals and man include *M. kansasii*, *M. avium intracellulare*, *M. fortuitum*, *M. marinum*, *M. chelonei*, and *M. scrofulaceum*. The pathogenic mycobacterial species frequently exhibit a high degree of homology in their respective DNA and corresponding protein sequences and some species, such as *M. tuberculosis* and *M. bovis*, are highly related.

“Attempts to eradicate tuberculosis using immunogenic compositions was initiated in 1921 after Calmette and Guerin successfully attenuated a virulent strain of *M. bovis* at the Institut Pasteur in Lille, France. This attenuated *M. bovis* became known as the Bacille Calmette Guerin, or BCG for short. Nearly eighty years later, immunogenic compositions derived from BCG remain the only prophylactic therapy for tuberculosis currently in use. In fact, all BCG immunogenic compositions available today are derived from the original strain of *M. bovis* developed by Calmette and Guerin at the Institut Pasteur.

“The World Health Organization considers the BCG immunogenic compositions an essential factor in reducing tuberculosis worldwide, especially in developing nations. In theory, the BCG immunogenic composition confers cell-mediated immunity against an attenuated mycobacterium that is immunologically related to *M. tuberculosis*. The resulting immune response should inhibit primary tuberculosis. Thus, if primary tuberculosis is inhibited, latent infections cannot occur and disease reactivation is avoided.

“Current BCG immunogenic compositions are provided as lyophilized cultures that are re-hydrated with sterile diluent immediately before administration. The BCG immunogenic composition is given at birth, in infancy, or in early childhood in countries that practice BCG vaccination, including developing and developed countries. Adult visitors to endemic regions who may have been exposed to high doses of infectious Mycobacteria may receive BCG as a prophylactic providing they are skin test non-reactive. Adverse reactions to the immunogenic composition are rare and are generally limited to skin ulcerations and lymphadenitis near the injection site. However, in spite of these rare adverse reactions, the BCG immunogenic composition has an unparalleled history of safety with over three billion doses having been administered worldwide since 1930.
“However, the unparalleled safety of traditional BCG immunogenic compositions is coming under increased scrutiny and has created a paradox for healthcare practitioners. The population segments most susceptible to mycobacterial infections are the immunocompromised and immunosuppressed. Persons suffering from early or late-stage HIV infections are particularly susceptible to infection. Unfortunately, many persons in the early-stage of HIV infection are unaware of their immune status. It is likely that these individuals may voluntarily undergo immunization using a live attenuated immunogenic composition such as BCG without being forewarned of their unique risks. Moreover, other mildly immunocompromised or immunosuppressed individuals may also unwittingly undergo immunization with BCG hoping to avoid mycobacterial disease. Therefore, safer, more efficacious BCG and BCG-like immunogenic compositions are desirable.

“Recently, significant attention has been focused on using transformed BCG strains to produce immunogenic compositions that express various cell-associated antigens. For example, C. K. Stover, et al. have reported a Lyme Disease immunogenic composition using a recombinant BCG (rBCG) that expresses the membrane associated lipoprotein OspA of Borrelia burgdorferi. Similarly, the same author has also produced a rBCG immunogenic composition expressing a pneumococcal surface protein (PspA) of Streptococcus pneumoniae. (Stover C K, Bansal G P, Langerman S, and Hanson M S. 1994. Protective immunity elicited by rBCG immunogenic compositions. In: Brown F. (ed): Recombinant Vectors in Immunogenic Composition Development. Dev Biol Stand. Dasel, Karger, Vol. 82:163-170)

“U.S. Pat. No. 5,504,005 (the “005’ patent’) and U.S. Pat. No. 5,854,055 (the “055 patent’) both issued to B. R. Bloom et al., disclose theoretical rBCG vectors expressing a wide range of cell associated fusion proteins from numerous species of microorganisms. The theoretical vectors described in these patents are either directed to cell-associated fusion proteins, as opposed to extracellular non-fusion protein antigens, and/or the rBCG is hypothetically expressing fusion proteins from distantly related species.

“Furthermore, neither the ’005 nor the ’055 patent disclose animal model safety testing, immune response development or protective immunity in an animal system that closely emulates human disease. In addition, only theoretical rBCG vectors expressing M. tuberculosis fusion proteins are disclosed in the ’005 and ’055 patents; no actual immunogenic compositions are enabled. Those immunogenic composition models for M. tuberculosis that are disclosed are directed to cell-associated heat shock fusion proteins, not extracellular non-fusion proteins.
“U.S. Pat. No. 5,830,475 (the ‘475 patent’) also discloses theoretical mycobacterial immunogenic compositions used to express fusion proteins. The immunogenic compositions disclosed are intended to elicit immune responses in non-human animals for the purpose of producing antibodies thereto and not shown to prevent intracellular pathogen diseases in mammals. Moreover, the ‘475 patent does not disclose recombinant immunogenic compositions that use protein specific promoters to express extracellular non-fusion proteins.

“U.S. Pat. No. 6,467,967 claims immunogenic compositions comprising a recombinant BCG having an extrachromosomal nucleic acid sequence comprising a gene encoding a M. tuberculosis 30 kDa major extracellular protein (also known as Antigen 85B), wherein the M. tuberculosis 30 kDa major extracellular protein is over-expressed and secreted. Moreover, U.S. Pat. No. 6,924,118 claims additional recombinant BCG that over-express other M. tuberculosis major extracellular proteins.

“Therefore, there remains a need for recombinant intracellular pathogen immunogenic compositions that induce protective immune responses.”

In addition to the background information obtained for this patent, NewsRx journalists also obtained the inventors’ summary information for this patent: “The present invention provides methods for producing recombinant immunogenic compositions for preventing or treating diseases of intracellular pathogens in humans and animals, immunogenic compositions against diseases of intracellular pathogens in humans and animals, and a new approach to producing immunogenic compositions against tuberculosis, leprosy, other mycobacterial diseases, and other intracellular pathogens.

“The present invention provides recombinant Bacille Calmette Guerin (rBCG) immunogenic compositions that a) express host immunostimulatory molecules, host molecules that direct the immune response toward a TH1 type of immune response, or host molecules that direct the immune response away from a TH2 type of immune response; b) express a host immunostimulatory molecule, a host molecule that directs the immune response toward a TH1 type of immune response, or a host molecule that directs the immune response away from a TH2 type of immune response and express a pathogen major extracellular protein; or c) express Mycobacterium tuberculosis major extracellular proteins.

“In one embodiment of the present invention, an immunogenic composition is provided comprising a recombinant BCG expressing at least one Mycobacteria major extracellular protein selected from the group consisting of 12 kDa protein, 14 kDa protein, 16 kDa protein, 23.5 kDa protein, 24 kDa protein, 30 kDa protein, 32A kDa protein, 32B kDa
protein, 45 kDa protein, 58 kDa protein, 71 kDa protein, 80 kDa protein, and 110 KD protein, and combinations thereof, and at least one cytokine; wherein the Mycobacteria major extracellular proteins are over-expressed and secreted. In another embodiment, the at least one cytokine is selected from the group consisting of interferon gamma, interleukin-2, interleukin-12, interleukin-4 receptor and granulocyte macrophage colony stimulating factor, and combinations thereof.

“In another embodiment, at least one of said at least one Mycobacteria major extracellular proteins are over-expressed and secreted. In another embodiment, at least one cytokine is selected from the group consisting of interferon gamma, interleukin-2, interleukin-12, interleukin-4 receptor and granulocyte macrophage colony stimulating factor, and combinations thereof.

“In another embodiment, at least one of said at least one Mycobacteria major extracellular proteins are expressed on one or more extrachromosomal nucleic acid sequences. In another embodiment, at least one of said cytokines are expressed on one or more extrachromosomal nucleic acid sequences. In yet another embodiment, more than one of the at least one Mycobacteria major extracellular proteins are expressed on one or more extrachromosomal nucleic acid sequences. In another embodiment, each of said at least one Mycobacteria major extracellular proteins are expressed from different extrachromosomal nucleic acid sequences. In another embodiment, the at least one Mycobacteria major extracellular proteins and the at least one cytokine are expressed from different extrachromosomal nucleic acid sequences. In another embodiment, the at least one Mycobacteria major extracellular proteins and the at least one cytokine are expressed from the same extrachromosomal nucleic acid sequence.

“In another embodiment of the present invention, at least one of the at least one Mycobacteria major extracellular proteins are integrated into the rBCG genome under the control of a strong promoter and over-expressed. In another embodiment, the at least one cytokine are integrated into the rBCG genome under the control of a strong promoter and over-expressed. In another embodiment, the at least one Mycobacteria major extracellular proteins and the at least one cytokine are integrated into the rBCG genome under the control of a strong promoter and over-expressed.

“In another embodiment, the at least one major extracellular proteins are non-fusion proteins. In another embodiment, the at least one major extracellular proteins are fusion proteins. In yet another embodiment, the at least one major extracellular proteins and at least one cytokine comprise a fusion protein.

“In another embodiment of the present invention, the Mycobacteria major extracellular protein is from a species of Mycobacterium selected from the group consisting of Mycobacterium tuberculosis, Mycobacterium bovis, Mycobacterium leprae, and Mycobacterium avium intracellulare. In another embodiment, the Mycobacteria major extracellular protein is the 30 kDa protein.

“In another embodiment, the Mycobacteria major extracellular protein is over-expressed and secreted such that a protective immune response is induced in a host.
“In one embodiment of the present invention, the immunogenic composition expresses the 30 kDa, 32A kDa and 32B kDa Mycobacteria major extracellular proteins, the interleukin 4 receptor and interferon gamma.

“In another embodiment of the present invention, the immunogenic composition expresses the 30 kDa Mycobacteria major extracellular protein, the interleukin 4 receptor and interferon gamma.

“In another embodiment of the present invention, the immunogenic composition expresses the 30 kDa and 23.5 kDa Mycobacteria major extracellular proteins, the interleukin 4 receptor and interferon gamma.

“In one embodiment of the present invention, an immunogenic composition is provided comprising a recombinant intracellular pathogen expressing at least one major extracellular protein of an intracellular pathogen and at least one cytokine wherein the major extracellular protein is over-expressed. In another embodiment, the at least one cytokine is selected from the group consisting of interferon gamma, interleukin-2, interleukin-12, interleukin-4 receptor and granulocyte macrophage colony stimulating factor, and combinations thereof.

“In one embodiment of the present invention, an immunogenic composition is provided comprising a recombinant intracellular pathogen wherein the recombinant intracellular pathogen expresses at least one major extracellular protein of an intracellular pathogen and at least one cytokine wherein nucleic acid sequences encoding for the at least one major extracellular protein and at least one cytokine are incorporated into the intracellular pathogen’s chromosome(s) under a strong promoter such that the major extracellular protein is over-expressed.

“In another embodiment, the recombinant intracellular pathogen is of the same species as the intracellular pathogen against which the immunogenic composition is directed. In another embodiment, the recombinant intracellular pathogen is of a different species than the intracellular pathogen against which the immunogenic composition is directed.

“In another embodiment of the present invention, the recombinant intracellular pathogen is selected from the group consisting of Mycobacterium bovis, M. tuberculosis, M. leprae, M. kansasii, M. avium, Mycobacterium sp., Legionella pneumophila, L. longbeachae, L. bozemanii, Legionella sp., Rickettsia rickettsii, Rickettsia typhi, Rickettsia sp., Ehrlichia chaffeensis, Ehrlichia phagocytophila geno group, Ehrlichia sp., Coxiella burnetii, Leishmania sp, Toxoplasma gondii, Trypanosoma cruzi, Chlamydia pneumoniae, Chlamydia sp, Listeria monocytogenes, Listeria sp, Histoplasma sp., Francisella tularensis, Brucella species, Yersinia pestis, Bacillus anthracis, and Salmonella typhi and adenovirus, vaccinia, avipox, adeno-associated virus, modified Vaccinia Strain Ankara, Semliki Forest virus, poxvirus, and herpes viruses.
“In one embodiment of the present invention, an immunogenic composition is provided comprising a rBCG expressing the 30 kDa, 32A kDa and 32B kDa Mycobacteria major extracellular proteins from at least one extrachromosomal nucleic acid sequence and further comprising an extrachromosomal nucleic acid sequence expressing a gene encoding for interferon gamma, wherein the Mycobacteria major extracellular proteins are over-expressed and secreted.

“In one embodiment of the present invention, an immunogenic composition is provided comprising a rBCG wherein the rBCG expresses the 30 kDa, 32A kDa and 32B kDa Mycobacteria major extracellular proteins and a gene encoding for interferon gamma, wherein nucleic acid sequences encoding for the 30 kDa, 32A kDa and 32B kDa Mycobacteria major extracellular proteins and the interferon gamma are incorporated into the intracellular pathogen’s chromosome(s) under a strong promoter such that the 30 kDa, 32A kDa and 32B kDa Mycobacteria major extracellular proteins are over-expressed and secreted.

“In one embodiment of the present invention, an immunogenic composition is provided comprising a rBCG comprising a first extrachromosomal nucleic acid sequence expressing a gene encoding the 30 kDa Mycobacteria major extracellular protein from an extrachromosomal nucleic acid sequence and a second extrachromosomal nucleic acid sequence expressing a gene encoding for interferon gamma, wherein the 30 kDa Mycobacteria major extracellular protein is over-expressed and secreted.

“In another embodiment of the present invention, an immunogenic composition is provided comprising a rBCG wherein the rBCG expresses the 30 kDa Mycobacteria major extracellular protein and a gene encoding for interferon gamma, wherein nucleic acid sequences encoding for the 30 kDa Mycobacteria major extracellular protein and interferon gamma are incorporated into the intracellular pathogen’s chromosome(s) under a strong promoter such that the 30 kDa Mycobacteria major extracellular protein is over-expressed and secreted.”


By a News Reporter-Staff News Editor at Politics & Government Week – University Of Medicine And Dentistry Of New Jersey has been issued patent application serial number 449852, according to news reporting originating out of Washington, D.C., by VerticalNews editors.

The patent’s inventors are Gennaro, Maria Laura (New York, NY).

This patent application was filed on April 18, 2012 and was cleared for further review on August 16, 2012.

From the background information supplied by the inventors, news correspondents obtained the following quote: “Diagnosis for the disease tuberculosis (TB) traditionally includes a combination of clinical, bacteriological and radiographic evidence, typically culture and smear tests, the tuberculin skin test (TST) and chest x-ray.

“Antibodies specific for a number of proteins expressed by M. tuberculosis are detectable in human serum. Antibody assays are speedy and relatively inexpensive, and thus are a potentially valuable diagnostic and screening technique. There are several diagnostic categories for TB: active disease, inactive (past) TB, and two categories characterized by the absence of radiographic chest abnormality: latent infection and infection-free. Detection of active TB is, of course, clinically important. Detection of inactive TB is clinically significant, because persons with inactive TB are more than an order of magnitude more likely to develop active TB than are persons who have latent TB. Distinguishing active TB from inactive TB is significant from a public-health standpoint, as it permits concentration of resources, which are often very limited in countries most severely impacted by TB, where the danger is greatest. Distinguishing inactive TB from states characterized by normal chest x-rays is similarly important from a public-health standpoint.

“Attempts to utilize detection of serum antibodies to diagnose a TB state have focused on finding an antigen or antigens whose binding correlates positively with that particular state, for example, antigens for whom positive ELISA results signals active TB. Diagnosis of TB states by antibody serum tests has suffered from lack of accuracy.

“An aspect of this invention is assays for detection of human serum antibodies with improved ability to predict TB states accurately, particularly to discriminate between active TB and inactive TB.

“Another aspect of this invention is reagent kits containing M. tuberculosis proteins as antigens for such antibody assays.”

Supplementing the background information on this patent application, VerticalNews reporters also obtained the inventors’ summary information for this patent: “TB states include five recognized classes. Class 1 (sometimes denominated Class 0-1) indicates absence of infection. In this application we refer to that state as ‘infection-free’. Class
2 is latent infection. The foregoing two classes both are characterized by the absence of radiographic chest abnormality, which we sometimes refer to as ‘chest x-ray normal’ or, for short, ‘CXR-normal.’ Class 3 is active TB. Class 4 is inactive TB. Class 5 is TB suspected, diagnosis pending. This five-class system was adopted by the board of directors of the American Thoracic Society in July 1999, in a joint statement with the U.S. Centers for Disease Control (CDC) titled ‘Targeted Tuberculin Testing and Treatment of Latent Tuberculosis Infection.’ The classification has been endorsed by the Council of the Infectious Diseases Society of America. See Am. J. Respir. Crit. Care Med. (April 2000) 164 (4 pt 2): S221-47. Class 4, inactive TB, as defined is ‘Tuberculosis; not clinically active. This classification is defined by a history of previous episode(s) of tuberculosis or abnormal stable radiographic findings in a person with a positive reaction to tuberculin skin test, negative bacteriologic studies (if done), and no clinical and/or radiographic evidence of current disease. Persons in Class 4 may never have received chemotherapy, may be receiving treatment for latent infection, or may have completed a previously prescribed course of chemotherapy.’

“This invention is human serum antibody assays for TB with improved ability to distinguish inactive TB from active TB as compared to known single-antibody assays and, preferably also from latent TB and infection-free categories. Assays according to this invention are based on and utilize the well-known antigen-antibody reaction. The type of protocol, that is, sandwich assay or competitive assay, is not critical. I utilize an ELISA (enzyme-linked immunosorbent assay) that is a sandwich format including as a first reagent immobilized antigen and as second reagent a labeled anti-antibody that binds to antibodies immobilized by the first reagent. However, other formats for detection of serum antibodies can be used. See, for example, U.S. Nos. Re. 3,654,090, 3,791,932, 3,850,752, 3,839,153, and 3,879,262.

“Assays of this invention utilize proteins of M. tuberculosis as reagents, either as antigen first reagent to immobilize serum antibodies or as antigen labeled reagents, or both. Assays of this invention are characterized by the use of at least 3 antigens; and by the inclusion of antigens of at least two types: first, at least one antigen that is specific for an antibody whose presence is an indicator of inactive TB relative to active TB and, second, at least one antigen that is specific for an antibody whose absence is an indicator of inactive TB relative to active TB. When utilized in my preferred sandwich assay, a positive response from an antigen or antigens of the first type coupled with a negative response (that is, absence of a positive response) from an antigen or antigens of the second type is indicative of inactive TB as distinguished from active TB. Certain preferred assays include one or more antigens of a third type whose positive response is an indicator of active TB or inactive TB, or both, as distinguished from latent TB or infection-free.
Antigens of the first type in some instances are antigens of the third type, although antigens of the third type need to be antigens of the first type. Similarly, antigens of the second type may in some instances be antigens of the third type.

“Assays according to this invention include performing separate reactions in separate locations or containers, for example, separate spots on a card or stick surface or separate wells of microtitre plates. In such a format, use of a color-forming label such as horseradish peroxidase is possible, as one can tell which antigen or antigens lead to a positive response, namely color. Assays according to this invention also include performing separate reactions commonly in separate locations of a single array, such as occurs when antigen first reagents are immobilized at identifiable, separate locations on the surface of an array, and the entire array is exposed to serum, washed, exposed to common second reagent, washed again, and read. In this approach the second reagent is labeled with a signaling label, for example, a fluorescent moiety or a radioactive isotope, so that positive results at individual locations of various first-reagent antigens can be detected.

“Preferred assays according to this invention are constructed so as to have two results, positive result or negative result, for each antigen. For the type of sandwich ELISA I have used and that is described in this application, one establishes the division point (cut-off point) between positive and negative and adjusts antigen concentration or other conditions in the assay so that only results above cut-off give a positive result. This can be illustrated by reference to Table 3. In Table 3, for AlaDH antigen, the median results were: for cases of active TB, 0.199; for cases of inactive TB, 0.140; and for cases that were CXR-normal, 0.106. In designing an assay the concentration of the antigen can be adjusted to provide the desired cut-off, that is, so that only cases of active TB will produce sufficient color to be judged ‘positive.’ All other cases will give insufficient (or no) color and be judged ‘negative’ in the assay. Therefore, the AlaDH antigen result, if positive, will be consistent with active TB but not inactive TB, and it will also be consistent with active TB but not a CXR-normal class. However, a positive or negative result will not distinguish inactive TB from CXR-normal classes, because results for all of them would be negative. In this application, including the claims, such positive results are considered to signify serological recognition by an antigen. Looking at the medians for ESAT-6 and 16 kDa, one can see that a properly adjusted concentration for the cut-off will mean that a positive result is consistent with inactive TB but inconsistent with both active TB and CXR-normal classes. In this case a negative result will not distinguish active TB from CXR-normal classes.

“For a result to be considered positive, each first-reagent antigen must lead to the appropriate signal. For example, for an assay to be considered indicative of inactive TB, of the antigens listed in Table 4,
those with an odds ratio (OR) greater than 1 must give a ‘high’ signal and those with an OR below 1 must give a Low signal (in the case of 38 kDa Ag a low or Medium signal); and of the antigens listed in Table 5, all must give a ‘High’ signal to distinguish inactive TB from a CXR-normal state.

“To improve confidence in results, one can include more antigens, utilize antigens whose OR differs from 1.0 more greatly, utilize a different alpha value or a combination of two or more of the foregoing.

“To develop an assay according to this invention, one can start with a group of characterized serum samples and a putative set of antigens, and obtain data such as is shown in Table 3. For subsets or for all the antigens, one then performs a statistical analysis, for example, the analysis discussed in connection with Tables 4 and 5. To bring another antigen (‘antigen X’) into the mix without having to generate Table 3 data for antigens already tested, one simply saves the serum samples originally used and tests antigen X against them. With only that extra testing a new set or new subsets can be analyzed statistically to produce expanded Tables 4 and 5. Evaluation of another protein of M. tuberculosis for inclusion in assays of this invention can be accomplished routinely according to the assay and data-analysis procedures set forth herein. The procedures include measuring serum levels of antibodies according to the ELISA described herein, expressed conventionally as ‘optical density’ or absorbance (as OD.sub.450), to obtain data such as reported in Table 3, wherein differences are considered significant only at p<0.05 with and without controlling for multiple comparisons using the Bonferroni approach; estimating multivariate logistic regression models using only those antigens identified as statistically significant; and using backward elimination so that the odds ratios associated with each and every antigen are statistically significant (CI not including 1.0) using one model or the other as shown in Table 4.

“Described below in the Examples is work with an initial panel of eight antigens. While the results are impressive with this panel, no attempt has yet been made to optimize our assay procedure by changing the panel. However, many TB antigens are known. From reported work with sera from mice, primates and humans utilizing other TB antigens, I have identified several candidates for evaluation in kits and assays according to this invention. These include Rv0440, Rv3881c and Rv2195 (Havlir, D. V. et al (1991) Infect. Immun. 59, 665-670); Lodes, M. J. et al (2001) J Clin Microbiol 39, 2485-2493; Rv2495c, Rv2195, Rv2700 and Rv3763 (Bothamley (2003) Lancet 361, 2082); (Bothamley, G. H. (2004) Clin Diagn Lab Immunol 11, 942-951); and Rv1837c and Rv3803c (Singh, K. K. et al. (2005) Clin Diagn Lab Immunol 12, 354-358).

“The experimental work reported in this application was with serum from a special and particularly difficult population of persons. Most
active TB cases were negative when tested for bacterium in sputum smear. Correctly diagnosing such individuals by chest x-ray is quite difficult and requires subjective judgment of a highly skilled physician. For this group of active cases, individual antigens are quite inefficient at identifying active cases in a population that includes inactive and CXR-normal classes of TB. As shown in Table 6 and described below, individual antigens indicated the active cases correctly only 6-15% of the time. The assay of this invention, including a panel that includes both antigens that positively correlate to inactive TB and antigens that negatively correlate to inactive TB, did threefold better, as much as 43% of the time. This improvement is practically significant. If used for checking immigrants, for example, nearly half of the active TB cases that would otherwise not be detected would be detected, even using the unoptimized antigen panel initially tested.

“This invention also includes assay kits comprising multiple M. tuberculosis antigens as first, immobilizing reagent or as second, labeled reagent, or both. Preferred kits include multiple M. tuberculosis antigens as first reagent and anti-human IgG antibodies as labeled second reagents.

“The details of one or more embodiments of the invention are set forth in the accompanying drawings and the description below. Other features, objects, and advantages of the invention will be apparent from the description and drawings, and from the claims.”

Chapter 5

Risk and Prevention

Harvard University, Boston: Risk factors and timing of default from treatment for non-multidrug-resistant tuberculosis in Moldova

By a News Reporter-Staff News Editor at Biotech Week – A new study on Tuberculosis and Lung Disease is now available. According to news reporting out of Boston, Massachusetts, by NewsRx editors, research stated, “The Republic of Moldova, in Eastern Europe, has among the highest reported nationwide proportions of tuberculosis (TB) patients with multidrug-resistant tuberculosis (MDR-TB) worldwide. Default has been associated with increased mortality and amplification of drug resistance, and may contribute to the high MDR-TB rates in Moldova.”

Our news journalists obtained a quote from the research from Harvard University, “To assess risk factors and timing of default from treatment for non-MDR-TB from 2007 to 2010. A retrospective analysis of routine surveillance data on all non-MDR-TB patients reported. A total of 14.7% of non-MDR-TB patients defaulted from treatment during the study period. Independent risk factors for default included sociodemographic factors, such as homelessness, living alone, less formal education and spending substantial time outside Moldova in the year prior to diagnosis; and health-related factors such as human immunodeficiency virus co-infection, greater lung pathology and increasing TB drug resistance. Anti-tuberculosis treatment is usually initiated within an institutional setting in Moldova, and the default risk was highest in the month following the phase of hospitalized treatment (among civilians) and after leaving prison (among those diagnosed while incarcerated).”

According to the news editors, the research concluded: “Targeted interventions to increase treatment adherence for patients at highest risk
of default, and improving the continuity of care for patients transitioning from institutional to community care may substantially reduce risk of default.”


Our news journalists report that additional information may be obtained by contacting H.E. Jenkins, Harvard University, Sch Public Hlth, Boston, MA 02115, United States. (2013 Apr 17)

**Imperial College London: Estimating risk over time using data from targeted surveillance systems: application to bovine tuberculosis in Great Britain**

By a News Reporter-Staff News Editor at Life Science Weekly – Current study results on Epidemiology have been published. According to news reporting originating from London, United Kingdom, by NewsRx correspondents, research stated, “For infections that are typically asymptomatic, targeted surveillance systems (whereby individuals at increased risk are tested more frequently) will detect infections earlier on average than systems with random testing or in systems where all individuals are tested at the same intervals. However, estimating temporal trends in infection risk using data from such targeted surveillance systems can be challenging.”

Our news editors obtained a quote from the research from Imperial College London, “This is similarly a problem for targeted surveillance to detect faults of individual industrial components. The incidence of bovine tuberculosis (TB) in British cattle has been generally increasing in the last thirty years. Cattle herds are routinely tested for evidence of exposure to the aetiological bacteria *Mycobacterium bovis*, in a targeted surveillance programme in which the testing interval is determined by past local TB incidence and local veterinary discretion. The UK Department for Environment, Food and Rural Affairs (Defra) report the monthly percentage of tests on officially TB-free (OTF) herds resulting in a confirmed positive test for *M. bovis* (i.e. the percentage of tested herds with OTF status withdrawn), which contains substantial fluctuations (three years apart) within the increasing trend. As the number of herds tested changes over time, this cyclic trend is difficult to interpret. Here we evaluate an alternative to the Defra method in which we distribute each incident event across the period at risk to infer the underlying trends in infection incidence using a stochastic model of cattle herd incidence and testing frequencies fitted to data on the monthly
number of herds tested and number of these with OTF status with-
drawn in 2003-2010.”

According to the news editors, the research concluded: “We show
that for an increasing underlying incidence trend, the current Defra
approach can produce artefactual fluctuations whereas the alternative
method described provides more accurate descriptions of the underlying
risks over time.”

For more information on this research see: Estimating risk over time
using data from targeted surveillance systems: application to bovine
- www.elsevier.com; Epidemics - http://www.elsevier.com/wps/
product/cws_home/714736)

The news editors report that additional information may be ob-
tained by contacting I.M. Blake, MRC Centre for Outbreak Analysis and
Modelling, Dept. of Infectious Disease Epidemiology, School of Public
Health, Imperial College London, London, UK. (2013 Apr 02)

University of New South Wales, Kensington: Risk factors
for tuberculosis

By a News Reporter-Staff News Editor at Life Science Weekly – Investi-
gators publish new report on Life Science. According to news originat-
ing from Kensington, Australia, by NewsRx correspondents, research
stated, “The risk of progression from exposure to the tuberculosis bacilli
to the development of active disease is a two-stage process governed by
both exogenous and endogenous risk factors. Exogenous factors play
a key role in accentuating the progression from exposure to infection
among which the bacillary load in the sputum and the proximity of an
individual to an infectious TB case are key factors.”

Our news journalists obtained a quote from the research from the
University of New South Wales, “Similarly endogenous factors lead
in progression from infection to active TB disease. Along with well-
established risk factors (such as human immunodeficiency virus (HIV),
malnutrition, and young age), emerging variables such as diabetes, in-
door air pollution, alcohol, use of immunosuppressive drugs, and to-
bacco smoke play a significant role at both the individual and popu-
lation level. Socioeconomic and behavioral factors are also shown to
increase the susceptibility to infection. Specific groups such as health
care workers and indigenous population are also at an increased risk of
TB infection and disease.”

According to the news editors, the research concluded: “This paper
summarizes these factors along with health system issues such as the
effects of delay in diagnosis of TB in the transmission of the bacilli.”

For more information on this research see: Risk factors for tubercu-
losis. Pulmonary Medicine, 2013;2013():828939. (Hindawi Publishing
The news correspondents report that additional information may be obtained from P. Narasimhan, School of Public Health and Community Medicine, The University of New South Wales, Kensington, Sydney, NSW 2052, Australia. (2013 Apr 02)


By a News Reporter-Staff News Editor at Tuberculosis Week – Investigators discuss new findings in Pulmonary Medicine. According to news reporting from Leicester, United Kingdom, by NewsRx journalists, research stated, “The effectiveness of tuberculosis (TB) contact screening programmes using interferon gamma release assays remains uncertain as prospective contact TB risk is not well characterised. To quantify 2-year TB risk and evaluate screening performance with single-step QuantiFERON TB Gold-In Tube (QFT) in adult contacts.”

The news correspondents obtained a quote from the research from Health Protection Agency, “To compare TB risk between QFT tested subgroups stratified by exposure type (smear positive pulmonary (SP) versus non-smear positive (NSP) TB) and age (younger (16-35 years) versus older (&gt;= 36 years)). Screening involved QFT testing in older contacts of SP and all younger contacts, 8-12 weeks after index notification. Chemoprevention (3RH) was offered to QFT positive (+) younger adults. TB risk was determined in a prospective cohort study. Results 43 TB events occurred in 1769 adult contacts observed for median 717 days (2-year rate (95% CI) =2.5% (1.7 to 3.2)). Index-contact strain matching was demonstrable for 18 of 22 (82%) paired samples. No contacts (0/98) receiving 3RH developed TB. 215 of 817 appropriately tested adults (26.3%) were QFT+. 14 of 112 untreated QFT+ adults developed TB (2-year rate (95% CI)=13.4% (7.7 to 21.1)). The model required 35 contacts screened with QFT to identify one contact developing TB at 2 years. TB rates were comparable in QFT+ contacts of SP and NSP (rate ratio (RR)=0.98, p=0.962). For QFT+ older contacts, the disease rate was lower (8.9% (3.3 to 19.1)) and similar to the overall group rate (RR=1.4, p=0.503).”

According to the news reporters, the research concluded: “QFT based single-step contact screening is effective in young adults.”

For more information on this research see: Single-step QuantiFERON screening of adult contacts: a prospective cohort study of tuberculosis risk. Thorax, 2013;68(3):240-246. Thorax can be contacted at: Bmj Publishing Group, British Med Assoc House, Tavistock Square,
World Health Organization, Geneva: Multidrug-resistant tuberculosis in Belarus: the size of the problem and associated risk factors

By a News Reporter-Staff News Editor at AIDS Weekly – A new study on World Health Organization is now available. According to news reporting out of Geneva, Switzerland, by NewsRx editors, research stated, “To assess the problem of multidrug-resistant tuberculosis (MDR-TB) throughout Belarus and investigate the associated risk factors. In a nationwide survey in 2010-2011, 1420 tuberculosis (TB) patients were screened and 934 new and 410 previously treated cases of TB were found to meet the inclusion criteria.”

Our news journalists obtained a quote from the research from World Health Organization, “Isolates of Mycobacterium tuberculosis from each eligible patient were tested for susceptibility to anti-TB drugs. Sociobehavioural information was gathered in interviews based on a structured questionnaire. MDR-TB was found in 32.3% and 75.6% of the new and previously treated patients, respectively, and, 11.9% of the 612 patients found to have MDR-TB had extensively drug-resistant-TB (XDR-TB). A history of previous treatment for TB was the strongest independent risk factor for MDR-TB (odds ratio, OR: 6.1; 95% confidence interval, CI: 4.8-7.7). The other independent risk factors were human immunodeficiency virus (HIV) infection (OR: 2.2; 95% CI: 1.4-3.5), age <35 years (OR: 1.4; 95% CI: 1.0-1.8), history of imprisonment (OR: 1.5; 95% CI: 1.1-2.0), disability sufficient to prevent work (OR: 1.9; 95% CI: 1.2-3.0), alcohol abuse (OR: 1.3; 95% CI: 1.0-1.8) and smoking (OR: 1.5; 95% CI: 1.1-2.0). MDR-TB is very common among TB patients throughout Belarus.”

According to the news editors, the research concluded: “The numerous risk factors identified for MDR-TB and the convergence of the epidemics of MDR-TB and HIV infection call not only for stronger collaboration between TB and HIV control programmes, but also for the implementation of innovative measures to accelerate the detection of TB resistance and improve treatment adherence.”

Sungkyunkwan University, Seoul: Tacrolimus as a risk factor for tuberculosis and outcome of treatment with rifampicin in solid organ transplant recipients

By a News Reporter-Staff News Editor at Biotech Week – Data detailed on Mycobacterium Infections have been presented. According to news reporting from Seoul, South Korea, by NewsRx journalists, research stated, “The purpose of this study was to investigate the incidence, risk factors, and treatment outcome of tuberculosis (TB) in solid organ transplant (SOT) recipients treated with rifampicin. The incidence density of TB was calculated by a retrospective cohort study.”

The news correspondents obtained a quote from the research from Sungkyunkwan University, “Risk factors for TB were analyzed by a nested casecontrol study. Treatment outcome and effects of anti-TB drugs on immunosuppressants and allograft were compared between patients whose initial 2-month intensive regimen included rifampicin and those whose intensive regimen did not. Among the 2144 SOT recipients over 16 years, 40 cases of TB were found (1.7%). The incidence density was 372 cases per 105 patient years (95% confidence interval [CI], 270503), which was 4 times higher than for the general Korean population (90 cases per 105 person years). The median time to the development of TB was 234 days (range, 333940 days). The use of tacrolimus (odds ratio [OR] 4.90; 95% CI, 1.7413.80; P = 0.003) and cytomegalovirus (CMV) infection within the prior 3 months (OR 4.62; 95% CI, 1.4414.87; P = 0.01) were found to be risk factors for TB. Patients whose intensive regimen included rifampicin were more likely to have an increased dose of calcineurin inhibitors than patients whose intensive regimen did not include rifampicin (13/15 [86.7%] vs. 3/14 [21.4%], P = 0.001). Graft rejection and mortality did not differ between the 2 groups. Use of tacrolimus and CMV infection were major risk factors for TB in SOT recipients.”

According to the news reporters, the research concluded: “The graft outcome and mortality did not differ whether rifampicin was used or not during the first 2-month intensive phase.”

For more information on this research see: Tacrolimus as a risk factor for tuberculosis and outcome of treatment with rifampicin in solid organ transplant recipients. Transplant Infectious Disease, 2012;14(6):626-634. Transplant Infectious Disease can be contacted at:
Christian Medical College, Tamil Nadu: Risk factors for tuberculosis among health care workers in South India: a nested case-control study

By a News Reporter-Staff News Editor at Asia Business Newsweekly – New research on Mycobacterium Infections is the subject of a report. According to news reporting out of Tamil Nadu, India, by VerticalNews editors, research stated, “The epidemiology of tuberculosis (TB) among health care workers (HCWs) in India remains under-researched. This study is a nested case control design assessing the risk factors for acquiring TB among HCWs in India.”

Our news journalists obtained a quote from the research from Christian Medical College, “It is a nested case control study conducted at a tertiary teaching hospital in India. Cases (n = 101) were HCWs with active TB. Controls (n = 101) were HCWs who did not have TB. randomly selected from the 6,003 subjects employed at the facility. Cases and controls were compared with respect to clinical and demographic variables. The cases and controls were of similar age. Logistic regression analysis showed that body mass index (BMI) <19 kg/m(2) (odds ratio [OR]: 2.96. 95% confidence interval [CI]: 1.49-5.87), having frequent contact with patients (OR: 2.83, 95% CI: 1.47-5.45) and being employed in medical wards (OR: 12.37, 95% CI: 1.38-110.17) or microbiology laboratories (OR: 5.65, 95% CI: 1.74-18.36) were independently associated with increased risk of acquiring TB. HCWs with frequent patient contact and those with BMI <19 kg/m2 were at high risk of acquiring active TB. Nosocomial transmission of TB was pronounced in locations, such as medical wards and microbiology laboratories.”

According to the news editors, the research concluded: “Surveillance of high-risk HCWs and appropriate infrastructure modifications may be important to prevent interpersonal TB transmission in health care facilities.”

Shandong University, Jinan: Adherence to Tuberculosis Treatment among Migrant Pulmonary Tuberculosis Patients in Shandong, China: A Quantitative Survey Study

By a News Reporter-Staff News Editor at China Weekly News – Investigators discuss new findings in Mycobacterium Infections. According to news reporting out of Jinan, People’s Republic of China, by Vertical-News editors, research stated, “Adherence to TB treatment is the most important requirement for efficient TB control. Migrant TB patients’ ‘migratory’ nature affects the adherence negatively, which presents an important barrier for National TB Control Program in China.”

Our news journalists obtained a quote from the research from Shandong University, “Therefore, TB control among migrants is of high importance. The aim of this study is to describe adherence to TB treatment among migrant TB patients and to identify factors associated with adherence. A total of 12 counties/districts of Shandong Province, China were selected as study sites. 314 confirmed smear positive TB patients were enrolled between August 2(nd) 2008 and October 17(th) 2008, 16% of whom were non-adherent to TB therapy. Risk factors for non-adherence were: the divorced or bereft of spouse, patients not receiving TB-related health education before chemotherapy, weak incentives for treatment adherence, and self supervision on treatment.”

According to the news editors, the research concluded: “Based on the risk factors identified, measures are recommended such as implementing health education for all migrant patients before chemotherapy and encouraging primary care workers to supervise patients.”

For more information on this research see: Adherence to Tuberculosis Treatment among Migrant Pulmonary Tuberculosis Patients in Shandong, China: A Quantitative Survey Study. Plos One, 2012;7(12):e52334. (Public Library of Science - www.plos.org; Plos One - www.plosone.org)

Our news journalists report that additional information may be obtained by contacting C. Zhou, Institute of Social Medicine and Health Service Management, School of Public Health, Shandong University, Jinan, People’s Taiwan. (2013 Jan 22)
Centers for Disease Control and Prevention, Atlanta: Acquired Resistance to Second-Line Drugs Among Persons With Tuberculosis in the United States

By a News Reporter-Staff News Editor at AIDS Weekly – Data detailed on Infectious Diseases have been presented. According to news reporting out of Atlanta, Georgia, by NewsRx editors, research stated, “Acquired resistance to second-line drugs (SLDs) is a problem in treating patients with drug-resistant tuberculosis worldwide. The objectives of this study were to identify risk factors for acquired resistance (AR) to injectable SLDs (INJ SLDs) and fluoroquinolones in the US National tuberculosis Surveillance System, 1993-2008.”

Our news journalists obtained a quote from the research from Centers for Disease Control and Prevention, “We selected cases for which the initial and final drug susceptibility test (DST) results had been reported. We defined AR as resistance at the final DST but susceptibility to the same drug at the initial DST. We analyzed AR using 2-way frequency tables and multivariable logistic regression. The baseline prevalence of multidrug-resistant (MDR) and extensively drug-resistant (XDR) tuberculosis was 12.6% (1864/14 770) and 0.38% (56/14 770), respectively. Of 2274 individuals without initial resistance to INJ SLDs, 49 (2.2%) acquired resistance. Of 1141 initially susceptible to fluoroquinolones, 32 (2.8%) acquired resistance. The AR to INJ SLDs was associated with age group 25-44 years (adjusted odds ratio [aOR], 2.7; 95% confidence interval [CI], 1.2-6.3), positive HIV (human immunodeficiency virus) status (aOR, 2.5; 95% CI, 1.3-4.7), MDR at treatment initiation (aOR, 5.5; 95% CI, 2.9-10.5), and treatment with any SLD (aOR, 2.4; 95% CI, 1.2-4.7). The AR to fluoroquinolones was associated with MDR tuberculosis at treatment initiation (aOR, 6.5; 95% CI, 2.9-14.6). Among patients with initial and final DST reported, the risk factors for AR to INJ SLDs included age, positive HIV status, MDR tuberculosis and initial treatment with any SLD, while the only predictor for AR to fluoroquinolones was MDR tuberculosis at treatment initiation.”

According to the news editors, the research concluded: “Providers should consider monitoring SLD DST for MDR tuberculosis patients in the indicated subgroups.”

Our news journalists report that additional information may be obtained by contacting J.V. Ershova, US Center Dis Control & Prevent, Atlanta, GA, United States. (2013 Jan 21)

Safdarjang Hospital, New Delhi: Genital tuberculosis in adolescent girls from low socioeconomic status with acute ectopic pregnancy presenting at a tertiary care hospital in urban Northern India: are we missing an opportunity to treat?

By a News Reporter-Staff News Editor at Tuberculosis Week – Research findings on Obstetrics and Gynecology are discussed in a new report. According to news originating from New Delhi, India, by NewsRx correspondents, research stated, “Predominant etiology of ectopic gestation is tubal damage, notably salpingitis, which may be of tubercular etiology. Aims and objectives To compare the incidence of genital tuberculosis (GTB) in two groups of adolescent patients: one undergoing surgery for acute ectopic pregnancy, the other undergoing suction evacuation for spontaneous miscarriage and to evaluate GTB as a risk factor for ectopic pregnancy in adolescent girls from low socioeconomic status presenting to a tertiary care hospital in Northern India.”

Our news journalists obtained a quote from the research from Safdarjang Hospital, “Prospective case-control study with 17 adolescent subjects from low socioeconomic status with acute presentation of ectopic pregnancy (group 1, study) undergoing laparotomy with 20 adolescent subjects with spontaneous miscarriage (group 2, control) undergoing suction evacuation. Subjects were tested for presence of GTB by presence of tubercular granuloma and/or positive growth on BACTEC radiometric assay from sample obtained from endometrial aspirate and products of conception in groups 1 and 2, respectively. Incidence of GTB was 35.29 % (6 out of 17) in the study group compared with 5 % in the control group (1 out of 20) (P = 0.03). The sample size of this pilot study is too small to arrive at the definite conclusion whether GTB is risk factor for acute ectopic in this population of patients. Larger studies are needed to validate this hypothesis.”

According to the news editors, the research concluded: “However, in the presence of risk factors/suggestive intraoperative findings, testing for TB in this set of population presenting with ectopic pregnancy may be justified to prevent further morbidity by initiating anti-tubercular therapy in high prevalence areas.”

For more information on this research see: Genital tuberculosis in adolescent girls from low socioeconomic status with acute ectopic pregnancy presenting at a tertiary care hospital in urban Northern India: are we missing an opportunity to treat? Archives of Gynecology
University of North Carolina, Chapel Hill: Nutritional Risk Factors for Tuberculosis Among Adults in the United States, 19711992

By a News Reporter-Staff News Editor at Tuberculosis Week – Researchers detail new data in Epidemiology. According to news originating from Chapel Hill, North Carolina, by NewsRx correspondents, research stated, “The risk of developing tuberculosis (TB) may be related to nutritional status. To determine the impact of nutritional status on TB incidence, the authors analyzed data from the First National Health and Nutrition Examination Survey (NHANES I) Epidemiologic Follow-up Study (NHEFS).”

Our news journalists obtained a quote from the research from the University of North Carolina, “NHANES I collected information on a probability sample of the US population in 19711975. Adults were followed up in 19821992. Incident TB cases were ascertained through interviews, medical records, and death certificates. TB incidences were compared across different levels of nutritional status after controlling for potential confounding using proportional hazards regression appropriate to the complex sample design. TB incidence among adults with normal body mass index was 24.7 per 100,000 person-years (95 confidence interval (CI): 13.0, 36.3). In contrast, among persons who were underweight, overweight, and obese, estimated TB incidence rates were 260.2 (95 CI: 98.6, 421.8), 8.9 (95 CI: 2.2, 15.6), and 5.1 (95 CI: 0.0, 10.5) per 100,000 person-years, respectively. Adjusted hazard ratios were 12.43 (95 CI: 5.75, 26.95), 0.28 (95 CI: 0.13, 0.63), and 0.20 (95 CI: 0.07, 0.62), respectively, after controlling for demographic, socioeconomic, and medical characteristics. A low serum albumin level also increased the risk of TB, but low vitamin A, thiamine, riboflavin, and iron status did not.”

According to the news editors, the researchers concluded: “A populations nutritional profile is an important determinant of its TB incidence.”
CHAPTER 5 RISK AND PREVENTION


The news correspondents report that additional information may be obtained from J.P. Cegielski, University of North Carolina, Dept. of Epidemiol, Gillings Sch Global Public Hlth, Chapel Hill, NC, United States. (2012 Oct 15)

**London School of Hygiene and Tropical Medicine:**

**Increased risk of default among previously treated tuberculosis cases in the Western Cape Province, South Africa**

By a News Reporter-Staff News Editor at Life Science Weekly – Data detailed on Tuberculosis and Lung Disease have been presented. According to news reporting out of London, United Kingdom, by NewsRx editors, research stated, “To investigate, in two urban communities with high tuberculosis (TB) incidence and high rates of TB recurrence, whether a history of previous TB treatment is associated with treatment default. Retrospective cohort study of TB cases with an episode of treatment recorded in the clinic-based treatment registers between 2002 and 2007.”

Our news journalists obtained a quote from the research from the London School of Hygiene and Tropical Medicine, “Probabilistic record linkage was used to ascertain treatment history of TB cases back to 1996. Based on the outcome of their most recent previous treatment episode, previously treated cases were compared to new cases regarding their risk of treatment default. Previous treatment success (adjusted odds ratio [aOR] 1.79; 95%CI 1.17-2.73), previous default (aOR 6.18, 95%CI 3.68-10.36) and previous failure (aOR 9.72, 95%CI 3.07-30.78) were each independently associated with treatment default (P < 0.001). Other factors independently associated with default were male sex (P = 0.003) and age 19-39 years (P < 0.001). Previously treated TB cases are at increased risk of treatment default, even after previous successful treatment. This finding is of particular importance in a setting where recurrent TB is very common.”

According to the news editors, the researchers concluded: “Adherence to treatment should be ensured in new and retreatment cases to increase cure rates and reduce transmission of TB in the community.”
For more information on this research see: Increased risk of default among previously treated tuberculosis cases in the Western Cape Province, South Africa. *International Journal of Tuberculosis and Lung Disease*, 2012;16(8):1059-1065. *International Journal of Tuberculosis and Lung Disease* can be contacted at: Int Union Against Tuberculosis Lung Disease (I U A T L D), 68 Boulevard Saint-Michel, 75006 Paris, France.

Our news journalists report that additional information may be obtained by contacting F.M. Marx, London Sch Hyg & Trop Med, Dept. of Infect Dis Epidemiol, London WC1, United Kingdom. (2012 Oct 02)

**Obafemi Awolowo University Hospital, Ile Ife: Tuberculosis in pregnancy: a review**

By a News Reporter-Staff News Editor at AIDS Weekly – New research on Immune System Diseases and Conditions is the subject of a report. According to news reporting originating in Ile Ife, Nigeria, by NewsRx journalists, research stated, “Tuberculosis (TB) was declared a public health emergency by WHO in 2005. The disease is a significant contributor to maternal mortality and is among the three leading causes of death among women aged 15-45 years in high burden areas.”

The news reporters obtained a quote from the research from Obafemi Awolowo University Hospital, “The exact incidence of tuberculosis in pregnancy, though not readily available, is expected to be as high as in the general population. Diagnosis of tuberculosis in pregnancy may be challenging, as the symptoms may initially be ascribed to the pregnancy, and the normal weight gain in pregnancy may temporarily mask the associated weight loss. Obstetric complications of TB include spontaneous abortion, small for date uterus, preterm labour, low birth weight, and increased neonatal mortality. Congenital TB though rare, is associated with high perinatal mortality. Rifampicin, INH and Ethambutol are the first line drugs while Pyrazinamide use in pregnancy is gaining popularity. Isoniazid preventive therapy is a WHO innovation aimed at reducing the infection in HIV positive pregnant women. Babies born to this mother should be commenced on INH prophylaxis for six months, after which they are vaccinated with BCG if they test negative.”

According to the news reporters, the researchers concluded: “Successful control of TB demands improved living conditions, public enlightenment, primary prevention of HIV/AIDS and BCG vaccination.”

Max-Planck-Institute for Infection Biology, Berlin: Enabling biomarkers for tuberculosis control

By a News Reporter-Staff News Editor at Clinical Trials Week – Research findings on Mycobacterium Infections are discussed in a new report. According to news reporting out of Berlin, Germany, by NewsRx editors, research stated, “Accelerated control of tuberculosis (TB) requires better control measures. Biomarkers, which reliably diagnose active TB or even predict risk of disease progression in individuals, could facilitate rapid diagnosis and treatment of TB patients and allow preventive measures for latently infected individuals with a high risk of TB.”

Our news journalists obtained a quote from the research from Max-Planck-Institute for Infection Biology, “Moreover, biomarkers could speed up clinical trials with novel drug and vaccine candidates. Three platforms of global biomarker profiling will be described, with an emphasis on the most recent achievements: transcriptomics, proteomics and metabolomics. Moreover, we will discuss the need for computational analyses to make the best use of the plethora of data generated by biomarker research. Aside from their potential prognostic and diagnostic value, biomarkers could provide deeper insight into pathological processes underlying disease, and hence form the basis for novel intervention measures that target host molecules and pathways. We propose that biosignatures, which discriminate active TB from both latent infection and uninfected status, as well as from other diseases, will become available within the next decade.”

According to the news editors, the researchers concluded: “However, simple, low-cost biomarker-based point-of-care diagnosis will probably not be achieved in the next few years.”

For more information on this research see: Enabling biomarkers for tuberculosis control. The International Journal of Tuberculosis and Lung Disease, 2012;16(9):1140-8.

Our news journalists report that additional information may be obtained by contacting J. Maertzdorf, Dept. of Immunology, Max Planck Institute for Infection Biology, Berlin, Germany. (2012 Aug 27)
National Institutes of Health, Bethesda: Frequency of adverse reactions to first- and second-line anti-tuberculosis chemotherapy in a Korean cohort

By a News Reporter-Staff News Editor at China Business Newsweekly – Investigators publish new report on Mycobacterium Infections. According to news reporting originating from Bethesda, Maryland, by Vertical-News correspondents, researchers stated “To determine the frequency of and risk factors for major adverse drug reactions (MADRs) associated with anti-tuberculosis treatment at a tuberculosis (TB) referral hospital in the Republic of Korea. Data from an ongoing natural history cohort study were analyzed for permanent regimen changes due to adverse drug reactions and confirmed by chart review.”

Our news editors obtained a quote from the research from the National Institutes of Health, “Among 655 subjects, there were 132 MADRs in 112 (17%) subjects. The most common MADRs were gastrointestinal (n = 53), musculoskeletal (n = 22), psychiatric (n = 10), visual (n = 9) and peripheral neuropathic (n = 8). MADRs were more frequent in subjects being treated with second-line regimens (16%) compared to first-line regimens (2.5%). Drugs frequently associated with MADRs were amikacin (3/10, 30%), linezolid (8/29, 28%), para-aminosalicylic acid (47/192, 24%), pyrazinamide (31/528, 5.8%), macrolides (2/44, 4.5%) and cycloserine (12/272, 4.4%). Fluoroquinolones accounted for a single MADR (1/377, 0.003%), despite widespread usage. In multivariate analysis, infection with multi- or extensively drug-resistant disease and previous history of anti-tuberculosis treatment were risk factors for MADR, with adjusted hazard ratios of respectively 2.2 (P = 0.02) and 1.6 (P = 0.04). MADRs are common during anti-tuberculosis chemotherapy in this population, occurring in more than one in six subjects.”

According to the news editors, the researchers concluded: “New and less toxic agents to treat drug-resistant TB are urgently needed.”


The news editors report that additional information may be obtained by contacting M.W. Carroll, NIAID, Off Cyber Infrastruct & Comp Biol, National Institutes of Health, Bethesda, MD, United States. (2012 Jul 31)
Montefiore Medical Center, Bronx: Independent association of younger age with hemoptysis in adults with pulmonary tuberculosis

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – Data detailed on Tuberculosis and Lung Disease have been presented. According to news reporting out of Bronx, New York, by NewsRx editors, researchers stated “The risk factors for mild to moderate hemoptysis in patients with pulmonary tuberculosis (PTB) are not entirely clear. To evaluate the independent association of risk factors with the occurrence of hemoptysis in PTB patients.”

Our news journalists obtained a quote from the research from Montefiore Medical Center, “Cross-sectional study of adult patients newly diagnosed with microbiologically proven PTB in a New York City hospital. Patients were categorized into subjects with and without hemoptysis and compared using univariate analysis. Independent associations of variables with hemoptysis were estimated using multivariate logistic regression. Of 194 subjects with PTB, 44 (23%) had hemoptysis. In univariate analysis, subjects with hemoptysis were significantly younger (P = 0.003), and more likely to be undocumented foreign-born (P = 0.038) compared to subjects without hemoptysis. In multivariate analysis, only younger age was independently associated with hemoptysis. This association was significant for a continuous decrease in age per year, or per decade (adjusted OR 1.59, P = 0.003). Younger age is an independent risk factor for hemoptysis in PTB.”

According to the news editors, the researchers concluded: “It is conceivable that a stronger inflammatory response in younger than in older age could contribute to pulmonary pathogenesis and injury in PTB.”


Our news journalists report that additional information may be obtained by contacting J.M. Achkar, Montefiore Med Center, Bronx, NY, United States. (2012 Jul 30)
History of tuberculosis as an independent prognostic factor for lung cancer survival

By a News Reporter-Staff News Editor at Tuberculosis Week – Research findings on Lung Cancer are discussed in a new report. According to news reporting originating from Rotterdam, Netherlands, by NewsRx correspondents, researchers stated “It is well known that pulmonary tuberculosis is associated with an increased risk of lung cancer. We investigated whether a history of pulmonary tuberculosis is an independent risk factor for lung cancer survival in Caucasian patients.”

Our news editors obtained a quote from the research by the authors, “The data of the prospective population-based cohort of The Rotterdam Study were used. During a mean follow-up time of 18 years, there were 214 incident cases of pathology-proven lung cancer in a source population of 7983 study participants. History of tuberculosis was assessed at baseline by interviewers using standardized questionnaires. Associations of lung cancer survival with the occurrence of pulmonary tuberculosis were assessed using Cox’s proportional hazard regression analysis adjusted for age, gender, pack-years, educational level and tumor stage. A history of tuberculosis was reported in 13 of the 214 subjects with lung cancer. The survival of patients with lung cancer was significantly shorter in subjects with a history of pulmonary tuberculosis (HR = 2.36, CI95%: 1.1-4.9), than in subjects without a history of pulmonary tuberculosis with a mean difference of 311 days.”

According to the news editors, the researchers concluded: “The presence of a history of pulmonary tuberculosis may be an important prognostic factor in the survival of lung cancer.”


The news editors report that additional information may be obtained by contacting M.E. Heuvers, Erasmus Med Univ Center, Dept. of Med Informat, Rotterdam, Netherlands. (2012 Jul 09)
Centers for Disease Control and Prevention, Beijing: Social Behaviour Risk Factors for Drug Resistant Tuberculosis in Mainland China: a Meta-analysis

By a News Reporter-Staff News Editor at Asia Business Newsweekly – Data detailed on Tuberculosis have been presented. According to news reporting originating from Beijing, People’s Republic of China, by VerticalNews correspondents, researchers stated “To determine risk factors associated with drug resistant tuberculosis (TB) in mainland China. PubMed and Chinese BioMedical databases were searched.”

Our news editors obtained a quote from the research by the authors from Centers for Disease Control and Prevention, “Cohort, case-control and cross-sectional studies providing effect estimates of risk factors for any-drug resistant or multidrug resistant (MDR) TB were included. The meta-analysis included 16 studies. Any-drug resistant TB was significantly associated with poor quality directly observed treatment, short-course (DOTS) (odds ratio [OR] 2.65, 95% confidence interval [CI] 1.22, 5.79), long term illness > 1 year (OR 2.71, 95% CI 1.34, 5.48), poor treatment adherence (OR 2.00, 95% CI 1.17, 3.40), previous treatment (OR 4.54, 95% CI 2.71, 7.61) and age 40 - 60 years (OR 1.62, 95% CI 1.10, 2.38). MDR-TB was significantly associated with poor quality DOTS (OR 1.84, 95% CI 1.36, 2.49), poor treatment adherence (OR 4.39, 95% CI 2.97, 6.50), previous treatment (OR 3.83, 95% CI 2.12, 6.89) and poverty (OR 1.87, 95% CI 1.38, 2.52).”

According to the news editors, the researchers concluded: “Previous treatment, poor quality DOTS, poor treatment adherence, long term illness, age 40 - 60 years and poverty are associated with a greater risk of drug resistant TB in mainland China.”


The news editors report that additional information may be obtained by contacting P. Zhao, Chaoyang Center Dis Control & Prevent, Beijing, People’s Republic of China. (2012 Jul 03)
University of Colorado, Aurora: Seasonality of Tuberculosis in the United States, 1993-2008

By a News Reporter-Staff News Editor at Pediatrics Week – New research on Tuberculosis is the subject of a report. According to news originating from Aurora, Colorado, by VerticalNews correspondents, researchers stated “Although seasonal variation in tuberculosis incidence has been described in several recent studies, the mechanism underlying this seasonality remains unknown. Seasonality of tuberculosis disease may indicate the presence of season-specific risk factors that could potentially be controlled if they were better understood.”

Our news journalists obtained a quote from the research by the authors from the University of Colorado, “We conducted this study to determine whether tuberculosis is seasonal in the United States and to describe patterns of seasonality in specific populations. We performed a time series decomposition analysis of tuberculosis cases reported to the Centers for Disease Control and Prevention from 1993 through 2008. Seasonal amplitude of tuberculosis disease (the difference between the months with the highest and lowest mean case counts), was calculated for the population as a whole and for populations with select demographic, clinical, and epidemiologic characteristics. A total of 243,432 laboratory-confirmed tuberculosis cases were reported over a period of 16 years. A mean of 21.4% more cases were diagnosed in March, the peak month, compared with November, the trough month. The magnitude of seasonality did not vary with latitude. The greatest seasonal amplitude was found among children aged < 5 years and in cases associated with disease clusters. Tuberculosis is a seasonal disease in the United States, with a peak in spring and trough in late fall. The latitude independence of seasonality suggests that reduced winter sunlight exposure may not be a strong contributor to tuberculosis risk.”

According to the news editors, the researchers concluded: “Increased seasonality among young children and clustered cases suggests that disease that is the result of recent transmission is more influenced by season than disease resulting from activation of latent infection.”


The news correspondents report that additional information may be obtained from M.D. Willis, University of Colorado, Div Pulm Sci & Crit Care Med, Aurora, CO, United States. (2012 Jun 23)
CHAPTER 5  RISK AND PREVENTION

Researchers Submit Patent Application, “Tuberculosis Vaccine”, for Approval

By a News Reporter-Staff News Editor at Life Science Weekly – From Washington, D.C., NewsRx journalists report that a patent application by the inventors Montanes, Carlos Martin (Zaragoza, ES); Gicquel, Brigitte (Zaragoza, ES); Herran, Esther Perez (Zaragoza, ES); Asensio, Jesus Gonzalo (Zaragoza, ES); Arribas, Ainhoa Arbues (Zaragoza, ES), filed on September 14, 2012, was cleared for further review on January 31, 2013.

The patent’s assignee for patent serial number 619615 is Universidad de Zaragoza.

News editors obtained the following quote from the background information supplied by the inventors: “The present invention relates to an isolated microorganism belonging to the Mycobacterium genus, characterised in that it comprises the inactivation of the Rv0757 gene that confers a PhoP- phenotype and the inactivation of a second gene that prevents DIM production (DIM- phenotype). Additionally, the present invention comprises the use of said microorganism for the preparation of a vaccine for the immunization or prevention of tuberculosis.

“The use of vaccines to prevent tuberculosis in humans has proved to be a tremendous challenge for almost a century now. BCG, derived from M. bovis, is currently the only tuberculosis vaccine in use and is the most widely used vaccine in the world. The development and generalised administration of the BCG vaccine since the beginning, of the 1920s represented a significant advance, with the prospect of being able to eradicate tuberculosis from the world. However, these initial promises were not achieved and, from the results of a large number of efficacy trials, it is clear that the BCG vaccine in its current form is of limited use in controlling the disease, particularly in respiratory forms in adults in third world areas where the disease is endemic. Fine, P. E. Variation in protection by BCG: implications of and for heterologous immunity. Lancet 1995, 346(8986), 1339-1345. With more knowledge of the virulence of M. tuberculosis and immune response models that lead to the generation of protective immunity, it is possible to develop better vaccines than BCG. The observation that higher protection levels are achieved when the host is vaccinated with BCG suggests that viability and persistence are fundamental properties required for the success of a tuberculosis vaccine. In the present invention, we use a M. tuberculosis strain with the inactivated Rv0757 (phoP) gene and a second independent mutation of phoP, which prevents DIM synthesis, as a prototype single dose live vaccine, and we show that, as well as being more attenuated than BCG in immunocompromised SCID mice,
it provided protection levels comparable to those conferred by BCG in mice and higher protection than BCG in guinea pigs.

“The phoP gene, together with phoR, forms part of a two-component system that shows a high degree of similarity to other two-component systems that control the transcription of key virulence genes in intracellular pathogens. It also controls the expression of many other genes that are not directly involved in virulence. Groisman, E. A. The pleiotropic two-component regulatory system PhoP-PhoQ. J Bacteriol 2001, 183(6), 1835-1842. The elimination of virulence genes does not seem to be, per se, the only method for the attenuation of M. tuberculosis. It was shown that a pantothenate auxotrophic mutant of M. tuberculosis, which is incapable of de novo synthesis of pantothenic acid, persisted in SCID mice, without managing to cause the disease. Sambandamurthy, V. K., Wang, X., Chen, B. et al. A pantothenate auxotroph of Mycobacterium tuberculosis is highly attenuated and protects mice against tuberculosis. Nat Med 2002, 8(10), 1171-1174. Individual leucine auxotrophs are also strongly attenuated and incapable of replication in vivo in SCID mice. Hondalus, M. K., Bardarov, S., Russell, R., Chan, J., Jacobs, W. R., Jr. & Bloom, B. R. Attenuation of and protection induced by a leucine auxotroph of Mycobacterium tuberculosis. Infect Immun 2000, 68(5), 2888-2898. Therefore, the principle that vaccine strains based on M. tuberculosis can be successfully attenuated whilst retaining genes that are suppressed in M. bovis BCG is now generally accepted.

“In the past, research into more effective vaccines than BCG was based on the notion that loss of virulence with BCG was in itself a factor that contributed to its lack of complete protective efficacy. Behr, M. A., Wilson, M. A., Gill, W. P. et al. Comparative genomics of BCG vaccines by whole-genome DNA microarray. Science 1999, 284(5419), 1520-1523. It was therefore reasoned that new attenuated mutants of M. tuberculosis, with less virulence, could be more effective as vaccines. However, a recent study has shown that natural infection with M. tuberculosis and vaccination with BCG do not differ in their capacity to bring about protective immunity against tuberculosis. Sampson, S. L., Dascher, C. C., Sambandamurthy, V. K. et al. Protection elicited by a double leucine and pantothenate auxotroph of Mycobacterium tuberculosis in guinea pigs. Infect Immun 2004, 72(5), 3031-3037. This raises questions as to whether or not it is possible to improve BCG by rational attenuation of M. tuberculosis. Within this context, the observation that the mutant M. tuberculosis strain of the present invention with the combination of 2 independent mutations 1.– in synthesis of the PhoP protein and 2.– in DIM synthesis is more attenuated than BCG in the SCID mouse model, even when applied at a dose 10 times higher than those of BCG, and the greater degree of protection than BCG in the guinea pig model is particularly surprising and significant.”
As a supplement to the background information on this patent application, NewsRx correspondents also obtained the inventors’ summary information for this patent: “The present invention relates to an isolated microorganism belonging to the Mycobacterium genus, characterised in that it comprises the inactivation of the Rv0757 gene that confers a PhoP- phenotype and the inactivation of a second gene that prevents DIM production (DIM- phenotype). Additionally, the present invention comprises the use of said microorganism for the preparation of a vaccine for the immunization or prevention of tuberculosis.

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**Patent Issued for Tuberculosis Vaccine**

By a News Reporter-Staff News Editor at Life Science Weekly – According to news reporting originating from Alexandria, Virginia, by
NewsRx journalists, a patent by the inventors Montanes, Carlos Martin (Saragossa, ES); Gicquel, Brigitte (Saragossa, ES); Herran, Esther Perez (Saragossa, ES); Asensio, Jesus Gonzalo (Saragossa, ES); Arribas, Ainhoa Arbues (Saragossa, ES), filed on March 14, 2007, was cleared and issued on October 16, 2012.

The assignee for this patent, patent number 8287886, is Universidad de Zaragoza (Saragossa, ES).

Reporters obtained the following quote from the background information supplied by the inventors: “The present invention relates to an isolated microorganism belonging to the Mycobacterium genus, characterised in that it comprises the inactivation of the Rv0757 gene that confers a PhoP- phenotype and the inactivation of a second gene that prevents DIM production (DIM- phenotype). Additionally, the present invention comprises the use of said microorganism for the preparation of a vaccine for the immunization or prevention of tuberculosis.

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Chapter 6

Surgery

University College London School of Medicine: Surgery and tuberculosis

By a News Reporter-Staff News Editor at Tuberculosis Week – Investigators discuss new findings in Mycobacterium Infections. According to news reporting from London, United Kingdom, by NewsRx journalists, research stated, “Tuberculosis (TB) remains a global emergency and continues to kill 1.7 million people globally each year. In the UK, figures for TB are increasing especially in urban areas.”

The news correspondents obtained a quote from the research from the University College London School of Medicine, “There have been advances in imaging techniques as well as increasingly invasive medical interventions in both the diagnosis and treatment of this complex disease. Surgery continues to play an evolving and more challenging role in TB management as minimally invasive procedures can be increasingly used in diagnosis and treatment.”

According to the news reporters, the research concluded: “Open surgical procedures continue to prove an important adjunct in the management of multidrug-resistant TB (MDR-TB) and the complications of TB.”

For more information on this research see: Surgery and tuberculosis. Current Opinion In Pulmonary Medicine, 2012;18(3):241-5. (Lippincott Williams and Wilkins - www.lww.com; Current Opinion In Pulmonary Medicine - http://journals.lww.com/co-pulmonarymedicine/pages/default.aspx)

Our news journalists report that additional information may be obtained by contacting I. Cummings, The London Chest Hospital and Dept. of Infectious Diseases, University College London Medical School, London, UK. (2013 Apr 22)
Mashhad University of Medical Sciences: Outcomes following surgery for complicated tuberculosis: analysis of 108 patients

By a News Reporter-Staff News Editor at Tuberculosis Week – Fresh data on Mycobacterium Infections are presented in a new report. According to news reporting originating in Mashhad, Iran, by NewsRx journalists, research stated, “Background Both incidence and complications of pleuropulmonary tuberculosis (TB) have increased due to recent increase of immunocompromising conditions. The aim of this study was to assess surgical outcomes in patients suffering from complicated pleuropulmonary TB. Methods This study included 108 patients with pleuropulmonary TB who underwent surgery.”

The news reporters obtained a quote from the research from the Mashhad University of Medical Sciences, “Age, sex, surgical indications, operative techniques, complications, mortality, and morbidity were evaluated. Results Male-female ratio was 1:11 with mean age of 40 years; 72.2 and 27.8% of the patients underwent surgery due to parenchymal and pleural complications. In the parenchymal group, the most common indication was parenchymal destruction (27.7%) and the most common procedure was lobectomy (50.9%). Out of 20 sputum smear-positive patients, 15 had multidrug-resistant tuberculosis (MDR-TB) and 5 had smear-positive open cavity. Overall 13 of the MDR-TB group and all smear-positive open cavity group became sputum-negative after the surgery. There were 13 patients with undiagnosed masses, among whom 3 patients had adenocarcinoma. In the pleural group, the most common surgical indication was empyema (13.8%) and the most common procedure was decortication and pleurectomy (13.8%). In the bronchopleural fistula group (6.4%), patients showed good results after surgery. There were 19.4% of patients who showed postoperative complications. The most common complication was residual space (5.5%). The main factors leading to major postoperative complications included positive preoperative sputum smear and history of immunocompromising condition.”

According to the news reporters, the research concluded: “Mortality rate was 2.7%. Conclusion Considering the favorable results achieved by surgery in patients with pleuropulmonary TB, this treatment can be recommended for this group of patients.”


Our news correspondents report that additional information may be obtained by contacting R. Bagheri, Dept. of Thoracic Surgery, Mashhad University of Medical Sciences, Mashhad, Iran. (2013 Apr 08)
University of Ulsan, Seoul: Comparison of the QuantiFERON-TB Gold In-Tube test with the tuberculin skin test for detecting latent tuberculosis infection prior to hematopoietic stem cell transplantation

By a News Reporter-Staff News Editor at Blood Weekly – Fresh data on Transplantation are presented in a new report. According to news reporting from Seoul, South Korea, by NewsRx journalists, research stated, “A total of 244 patients including 100 (41%) autologous hematopoietic stem cell transplant (HCT) recipients and 144 (59%) allogeneic HCT recipients were enrolled over a 28-month period. During the study period, no prophylaxis for latent tuberculosis (TB) infection was administrated.”

The news correspondents obtained a quote from the research from the University of Ulsan, “Of these, 201 (82%) had Bacillus Calmette-Guerin (BCG) scars or prior histories of BCG vaccination. The tuberculin skin test (TST) and the QuantiFERON-TB Gold In-Tube (QFT-GIT) test were performed simultaneously in all 244 patients. TST indurations were \( \geq 5 \) mm in 39 of these patients (15%), and in 25 (10%) indurations were \( \geq 10 \) mm. In addition, 40 (16%) had positive QFT-GIT outcomes, and 34 (14%) indeterminate outcomes. If the 34 patients with indeterminate QFT-GIT results were excluded from the overall agreement analysis, the agreement between the TST results (induration size \( \geq 5 \) mm) and the QFT-GIT results in the 210 patients with clear QFT results was poor (kappa = 0.08, 95% confidence interval [CI] -0.06 to 0.24), as it was for the patients with indurations \( \geq 10 \) mm (kappa = 0.15, 95% CI -0.004 to 0.31). During follow up, 2 patients developed TB after HCT. The incidence of TB in the patients with positive QFT-GIT outcomes was 2.80 per 100 person-years (95% CI 0.07-15.81), whereas among those with positive TST (\( \geq 5 \) mm) results, it was 0 per 100 person-years (95% CI 0-8.00). However, this finding should be cautiously interpreted because of the relatively short follow up and the fact that the sample size of the study cohort did not have adequate power.”

According to the news reporters, the research concluded: “Our data show that, although the frequencies of positive outcomes in the 2 TB screening tests were similar, the overall agreement between the TST and the QFT-GIT test was poor, regardless of BCG vaccination history.”

Department of Surgery, Chiayi: The Role of Video-Assisted Thoracoscopic Surgery in Therapeutic Lung Resection for Pulmonary Tuberculosis

By a News Reporter-Staff News Editor at Biotech Week – Researchers detail new data in Mycobacterium Infections. According to news reporting originating from Chiayi, Taiwan, by NewsRx correspondents, research stated, “Video-assisted thoracoscopic surgery (VATS) has been considered an effective diagnostic modality for pulmonary tuberculosis. Its feasibility in therapeutic lung resection, however, has not been validated.”

Our news editors obtained a quote from the research from the Department of Surgery, “The medical records of patients who underwent VATS or a thoracotomy for therapeutic resection of pulmonary tuberculosis between January 2007 and March 2011 were reviewed for age, sex, indications for surgery, approach and procedures, preoperative sputum culture status, operative time, blood loss, hospital stay, and complications. One hundred twenty-three patients were enrolled. Sixty-three were successfully treated using VATS and 60 were converted to thoracotomy. The number of VATS wedge resections was significantly higher ($p = 0.004$). Patients who underwent VATS had significantly less blood loss, shorter hospital stays, and fewer complications ($p = 0.031$, 0.000, and 0.022, respectively). Lesions treated with a pneumonectomy or that required thoracoplasty failed to be done using VATS ($p = 0.054$ and 0.002, respectively). Patients who underwent VATS had slightly more isolated lobectomies and significantly ($p = 0.005$) shorter hospital stays than did thoracotomy patients. Concomitant and isolated segmentectomies were done using VATS, but there were significantly fewer than for thoracotomy patients ($p = 0.033$). Video-assisted thoracoscopic surgery is effective for therapeutic wedge resections, isolated lobectomies, and simple segmentectomies and lobectomies combined with wedge resections or segmentectomies for pulmonary tuberculosis.”

According to the news editors, the research concluded: “Tuberculosis lesions that require a pneumonectomy or thoracoplasty are still major challenges for VATS.”

The news editors report that additional information may be obtained by contacting Y.T. Yen, Chia Yi Christian Hosp, Div Thorac Surg, Dept. of Surg, Chiayi, Taiwan. (2013 Feb 20)

**Regina Elena National Intitute for Cancer Treatment and Research, Rome: Chemotherapeutically Induced Cutaneous Tuberculosis after BCG Injection in a Patient with Pelvic Osteosarcoma**

By a News Reporter-Staff News Editor at Tuberculosis Week – Data detailed on Bacterial Skin Diseases have been presented. According to news originating from Rome, Italy, by NewsRx correspondents, research stated, “Tuberculosis (TB) is a serious infection afflicting a multitude of people worldwide. Recently, its prevalence has increased.”

Our news journalists obtained a quote from the research from Regina Elena National Intitute for Cancer Treatment and Research, “The incidence of skin involvement generally is low. Bacillus Calmette-Guerin (BCG) is a live attenuated strain of Mycobacterium bovis that typically is administered as a vaccine to stimulate the immune system when treating some early neoplasms or to guard against tuberculosis. Case report and literature review. The authors describe a young man with osteosarcoma of the left hemipelvis who received intradermal BCG injection for immune stimulation prior to surgery. In the course of neoadjuvant chemotherapy, he developed cutaneous tuberculosis.”

According to the news editors, the research concluded: “It is our opinion that BCG injection should be avoided in all patients requiring surgery, especially in oncologic patients, where the immunodeficiency brought on by chemotherapy predisposes to active opportunistic infection.”

For more information on this research see: Chemotherapeutically Induced Cutaneous Tuberculosis after BCG Injection in a Patient with Pelvic Osteosarcoma. *Surgical Infections*, 2012;13(6):406-408. *Surgical Infections* can be contacted at: Mary Ann Liebert Inc, 140 Huguenot Street, 3RD Fl, New Rochelle, NY 10801, USA. (Mary Ann Liebert, Inc. - www.liebertpub.com; Surgical Infections - http://www.liebertpub.com/overview/surgical-infections/53/)
The news correspondents report that additional information may be obtained from G. Zoccali, Regina Elena Inst Canc Res, Medical Oncol Sect A, Rome, Italy. (2013 Feb 11)

**Department of Internal Medicine, Madrid: Drug treatment of multidrug-resistant osteoarticular tuberculosis: a systematic literature review**

By a News Reporter-Staff News Editor at Tuberculosis Week – Current study results on Mycobacterium Infections have been published. According to news reporting originating from Madrid, Spain, by NewsRx correspondents, research stated, “To review the literature in order to determine the best treatment options for multidrug-resistant tuberculosis (MDR-TB) of the skeletal system. We searched the PubMed database for all case reports of osteoarticular MDR-TB that provided information on drug treatment and clinical outcome.”

Our news editors obtained a quote from the research from the Department of Internal Medicine, “We identified six cases with spinal MDR-TB and seven with extraspinal MDR-TB and reviewed their susceptibility tests, treatments administered, surgical treatments, and clinical outcomes. All patients had a successful clinical outcome (either cured or improved) except one who died due to septicemia. One patient with spinal MDR-TB and four patients with extraspinal MDR-TB had a successful outcome with medical treatment alone. Two patients who received treatment for a shorter time or with fewer drugs than recommended were cured with the addition of surgery. Osteoarticular MDR-TB is very infrequently reported in the literature.”

According to the news editors, the research concluded: “The few cases reviewed suggest that it is possible to achieve a good outcome with second-line anti-tuberculous drugs, and that surgery might be useful for cases in which an optimized medical treatment is not possible.”


The news editors report that additional information may be obtained by contacting I. Suarez-Garcia, Hosp Cantoblanco La Paz, Dept. of Internal Med, TB Unit, Madrid, Spain. (2013 Jan 07)
Central South University, Changsha: Surgical management by one-stage posterior transforaminal lumbar debridement, interbody fusion, and posterior instrumentation for lumbo-sacral tuberculosis in the aged

By a News Reporter-Staff News Editor at Tuberculosis Week – Data detailed on Mycobacterium Infections have been presented. According to news reporting out of Changsha, People’s Republic of China, by NewsRx editors, research stated, “To evaluate the clinical study efficacy and feasibility of 17 aged patients with lumbo-sacral tuberculosis treated by one-stage posterior transforaminal lumbar debridement, interbody fusion, and posterior instrumentation. Methods 17 aged patients who suffered from lumbo-sacral tuberculosis were admitted into our hospital between March 2003 and October 2010.”

Our news journalists obtained a quote from the research from Central South University, “All of them were treated by one-stage posterior transforaminal lumbar debridement, interbody fusion, and posterior instrumentation. Then the clinical efficacy with statistical analysis was evaluated based on the materials on the lumbo-sacral angle, neurological status that was recorded by Frankel grade system, and erythrocyte sedimentation rate (ESR), which were collected at certain time. The average follow-up period was 47.5 +/- A 17.1 months (17-71 months), In the 17 cases, no postoperative complications related to instrumentation occurred and neurologic function was improved in various degrees. The mean preoperative lumbo-sacral angle was 20.5A degrees A A +/- A 1.7A degrees (range 18.0A degrees-23.0A degrees). The lumbo-sacral angle became 29.1A degrees A A +/- A 1.5A degrees (range 26.4A degrees-31.0A degrees) postoperatively. The average pretreatment ESR was 57.4 +/- A 16.8 mm/h (33-95 mm/h), which got normal (9.2 +/- A 3.1 mm/h) within 3 months in all patients. All patients got bony fusion within 6-8 months after surgery.”

According to the news editors, the research concluded: “One-stage posterior transforaminal lumbar debridement, interbody fusion, and posterior instrumentation can be an effective treatment method for the treatment of lumbo-sacral tuberculosis in the aged patients.”

For more information on this research see: Surgical management by one-stage posterior transforaminal lumbar debridement, interbody fusion, and posterior instrumentation for lumbo-sacral tuberculosis in the aged. Archives of Orthopaedic and Trauma Surgery, 2012;132(12):1677-1683. Archives of Orthopaedic and Trauma Surgery can be contacted at: Springer, 233 Spring St, New York, NY 10013, USA. (Springer - www.springer.com; Archives of Orthopaedic and Trauma Surgery - http://www.springerlink.com/content/0936-8051/)
Our news journalists report that additional information may be obtained by contacting H.Q. Zhang, Central South University, Dept. of Spine Surg, Xiangya Hosp, Changsha 410008, Hunan, People’s Republic of China. (2012 Dec 31)

Department of Health, Melbourne: Diagnosis of tuberculous lymphadenitis using fine needle aspiration biopsy

By a News Reporter-Staff News Editor at Tuberculosis Week – Researchers detail new data in Internal Medicine. According to news originating from Melbourne, Australia, by NewsRx correspondents, research stated, “Tuberculous lymphadenitis is the commonest form of extrapulmonary tuberculosis. However, the optimal approach to diagnosis, employing biopsy by either fine needle aspiration (FNA) or surgical excision, remains uncertain.”

Our news journalists obtained a quote from the research from the Department of Health, “To evaluate the diagnostic value of biopsy using each of the component diagnostic modalities of FNA (microscopy, cytology and culture), and compare these with excision biopsy in the diagnosis of tuberculous lymphadenitis in a predominantly migrant population in Melbourne. A retrospective examination of tuberculous lymphadenitis cases presenting to Western Health over 12 years was conducted. Using a reference method of positive culture of Mycobacterium tuberculosis, the diagnostic sensitivities of each modality employed in FNA were determined. Forty-two subjects having FNA and 30 having excision biopsy as the initial investigation were compared. Among specimens obtained by FNA, sensitivity of microscopy was 18% (95% confidence interval (CI): 5-40%) and sensitivity of cytology was 38% (95% CI: 20-59%). For specimens obtained by excision biopsies, sensitivities for microscopy and histology were 17% (95% CI: 2-32%) and 96% (95% CI: 88-100%) respectively. Sensitivity of culture performed on FNA specimens was 86% (95% CI: 65-97%). Given the relatively high sensitivity of mycobacterial cultures from FNA, this study supports its routine use as the initial investigation in most patients with suspected tuberculous lymphadenitis.”

According to the news editors, the research concluded: “Microscopy and cytology add relatively little to the clinical utility of FNA.”

Carol Davila University of Medicine and Pharmacy, Bucharest: The risk of tuberculosis in transplant candidates and recipients: a TBNET consensus statement

By a News Reporter-Staff News Editor at Hematology Week – Current study results on Respiratory Research have been published. According to news reporting from Bucharest, Romania, by NewsRx journalists, research stated, “Tuberculosis (TB) is a possible complication of solid organ and hematopoietic stem cell transplantation. The identification of candidates for preventive chemotherapy is an effective intervention to protect transplant recipients with latent infection with Mycobacterium tuberculosis from progressing to active disease.”

The news correspondents obtained a quote from the research from the Carol Davila University of Medicine and Pharmacy, “The best available proxy for diagnosing latent infection with M. tuberculosis is the identification of an adaptive immune response by the tuberculin skin test or an interferon-gamma based ex vivo assay. Risk assessment in transplant recipients for the development of TB depends on, among other factors, the locally expected underlying prevalence of infection with M. tuberculosis in the target population. In areas of high prevalence, preventive chemotherapy for all transplant recipients may be justified without immunodiagnostic testing while in areas of medium and low prevalence, preventive chemotherapy should only be offered to candidates with positive M. tuberculosis-specific immune responses. The diagnosis of TB in transplant recipients can be challenging. Treatment of TB is often difficult due to substantial interactions between anti-TB drugs and immunosuppressive medications.”

According to the news reporters, the research concluded: “This management guideline summarises current knowledge on the prevention, diagnosis and treatment of TB related to solid organ and hematopoietic stem cell transplantation and provides an expert consensus on questions where scientific evidence is still lacking.”

Department of Pediatric Surgery. New Delhi: Imaging features of pediatric musculoskeletal tuberculosis

By a News Reporter-Staff News Editor at Pediatrics Week – Investigators publish new report on Mycobacterium Infections. According to news reporting originating from New Delhi, India, by VerticalNews correspondents, research stated, “Tuberculosis (TB) is widely prevalent in developing nations and has recently made a comeback in industrialized countries, with the rise in immunocompromized patients. Musculoskeletal TB in children presents a diagnostic challenge because it is difficult to recognize in the early stages of the disease, and imaging features mimic other entities.”

Our news editors obtained a quote from the research from the Department of Pediatric Surgery, “The clinical onset is insidious, with an indolent course and a resultant late presentation. It leads to significant morbidity; a delay in diagnosis can cause potentially serious neurological complications and bone and joint destruction. Conventional radiographs are the initial imaging modality and US, CT and MRI are used in conjunction to better delineate the disease extent and morphology. Radiologists should be familiar with the spectrum of imaging features of TB, including plain radiographs and MRI, and aid the clinician in making an early diagnosis.”

According to the news editors, the research concluded: “Aspiration or biopsy with examination for acid-fast bacillus and histological evaluation is required to confirm the diagnosis.”

For more information on this research see: Imaging features of pediatric musculoskeletal tuberculosis. Pediatric Radiology, 2012;42(10):1235-1249. Pediatric Radiology can be contacted at: Springer, 233 Spring St, New York, NY 10013, USA. (Springer - www.springer.com; Pediatric Radiology - http://www.springerlink.com/content/0301-0449/)

The news editors report that additional information may be obtained by contacting A. Prasad, Chacha Nehru Bal Chikitsalaya, Dept. of Pediat Surg, New Delhi, India. (2012 Nov 17)
Department of Plastic Surgery, Slough: Nasopharyngeal tuberculosis presenting with auditory symptoms

By a News Reporter-Staff News Editor at Life Science Weekly – Current study results on Tuberculosis have been published. According to news reporting originating from Slough, United Kingdom, by NewsRx correspondents, research stated, “We present an unusual case of a 54-year-old Chinese lady presenting to the ears, nose and throat clinic after family members noticed that her hearing had progressively deteriorated over the preceding weeks. She also complained of tinnitus.”

Our news editors obtained a quote from the research from the Department of Plastic Surgery, “Examination of the ears, nose and throat was unremarkable. Flexible nasoendoscopy demonstrated swelling in the postnasal space, which, following biopsy, was shown to be pathognomonic of tuberculosis.”

According to the news editors, the research concluded: “This was successfully treated with multidisciplinary input and the patient made a complete recovery.”

For more information on this research see: Nasopharyngeal tuberculosis presenting with auditory symptoms. *Bmj Case Reports*, 2012;2012(). (BMJ Publishing Group - http://group.bmj.com/; *Bmj Case Reports* - http://casereports.bmj.com/)

The news editors report that additional information may be obtained by contacting M. Pankhania, Dept. of Plastic Surgery, Wexham Park Hospital, Slough, UK. (2012 Oct 30)

Christian Medical College, Tamil Nadu: Tuberculosis in a renal allograft recipient presenting with intussusception

By a News Reporter-Staff News Editor at Biotech Week – Investigators publish new report on Tuberculosis. According to news originating from Tamil Nadu, India, by NewsRx correspondents, research stated, “Extra-pulmonary tuberculosis (TB) is more common in renal allograft recipients and may present with dissemination or an atypical features. We report a renal allograft recipient with intestinal TB presenting 3 years after transplantation with persistent fever, weight loss, diarrhea, abdominal pain and mass in the abdomen with intestinal obstruction.”

Our news journalists obtained a quote from the research from Christian Medical College, “He was diagnosed to be having an ileocolic intussusception which on resection showed a granulomatous inflammation with presence of acid-fast bacilli (AFB) typical of *Mycobacterium tuberculosis*. In addition, AFB was detected in the tracheal aspirate, indicating dissemination. He received anti-TB therapy (ATT) from the fourth postoperative day. However, he developed a probable immune reconstitution inflammatory syndrome (IRIS) with multiorgan failure and died
on 11(th) postoperative day. This is the first report of intestinal TB presenting as intussusception in a renal allograft recipient. The development of IRIS after starting ATT is rare in renal allograft recipients.”

According to the news editors, the research concluded: “This report highlights the need for a high index of suspicion for diagnosing TB early among renal transplant recipients and the therapeutic dilemma with overwhelming infection and development of IRIS upon reduction of immunosuppression and starting ATT.”

For more information on this research see: Tuberculosis in a renal allograft recipient presenting with intussusception. Indian Journal of Nephrology, 2012;22(1):52-6.

The news correspondents report that additional information may be obtained from A. Mohapatra, Dept. of Nephrology, Christian Medical College, Vellore, Tamil Nadu, India. (2012 Oct 24)

Central South University, Changsha: Two-stage surgical management using posterior instrumentation, anterior debridement and allografting for tuberculosis of the lower lumbar spine in children of elementary school age: minimum 3-year follow-up of 14 patients

By a News Reporter-Staff News Editor at Pediatrics Week – Researchers detail new data in Mycobacterium Infections. According to news reporting originating in Changsha, People’s Republic of China, by Vertical-News journalists, research stated, “Various surgical methods have been described for the management of lumbar tuberculous spondylitis in the literature. However, there were few reports on the two-stage surgical treatment of lumbar tuberculosis in children of elementary school age.”

The news reporters obtained a quote from the research from Central South University, “We present a retrospective clinical study of 14 patients with lumbar and lumbosacral tuberculous spondylitis treated by two-stage surgery (first stage: posterior instrumentation; second stage: anterior debridement and allografting). The purpose is to determine the clinical efficacy of such surgical treatment for lumbar tuberculosis in children. Our series was comprised 9 males and 5 females with an average age of 7.5 years treated with the abovementioned surgical procedure. All patients had lumbar and lumbosacral involvement with one patient having spondylitis at L2-3, three at L3-4, seven at L4-5, and three at L5-S1. All patients had single motion segment involvement. The Frankel scoring system was used to assess the neurological deficits. Frankel’s grade B in two patients, grade C in four and grade D in eight. The following data were followed-up for an average period of 50.1 months (42-64 months) in these patients: healing of disease, deformity correction and its maintenance, neurologic function, and spinal
bony fusion. The average preoperative local deformity angle was -13.8 degrees, correcting to 3.4 degrees postoperatively and 1.5 degrees at the final follow-up. With the exception of one patient who received a D at the final follow-up, all cases obtained complete neurological recovery. No breakage and looseness of internal fixation was found. Bony fusion was achieved in all cases within 6 months postoperatively. There was no recurrent tuberculous infection. Two-stage (posterior and anterior) surgery is a safe and effective procedure for the patient of elementary school age suffering from lumbar and lumbosacral tuberculous spondylitis, especially for the patients in poor general condition."

According to the news reporters, the researchers concluded: “The procedure has the advantage of minor surgical invasion, effective kyphosis correction and less complications.”

For more information on this research see: Two-stage surgical management using posterior instrumentation, anterior debridement and allografting for tuberculosis of the lower lumbar spine in children of elementary school age: minimum 3-year follow-up of 14 patients. Archives of Orthopaedic and Trauma Surgery, 2012;132(9):1273-1279. Archives of Orthopaedic and Trauma Surgery can be contacted at: Springer, 233 Spring St, New York, NY 10013, USA. (Springer - www.springer.com; Archives of Orthopaedic and Trauma Surgery - http://www.springerlink.com/content/0936-8051/)

Our news correspondents report that additional information may be obtained by contacting H.Q. Zhang, Central South University, Dept. of Spine Surg, Xiangya Hosp, Changsha, Hunan, People’s Republic of China. (2012 Oct 06)

Department of Nephrology, Dubai: Tuberculosis of the arterio-venous graft in a renal transplant recipient

By a News Reporter-Staff News Editor at Biotech Week – New research on Mycobacterium Infections is the subject of a report. According to news originating from Dubai, United Arab Emirates, by NewsRx correspondents, research stated, “A 44-year-old Pakistani lady with end-stage renal disease secondary to rapidly proliferative glomerulonephritis underwent successful renal transplantation. Three years later, she was referred to the surgeon with an abscess in the axillary region at the site of a previous arterio-venous (AV) graft.”

Our news journalists obtained a quote from the research from the Department of Nephrology, “She underwent repeated incision and drainage of the abscess, which was constantly recurring. Nine months later, she presented with a tender swelling at the site of the AV graft with purulent discharge. The graft was removed; culture and histology confirmed the presence of tuberculosis (TB).”
According to the news editors, the researchers concluded: “This patient presents a rare case of TB infection in the AV graft.”


The news correspondents report that additional information may be obtained from F. Alalawi, Dept. of Nephrology, Dubai Hospital, Dubai Health Authority, Dubai, United Arab Emirates. *(2012 Oct 03)*

**All India Institute of Medical Sciences, New Delhi: Comparison of PET/CT with other imaging modalities in women with genital tuberculosis**

By a News Reporter-Staff News Editor at Tuberculosis Week – Current study results on Mycobacterium Infections have been published. According to news reporting out of New Delhi, India, by NewsRx editors, research stated, “To compare findings with 2-deoxy-2-(F-18)fluoro-D-glucose positron emission tomography combined with computed tomography (F-18-FDG-PET/CT) with findings obtained using ultrasound (US), magnetic resonance imaging (MRI), and CT in patients with proven tubercular tubo-ovarian masses. Seventeen patients with proven tubercular tubo-ovarian masses underwent F-18-FDG-PET/CT imaging and the findings were compared with US (for all patients), MRI (for 9 patients), CT (for 4 patients), and laparotomy or laparoscopic findings (for 14 patients).”

Our news journalists obtained a quote from the research from the All India Institute of Medical Sciences, “Eleven patients (64.7%) had unilateral tubo-ovarian masses, with activity in 6 masses (35.3%); 4 patients (23.5%) had bilateral tubo-ovarian masses, with activity in all masses; and 2 patients (11.76%) had unilateral space-occupying lesions, with activity in 1 lesion. The detection rates of tubo-ovarian masses with F-18-FDG-PET/CT were similar to, but the characterization of adnexal masses was less than, those obtained with CT or MRI. Finally, F-18-FDG-PET/CT was equally accurate as laparoscopy or laparotomy in detecting the presence, laterality, and activity of tubo-ovarian masses.”

According to the news editors, the researchers concluded: “Imaging with F-18-FDG-PET/CT is noninvasive and appears to be clinically useful for the diagnosis of tubercular tubo-ovarian masses.”

For more information on this research see: Comparison of PET/CT with other imaging modalities in women with genital tuberculosis. *International Journal of Gynecology & Obstetrics*, 2012;118(2):123-128. *International Journal of Gynecology & Obstetrics* can be contacted at:
Ohio State University, Columbus: Tuberculosis In Pediatric Solid Organ And Hematopoietic Stem Cell Transplant Recipients

By a News Reporter-Staff News Editor at Chemicals & Chemistry – New research on Stem Cell Research is the subject of a report. According to news reporting out of Columbus, Ohio, by VerticalNews editors, researchers stated “The burden of tuberculosis after pediatric solid organ transplant or hematopoietic stem cell transplantation has not been well characterized.”

Our news journalists obtained a quote from the research from Ohio State University, “We report 7 pediatric cases with disseminated (4/7) or pulmonary (3/7) tuberculosis after solid organ transplant (n = 6) or hematopoietic stem cell transplantation (n = 1) during 26 years. The outcome was favorable in 6 patients.”

According to the news editors, the researchers concluded: “Isoniazid-induced hepatitis and rifampin interactions were common.”

For more information on this research see: Tuberculosis In Pediatric Solid Organ And Hematopoietic Stem Cell Transplant Recipients. Pediatric Infectious Disease Journal, 2012;31(7):774-777. Pediatric Infectious Disease Journal can be contacted at: Lippincott Williams & Wilkins, 530 Walnut St, Philadelphia, PA 19106-3621, USA. (Lippincott Williams and Wilkins - www.lww.com; Pediatric Infectious Disease Journal - http://journals.lww.com/pidj/pages/default.aspx)

Our news journalists report that additional information may be obtained by contacting R. Vecino, Ohio State University, Coll Med, Center Vaccines & Immun, Nationwide Childrens HospDiv Pediat Infect Dis, Columbus, OH 43210, United States. (2012 Aug 03)
Sacred Heart Catholic University, Rome: Surgical treatment of tuberculous spondylodiscitis

By a News Reporter-Staff News Editor at Biotech Week – Fresh data on Osteoarticular Tuberculosis are presented in a new report. According to news reporting from Rome, Italy, by NewsRx journalists, researchers stated “Most patients affected by spinal tuberculosis can be successfully treated conservatively with chemotherapy, external bracing and prolonged rest. Nevertheless, kyphotic deformity, spinal instability and neurological deficit remain a common complication associated with conservative approach.”

The news correspondents obtained a quote from the research by the authors from Sacred Heart Catholic University, “To illustrate different indications and treatment modalities for tuberculous spondylodiscitis, focusing on the role of surgery as an adjuvant of effective chemotherapy in the management of selected patients. Various early and late surgical procedures are recommended to treat spinal tuberculosis. The Authors analyzed surgical indications, approaches, complications and outcomes comparing their experience with available Literature. Conservative management is preferable in patients without vertebral instability and deformity; in presence of abscesses, invasive radiological techniques in combination with abscess drainage and chemotherapy are recommended. In patients with vertebral collapse, kyphotic deformity or abscess formation, vertebral instability or neurological deficits, anterior radical debridement, anterior strut grafting and anterior instrumentation is an optimal standardized procedure. In patients with involvement of more than two vertebral levels or lumbosacral junction and in those whose sagittal alignment is markedly deformed with segmental kyphosis, and in patients who have difficulty in undergoing anterior instrumentation, posterior instrumentation is recommended in combination with anterior radical debridement and anterior strut grafting in one or two staged procedures. Since surgery for spinal tuberculosis is demanding, it should be performed only after taking into account the risks and benefits in operable patients.”

According to the news reporters, the researchers concluded: “Various surgical procedures are recommended to treat spinal tuberculosis but the common goals are to eradicate the infection and to prevent or to treat neurologic deficits or spinal deformity.”

For more information on this research see: Surgical treatment of tuberculous spondylodiscitis. European Review for Medical and Pharmacological Sciences, 2012;16(1):79-85. European Review for Medical and Pharmacological Sciences can be contacted at: Verduci Publisher, Via Gregorio Vii, Rome, 186-00165, Italy.

Our news journalists report that additional information may be obtained by contacting E. Pola, Sacred Heart Catholic University, Sch
CHAPTER 6    SURGERY

Chapter 7

Therapies and Treatments

Johns Hopkins University School of Medicine, Baltimore: Rifapentine is not more active than rifampin against chronic tuberculosis in guinea pigs

By a News Reporter-Staff News Editor at Life Science Weekly – New research on Mycobacterium Infections is the subject of a report. According to news originating from Baltimore, Maryland, by NewsRx correspondents, research stated, “Rifamycins are key sterilizing drugs in the current treatment of active tuberculosis (TB). Daily dosing of rifapentine (P), a potent rifamycin with high intracellular accumulation, in place of rifampin and isoniazid (H), in the standard antitubercular regimen significantly shortens the duration of treatment needed to prevent relapse in a murine model of active TB.”

Our news journalists obtained a quote from the research from the Johns Hopkins University School of Medicine, “We undertook the current study to compare directly the activities of human-equivalent doses of P and R in a guinea pig model of chronic TB, in which bacilli are predominantly extracellular within human-like necrotic granulomas. Hartley strain guinea pigs were aerosol infected with ~200 bacilli of Mycobacterium tuberculosis H37Rv, and treatment given 5 days/week was initiated 6 weeks later. R at 100 mg/kg of body weight and P at 100 mg/kg were given orally alone or in combination with isoniazid (H) at 60 mg/kg and pyrazinamide (Z) at 300 mg/kg. Culture-positive relapse was assessed in subgroups of guinea pigs after completion of 1 and 2 months of treatment. Human-equivalent doses of R and P showed equivalent bactericidal activity when used alone and in combination therapy. In guinea pigs treated with rifampin, isoniazid, and pyrazinamide (RHZ) or PHZ, microbiological relapse occurred in the lungs of 8/10 animals..."
treated for 1 month and in 0/10 animals treated for 2 months. Substitution of P for R in the standard antitubercular regimen did not shorten the time to cure in this guinea pig model of chronic TB.”

According to the news editors, the research concluded: “Data from ongoing clinical trials comparing the activity of these two drugs are awaited to determine the relevance of the guinea pig TB model in preclinical drug screening.”

For more information on this research see: Rifapentine is not more active than rifampin against chronic tuberculosis in guinea pigs. *Antimicrobial Agents and Chemotherapy*, 2012;56(7):3726-31. (American Society for Microbiology - www.asm.org; Antimicrobial Agents and Chemotherapy - aac.asm.org)

The news correspondents report that additional information may be obtained from N.K. Dutta, Departments of Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland, United States. *(2013 Apr 23)*

**University of Florence: Serial QuantiFERON TB-Gold in-tube testing during LTBI therapy in candidates for TNFi treatment**

By a News Reporter-Staff News Editor at Life Science Weekly – Researchers detail new data in Infection Research. According to news originating from Florence, Italy, by NewsRx correspondents, research stated, “To evaluate the T-cell interferon (IFN)-gamma response to Mycobacterium tuberculosis-specific antigens during latent tuberculosis infection (LTBI) therapy in candidates for tumor necrosis factor-alpha inhibitors (TNFi). 1490 Patients were screened for LTBI.”

Our news journalists obtained a quote from the research from the University of Florence, “One-hundred and sixty-six of them were treated for LTBI and followed-up with QuantiFERON-TB Gold (QFT-IT) testing at baseline (T0) and therapy completion (T1); 92 subjects were also tested 3-6 months after therapy completion (T2). At T1 the QFT-IT reversion and conversion rates were 24% (27/111) and 18% (10/55), respectively. By multivariate analysis, the likelihood of reversion significantly decreased with older age (&gt;50-60), larger TST size (&gt;15 mm) and higher IFN-gamma value at T0 (&gt;1 IU/ml); the likelihood of conversion increased with higher IFN-gamma levels at T0 (1 IU/ml) and in female patients. Quantitative data among those who scored QFT-IT-positive at T0 showed a decreasing trend of IFN-gamma levels between T0 and T1 that reached statistical significance when T0 was compared to T2, and T1 to T2. The data confirm the difficulty of interpreting the modulation of IFN-gamma levels during LTBI therapy.”
According to the news editors, the research concluded: “Currently, there is no evidence to support the use of QFT-IT in the clinical practice of monitoring LTBI treatment in candidates for TNFi.”


The news correspondents report that additional information may be obtained from F. Bartalesi, Univ Firenze, Dipartimento Med Interna, I-50134 Florence, Italy. (2013 Apr 23)

**University of KwaZulu-Natal, Scottsville: In Vitro Antimicrobial Activity of Extracts from Plants Used Traditionally in South Africa to Treat Tuberculosis and Related Symptoms**

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators discuss new findings in Complementary and Alternative Medicine. According to news reporting out of Scottsville, South Africa, by NewsRx editors, research stated, “Respiratory ailments are major human killers, especially in developing countries. Tuberculosis (TB) is an infectious disease causing a threat to human healthcare.”

Our news journalists obtained a quote from the research from the University of KwaZulu-Natal, “Many South African plants are used in the traditional treatment of TB and related symptoms, but there has not been a sufficient focus on evaluating their antimicrobial properties. The aim of this study was to evaluate the antimicrobial properties of plants used traditionally to treat TB and related symptoms against microorganisms (Klebsiella pneumoniae, Staphylococcus aureus, and Mycobacterium aurum A+) associated with respiratory infections using the microdilution assay. Ten plants were selected based on a survey of available literature of medicinal plants used in South Africa for the treatment of TB and related symptoms. The petroleum ether, dichloromethane, 80% ethanol, and water extracts of the selected plants were evaluated for antibacterial activity. Out of 68 extracts tested from different parts of the 10 plant species, 17 showed good antimicrobial activities against at least one or more of the microbial strains tested, with minimum inhibitory concentration ranging from 0.195 to 12.5 mg/mL. The good antimicrobial properties of Abrus precatorius, Terminalia phanerophlebia, Indigofera arrecta, and Pentanisia pruneloides authenticate their traditional use in the treatment of respiratory diseases.”
According to the news editors, the research concluded: “Thus, further pharmacological and phytochemical analysis is required.”

For more information on this research see: In Vitro Antimicrobial Activity of Extracts from Plants Used Traditionally in South Africa to Treat Tuberculosis and Related Symptoms. Evidence-Based Complementary and Alternative Medicine, 2013();1-8. Evidence-Based Complementary and Alternative Medicine can be contacted at: Hindawi Publishing Corporation, 410 Park Avenue, 15TH Floor, #287 Pmb, New York, NY 10022, USA. (Hindawi Publishing - www.hindawi.com; Evidence-Based Complementary and Alternative Medicine - http://www.hindawi.com/journals/ecam/)

Our news journalists report that additional information may be obtained by contacting B. Madikizela, Univ KwaZulu Natal Pietermaritzburg, Sch Life Sci, Res Center Plant Growth & Dev, ZA-3209 Scottsville, South Africa. (2013 Apr 23)

Ohio State University, Columbus: Impact of cigarette smoking on rates and clinical prognosis of pulmonary tuberculosis in Southern Mexico

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – Fresh data on Infection Research are presented in a new report. According to news originating from Columbus, Ohio, by NewsRx correspondents, research stated, “To examine the relationship between cigarette smoking and incidence and mortality rates of pulmonary tuberculosis (TB) and treatment outcomes. From 1995 to 2010, we analyzed data from 1062 patients with TB and from 2001 to 2004, 2951 contacts in Southern Mexico.”

Our news journalists obtained a quote from the research from Ohio State University, “Patients with acid-fast bacilli or Mycobacterium tuberculosis in sputum samples underwent epidemiological, clinical and mycobacteriological evaluation and received treatment by the local DOTS program. Consumers of 1-10 (LS) or 11 or more (HS) cigarettes per day incidence (1.75 and 11.79) and mortality (HS, 17.74) smoker-non-smoker rate ratios were significantly higher for smokers. Smoker population was more likely to experience unfavorable treatment outcomes (HS, adjusted OR 2.36) and retreatment (LS and HS, adjusted hazard ratio (HR) 2.14 and 2.37). Contacts that smoked had a higher probability of developing active TB (HR 2.38) during follow up.”

According to the news editors, the research concluded: “Results indicate the need of incorporating smoking prevention and cessation, especially among men, into international TB control strategies.”

The news correspondents report that additional information may be obtained from R.A. Bonacci, Ohio State University, Dept. of Microbiol, Columbus, OH 43210, United States. (2013 Apr 22)

**University of KwaZulu-Natal, Durban: Strategies for reducing treatment default in drug-resistant tuberculosis: systematic review and meta-analysis**

By a News Reporter-Staff News Editor at Biotech Week – Fresh data on Multidrug Resistant Tuberculosis are presented in a new report. According to news reporting out of Durban, South Africa, by NewsRx editors, research stated, “Scaling up treatment for multidrug-resistant tuberculosis is a global health priority. However, current treatment regimens are long and associated with side effects, and default rates are consequently high.”

Our news journalists obtained a quote from the research from the University of KwaZulu-Natal, “This systematic review aimed to identify strategies for reducing treatment default. We conducted a systematic search up to May 2012 to identify studies describing interventions to support patients receiving treatment for multidrug-resistant tuberculosis (MDR-TB). The potential influence of study interventions were explored through subgroup analyses. A total of 75 studies provided outcomes for 18294 patients across 31 countries. Default rates ranged from 0.5% to 56%, with a pooled proportion of 14.8% (95%CI 12.4-17.4). Strategies identified to be associated with lower default rates included the engagement of community health workers as directly observed treatment (DOT) providers, the provision of DOT throughout treatment, smaller cohort sizes and the provision of patient education. Current interventions to support adherence and retention are poorly described and based on weak evidence. This review was able to identify a number of promising, inexpensive interventions feasible for implementation and scale-up in MDR-TB programmes.”

According to the news editors, the research concluded: “The high default rates reported from many programmes underscore the pressing need to further refine and evaluate simple intervention packages to support patients.”

For more information on this research see: Strategies for reducing treatment default in drug-resistant tuberculosis: systematic review
Factors affecting defaulting from DOTS therapy under the national programme of tuberculosis control in Alexandria, Egypt

By a News Reporter-Staff News Editor at Life Science Weekly – Fresh data on Health and Medicine are presented in a new report. According to news reporting out of Dubai, United Arab Emirates, by NewsRx editors, research stated, “This unmatched case-control study aimed to identify factors affecting default from therapy under the national programme of TB control in Alexandria, Egypt. Record reviews and structured interviews were made with 57 defaulters and 187 randomly selected controls.”

Our news journalists obtained a quote from the research, “Univariate analysis showed 13 out of 54 factors, investigated were significantly associated with defaulting and, after stepwise logistic regression, 5 factors remained in the model: younger age (adjusted OR=0.16), rural area of residence (OR=12.9), long waiting times (OR=5.81), poor physician-patient communication (OR=3.06) and fear of information leakage (OR=3.62). Reasons cited by defaulters included long distance to the clinic, unsuitable clinic times and long waiting times.”

According to the news editors, the research concluded: “The main factors associated with defaulting from the national programme of TB control in Alexandria, Egypt were service-related factors, which are amenable to improvement.”


Our news journalists report that additional information may be obtained by contacting M.N. El-Din, e-School of Health and Environmental Studies, Hamdan Bin Mohammed e-University, Dubai, United Arab Emirates. (2013 Apr 16)
Korea Research Institute of Chemical Technology, Daejeon: Design, synthesis, and structure-activity relationship studies of tryptanthrins as antitubercular agents

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators publish new report on Natural Products. According to news reporting originating in Daejeon, South Korea, by NewsRx journalists, research stated, “The natural product tryptanthrin (1a) represents a potential lead for new tuberculosis (TB) drugs since tryptanthrin and its synthetic analogues possess potent in vitro activity against *Mycobacterium tuberculosis* (Mtb). However, in spite of their in vitro activity, none of these agents have been shown to be efficacious in vivo against animal models of TB.”

The news reporters obtained a quote from the research from the Korea Research Institute of Chemical Technology, “Described herein are syntheses of new tryptanthrin analogues together with a systematic investigation of their in vitro antitubercular activity and ADME properties followed by pharmacokinetic characterization in rodents for the most promising compounds. Those with the best potency and oral bioavailability were progressed to evaluations of efficacy against acute murine TB. The work aimed to prove the concept that this compound class can limit growth of Mtb during infection as well as to establish the SAR for in vitro activity against Mtb and the range of in vitro ADME parameters for this class of natural products. Novel C-11-deoxy (5b) and A-ring-saturated (6) tryptanthrin analogues were discovered that maintained activity against Mtb and showed improved solubility compared to tryptanthrin as well as evidence of oral bioavailability in rodents. However, neither 5b nor 6 demonstrated efficacy against acute murine TB following administration at doses up to 400 mg/kg daily for 4 weeks.”

According to the news reporters, the research concluded: “Although 5b and 6 failed to inhibit replication or kill Mtb in vivo, they illuminate a path to new structural variations of the tryptanthrin scaffold that may maximize the potential of this class of compounds against TB.”


Our news correspondents report that additional information may be obtained by contacting J.M. Hwang, Cancer and Infectious Diseases Therapeutics Research Group, Korea Research Institute of Chemical Technology, Daejeon 305-600, South Korea. (2013 Apr 16)
National Health Laboratory Service, Johannesburg: Point-of-care Xpert ® MTB/RIF for smear-negative tuberculosis suspects at a primary care clinic in South Africa

By a News Reporter-Staff News Editor at Life Science Weekly – Current study results on Tuberculosis and Lung Disease have been published. According to news originating from Johannesburg, South Africa, by NewsRx correspondents, research stated, “To assess the clinical utility and cost of point-of-care Xpert ® MTB/RIF for the diagnosis of smear-negative tuberculosis (TB). Cohort study of smear-negative TB suspects at a South African primary care clinic.”

Our news journalists obtained a quote from the research from National Health Laboratory Service, “Participants provided one sputum sample for fluorescent smear microscopy and culture and an additional sample for Xpert. Outcomes of interest were TB diagnosis, linkage to care, patient and provider costs. Among 199 smear-negative TB suspects, 16 were positive by Xpert, 15 by culture and 7 by microscopy. All cases identified by Xpert began anti-tuberculosis treatment the same or next day; only one of five Xpert-negative culture-positive cases started treatment after 34 days. Xpert at point of care offered similar diagnostic yield but a faster turnaround time than smear and culture performed at a centralized laboratory. Compared to smear plus culture, Xpert (at US$9.98 per cartridge) was US$3 less expensive per valid result (US$21 vs. US$24) and only US$6 more costly per case identified (US$266 vs. US$260). Xpert is an effective method of diagnosing smear-negative TB. It is cost saving for patients, especially if performed at point of care, but it is costly for health care providers.”

According to the news editors, the research concluded: “Data-driven studies are needed to determine its cost-effectiveness in resource-poor settings with diverse diagnostic practices.”


The news correspondents report that additional information may be obtained from A. Van Rie, Natl Hlth Lab Serv, Johannesburg, South Africa. (2013 Apr 16)
University of Amsterdam: Free tuberculosis diagnosis and treatment are not enough: patient cost evidence from three continents

By a News Reporter-Staff News Editor at Life Science Weekly – Researchers detail new data in Tuberculosis and Lung Disease. According to news reporting originating from Amsterdam, Netherlands, by NewsRx correspondents, research stated, “The National Tuberculosis Programs of Ghana, Viet Nam and the Dominican Republic. To assess the direct and indirect costs of tuberculosis (TB) diagnosis and treatment for patients and households.”

Our news editors obtained a quote from the research from the University of Amsterdam, “Each country translated and adapted a structured questionnaire, the Tool to Estimate Patients’ Costs. A random sample of new adult patients treated for at least 1 month was interviewed in all three countries. Across the countries, 27-70% of patients stopped working and experienced reduced income, 5-37% sold property and 17-47% borrowed money due to TB. Hospitalisation costs (US$42-118) and additional food items formed the largest part of direct costs during treatment. Average total patient costs (US$538-1268) were equivalent to approximately 1 year of individual income. We observed similar patterns and challenges of TB-related costs for patients across the three countries.”

According to the news editors, the research concluded: “We advocate for global, united action for TB patients to be included under social protection schemes and for national TB programmes to improve equitable access to care.”


The news editors report that additional information may be obtained by contacting V. Mauch, University of Amsterdam, Academy Med Center, Amsterdam Inst Global Hlth & Dev, NL-1105 AZ Amsterdam, Netherlands. (2013 Apr 16)
University of Skovde: Food incentives improve adherence to tuberculosis drug treatment among homeless patients in Russia

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators publish new report on Caring Science. According to news reporting from Skovde, Sweden, by NewsRx journalists, research stated, “The aim of the study was to evaluate the impact of food incentives on adherence to tuberculosis (TB) drug treatment among homeless patients with TB. Food packages were thus given as a part of directly observed therapy to 142 homeless patients with TB at a dispensary in Saint Petersburg, Russian Federation.”

The news correspondents obtained a quote from the research from the University of Skovde, “In addition, a social worker provided the patients with information and legal assistance, for example help with internal passports. Among the 142 patients, 66 were included in the study at the dispensary during their entire treatment period, while 76 patients were included in the study during shorter periods mainly because of transfer to inpatient care. In the first group, 59% of the patients continued the TB drug treatment without interruption in contrast to 31% in a control group. In the second group, that is those studied during shorter periods, 95% continued the TB drug treatment without interruption while attached to the dispensary. Food was introduced in the TB programme of the City of St. Petersburg as a consequence of this study.”

According to the news reporters, the research concluded: “It can be stated that the food incentive had a strong positive impact on the adherence to TB drug treatment among these socially marginalized patients. The social support contributed in all probability also to the positive results.”


Our news journalists report that additional information may be obtained by contacting B. Garden, Dept. of Life Sciences, University of Skovde, Skovde, Sweden. (2013 Apr 16)
Northrop Grumman, Atlanta: Epidemiology of recurrent tuberculosis in the United States, 1993-2010

By a News Reporter-Staff News Editor at Tuberculosis Week – Investigators publish new report on Tuberculosis and Lung Disease. According to news originating from Atlanta, Georgia, by NewsRx correspondents, research stated, “Recurrent tuberculosis (TB) can result from reactivation of a previous TB episode or reinfection with a new Mycobacterium tuberculosis strain. A retrospective analysis of all recurrent TB cases reported in the United States during 1993-2010 was conducted.”

Our news journalists obtained a quote from the research from Northrop Grumman, “The proportion of recurrent cases remained stable during the study period (annual range 4.2-5.7%). Compared with persons without a previous diagnosis of TB, persons with recurrent TB experienced lower treatment completion within 12 months and higher mortality during the recurrent episode.”

According to the news editors, the research concluded: “Persons with recurrent TB have poorer outcomes, suggesting the need for targeted interventions to ensure treatment completion.”


The news correspondents report that additional information may be obtained from L. Kim, Northrop Grumman Corp, Public Hlth Operating Unit, Atlanta, GA, United States. (2013 Apr 15)

University of Parma: Application of a stochastic modeling to assess the evolution of tuberculous and non-tuberculous mycobacterial infection in patients treated with tumor necrosis factor inhibitors

By a News Reporter-Staff News Editor at Tuberculosis Week – New research on Mycobacterium Infections is the subject of a report. According to news reporting originating in Parma, Italy, by NewsRx journalists, research stated, “In this manuscript we apply stochastic modeling to investigate the risk of reactivation of latent mycobacterial infections in patients undergoing treatment with tumor necrosis factor inhibitors. First, we review the perspective proposed by one of the authors in a previous work and which consists in predicting the occurrence of reactivation of latent tuberculosis infection or newly acquired tuberculosis during treatment; this is based on variational procedures on a simple set of parameters (e.g. rate of reactivation of a latent infection).”
The news reporters obtained a quote from the research from the University of Parma, “Then, we develop a full analytical study of this approach through a Markov chain analysis and we find an exact solution for the temporal evolution of the number of cases of tuberculosis infection (re)activation. The analytical solution is compared with Monte Carlo simulations and with experimental data, showing overall excellent agreement. The generality of this theoretical framework allows to investigate also the case of non-tuberculocous mycobacteria infections; in particular, we show that reactivation in that context plays a minor role. This may suggest that, while the screening for tuberculous is necessary prior to initiating biologics, when considering non-tuberculocous mycobacteria only a watchful monitoring during the treatment is recommended.”

According to the news reporters, the research concluded: “The framework outlined in this paper is quite general and could be extremely promising in further researches on drug-related adverse events.”


Our news correspondents report that additional information may be obtained by contacting E. Agliari, Dipartimento di Fisica, Universita di Parma, Parma, Italy. *(2013 Apr 15)*

**Colorado State University, Fort Collins: A physiologically based pharmacokinetic model of rifampin in mice**

By a News Reporter-Staff News Editor at Biotech Week – Current study results on Antimicrobial Agents and Chemotherapy have been published. According to news reporting originating from Fort Collins, Colorado, by NewsRx correspondents, research stated, “One problem associated with regimen-based development of antituberculosis (anti-TB) drugs is the difficulty of a systematic and thorough in vivo evaluation of the large number of possible regimens that arise from consideration of multiple drugs tested together. A mathematical model capable of simulating the pharmacokinetics and pharmacodynamics of experimental combination chemotherapy of TB offers a way to mitigate this problem by extending the use of available data to investigate regimens that are not initially tested.”

Our news editors obtained a quote from the research from Colorado State University, “In order to increase the available mathematical tools needed to support such a model for preclinical anti-TB drug development, we constructed a preliminary whole-body physiologically based
pharmacokinetic (PBPK) model of rifampin in mice, using data from the literature. Interindividual variability was approximated using Monte Carlo (MC) simulation with assigned probability distributions for the model parameters. An MC sensitivity analysis was also performed to determine correlations between model parameters and plasma concentration to inform future model development. Model predictions for rifampin concentrations in plasma, liver, kidneys, and lungs, following oral administration, were generally in agreement with published experimental data from multiple studies. Sensitive model parameters included those descriptive of oral absorption, total clearance, and partitioning of rifampin between blood and muscle.”

According to the news editors, the research concluded: “This PBPK model can serve as a starting point for the integration of rifampin pharmacokinetics in mice into a larger mathematical framework, including the immune response to Mycobacterium tuberculosis infection, and pharmacokinetic models for other anti-TB drugs.”


The news editors report that additional information may be obtained by contacting M.A. Lyons, Mycobacteria Research Laboratories, Dept. of Microbiology, Immunology and Pathology, Colorado State University, Fort Collins, Colorado, United States. (2013 Apr 10)

Central South University, Changsha: One-stage surgical treatment for upper thoracic spinal tuberculosis by internal fixation, debridement, and combined interbody and posterior fusion via posterior-only approach

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators publish new report on Musculoskeletal Diseases and Conditions. According to news reporting originating from Changsha, People’s Republic of China, by NewsRx correspondents, research stated, “To investigate the clinical efficacy and feasibility of one-stage surgical treatment for upper thoracic spinal tuberculosis by internal fixation, debridement, and combined interbody and posterior fusion via a posterior-only approach. Fourteen patients (eight males, six females) with upper thoracic tuberculosis whose lesions were confined to two adjacent segments were admitted to our hospital.”

Our news editors obtained a quote from the research from Central South University, “Their ages ranged from 23 to 72 years (average, 50 years). The American Spinal Injury Association (ASIA) impairment scale was used to assess neurological function. ASIA classification showed that preoperatively, one patient was grade A, two patients
were grade B, eight patients were grade C, and three patients were grade D. All patients were treated with one-stage surgical treatment by internal fixation, debridement, and combined interbody and posterior fusion via a posterior-only approach. Patients were evaluated preoperatively and postoperatively by measurement of thoracic kyphotic angles using Cobb angle evaluation, determination of erythrocyte sedimentation rate (ESR), evaluation of ASIA impairment scale, and radiological examination. Operation time ranged from 70 to 135 min (average, 110 min). Intraoperative blood loss ranged from 200 to 950 mL (average, 450 mL). All patients were followed up for 22 to 48 months postoperatively (average, 31.5 months). No sinus tract formation, cerebrospinal meningitis, or recurrence of tuberculosis occurred. All patients had significant postoperative improvement in ASIA classification scores. The thoracic kyphotic angles were significantly decreased to 12A degrees-26A degrees postoperatively, and at final follow-up were 13A degrees-28A degrees. The ESR recovered to normal within 6 months postoperatively in all patients. Bone fusion was achieved within 3-8 months (average, 5.5 months).

According to the news editors, the research concluded: “One-stage surgical treatment for upper thoracic spinal tuberculosis by internal fixation, debridement, and combined interbody and posterior fusion via a posterior-only approach can be an effective and feasible treatment method.”

For more information on this research see: One-stage surgical treatment for upper thoracic spinal tuberculosis by internal fixation, debridement, and combined interbody and posterior fusion via posterior-only approach. European Spine Journal, 2013;22(3):616-623. European Spine Journal can be contacted at: Springer, 233 Spring St, New York, NY 10013, USA. (Springer - www.springer.com; European Spine Journal - http://www.springerlink.com/content/0940-6719/)

The news editors report that additional information may be obtained by contacting H.Q. Zhang, Central South University, Xiangya Hosp, Dept. of Spine Surg, Changsha 410008, Hunan, People’s Republic of China. (2013 Apr 09)

Charles University, Prague: Quantiferon TB Gold and tuberculin skin tests for the detection of latent tuberculosis infection in patients treated with tumour necrosis factor alpha blocking agents

By a News Reporter-Staff News Editor at Life Science Weekly – A new study on Mycobacterium Infections is now available. According to news reporting out of Prague, Czech Republic, by NewsRx editors, research stated, “The risk of activation of latent tuberculosis infection (LTBI) is
increased in patients treated with anti-TNF-alpha drugs. Tuberculin skin test (TST) and Quantiferon-TB Gold test (QFT) are used to detect LTBI before and during anti-TNF-alpha treatment.

Our news journalists obtained a quote from the research from Charles University, “We describe here a relation of these tests at various timepoints and also longitudinal QFT data. Study group consisted of 305 patients with several rheumatic inflammatory diseases treated and/or scheduled for anti-TNF-alpha drugs. The QFT was performed in 303 patients during therapy and in 177 patients also during screening. The TST was used in 284 patients. Both tests simultaneously were utilised in 360 instances. Twenty-two patients were QFT positive; 3.9% before and 5.9% during anti-TNF-alpha treatment. Two patients who became QFT positive developed active tuberculosis. The TST was positive in 42% and 38% of patients before and during treatment, respectively. There was poor agreement between the two tests. Patients on glucocorticoids had a negative TST more frequently. The IFN-gamma response to mycobacterial antigens significantly increased after application of tuberculin, but never reached the positive threshold. There was a significant increase in mitogen-induced IFN-γ production after initiation of anti-TNF-alpha therapy. Poor correlation between the QFT and TST renders the TST non-specific for LTBI. QFT is more specific to detect LTBI and conversion to a positive result may predict active TB. An increase in IFN-gamma production in response to mycobacterial antigens is seen when the TST is performed before the QFT.”

According to the news editors, the research concluded: “Mitogen-induced IFN-gamma production increases after initiation of anti-TNF-alpha therapy.”

For more information on this research see: Quantiferon TB Gold and tuberculin skin tests for the detection of latent tuberculosis infection in patients treated with tumour necrosis factor alpha blocking agents. Clinical and Experimental Rheumatology, 2013;31(1):111-117. Clinical and Experimental Rheumatology can be contacted at: Clinical & Exper Rheumatology, Via Santa Maria 31, 56126 Pisa, Italy.

Our news journalists report that additional information may be obtained by contacting M. Klein, Charles Univ Prague, Dept. of Rheumatol, Fac Med 1, Prague, Czech Republic. (2013 Apr 09)

Seoul National University College of Medicine: Clinical effects of gemifloxacin on the delay of tuberculosis treatment

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators discuss new findings in Medical Science. According to
news reporting originating in Seoul, South Korea, by NewsRx journalists, research stated, “Although gemifloxacin has low in vitro activity against Mycobacterium tuberculosis, the effect of gemifloxacin on the delay of tuberculosis (TB) treatment has not been validated in a clinical setting. The study group included patients with culture-confirmed pulmonary TB who initially received gemifloxacin for suspected community-acquired pneumonia (CAP).”

The news reporters obtained a quote from the research from the Seoul National University College of Medicine, “Two control groups contained patients treated with other fluoroquinolones or nonfluoroquinolone antibiotics. Sixteen cases were treated with gemifloxacin for suspected CAP before TB diagnosis. Sixteen and 32 patients were treated with other fluoroquinolones and nonfluoroquinolones, respectively. The median period from the initiation of antibiotics to the administration of anti-TB medication was nine days in the gemifloxacin group, which was significantly different from the other fluoroquinolones group (35 days). The median times for the nonfluoroquinolone group and the gemifloxacin group were not significantly different. There were no significant differences between the gemifloxacin and other fluoroquinolone group in terms of symptomatic and radiographic improvements. However, the frequency of radiographic improvement in the other fluoroquinolones group tended to be higher than in the gemifloxacin group.”

According to the news reporters, the research concluded: “Gemifloxacin might be the preferred fluoroquinolone for treating CAP, to alleviate any concerns about delaying TB treatment.”


Our news correspondents report that additional information may be obtained by contacting S.Y. Kim, Division of Pulmonary and Critical Care Medicine, Dept. of Internal Medicine and Lung Institute of Medical Research Center, Seoul National University College of Medicine, Seoul, South Korea. (2013 Apr 09)


By a News Reporter-Staff News Editor at AIDS Weekly – New research on Infectious Diseases is the subject of a report. According to news reporting originating from Richmond, California, by NewsRx correspondents, research stated, “To inform efforts to prevent antituberculosis drug resistance acquired during treatment, particularly multidrug-resistant (MDR) tuberculosis, we analyzed surveillance records from
the US state with the highest morbidity. Surveillance data from the California tuberculosis registry of cases reported between 1994 and 2006 were examined retrospectively.”

Our news editors obtained a quote from the research from the California Department of Public Health, “Crude risks of acquired resistance were estimated. Multivariate logistic regression was used to estimate odds ratios of demographic, clinical, and case management characteristics associated with acquired drug resistance (ADR), and secular trends in the incidence of ADR were assessed. One in 688 patients acquired MDR tuberculosis, with crude risks varying greatly by initial drug susceptibility test results: 1 in 1909 if initially susceptible to isoniazid and rifampin, 1 in 113 if initially isoniazid resistant, and 1 in 23 if initially rifampicin resistant. Acquired isoniazid and rifampicin monoresistance occurred in 1 in 1018 and 1 in 1455 patients, respectively. Independent predictors of acquired MDR tuberculosis were initial isoniazid resistance (odds ratio [OR], 19.2; 95% confidence interval [CI], 8.25-44.7; P<.001), initial rifampicin resistance (OR, 35.9; 95% CI, 8.61-150; P<.001), human immunodeficiency virus (HIV) infection (OR, 5.07; 95% CI, 1.73-14.9; P = .003), and cavitary disease in the absence of directly observed therapy throughout therapy (OR, 2.65; 95% CI, 1.05-6.69; P = .04). The annual incidence of ADR declined over the study period. Although ADR is rare and declining in California, its costly consequences warrant improvements in treatment practices.”

According to the news editors, the research concluded: “Our findings suggest that we ensure DOT throughout the course of therapy for patients with baseline drug resistance, cavitary disease, or HIV infection.”


The news editors report that additional information may be obtained by contacting T.C. Porco, Calif Dept. of Public Hlth, Center Infect Dis, TB Control Branch, Richmond, CA 94804, United States. (2013 Apr 08)
By a News Reporter-Staff News Editor at Diabetes Week – Fresh data on Diabetes are presented in a new report. According to news reporting out of Cleveland, Ohio, by NewsRx editors, research stated, “Recurrent tuberculosis disease occurs within 2 years in as few as 1% and as many as 29% of individuals successfully treated for multidrug-resistant (MDR) tuberculosis. A better understanding of treatment-related factors associated with an elevated risk of recurrent tuberculosis after cure is urgently needed to optimize MDR tuberculosis therapy.”

Our news journalists obtained a quote from the research from Case Western Reserve University, “We conducted a retrospective cohort study among adults successfully treated for MDR tuberculosis in Peru. We used multivariable Cox proportional hazards regression analysis to examine whether receipt of an aggressive MDR tuberculosis regimen for \geq\ 18 months following sputum conversion from positive to negative was associated with a reduced rate of recurrent tuberculosis. Among 402 patients, the median duration of follow-up was 40.5 months (interquartile range, 21.2-53.4). Receipt of an aggressive MDR tuberculosis regimen for \geq\ 18 months following sputum conversion was associated with a lower risk of recurrent tuberculosis (hazard ratio, 0.40 [95% confidence interval, 0.17-0.96]; P = .04). A baseline diagnosis of diabetes mellitus also predicted recurrent tuberculosis (hazard ratio, 10.47 [95% confidence interval, 2.17-50.60]; P = .004). Individuals who received an aggressive MDR tuberculosis regimen for \geq\ 18 months following sputum conversion experienced a lower rate of recurrence after cure. Efforts to ensure that an aggressive regimen is accessible to all patients with MDR tuberculosis, such as minimization of sequential ineffective regimens, expanded drug access, and development of new MDR tuberculosis compounds, are critical to reducing tuberculosis recurrence in this population.”

According to the news editors, the research concluded: “Patients with diabetes mellitus should be carefully managed during initial treatment and followed closely for recurrent disease.”


Our news journalists report that additional information may be obtained by contacting M.F. Franke, Case Western Reserve University, TB Res Unit, Cleveland, OH 44106, United States. (2013 Apr 08)
Department of Pharmacology, Fort Collins: In vivo/in vitro pharmacokinetic and pharmacodynamic study of spray-dried poly-(DL-lactic-co-glycolic) acid nanoparticles encapsulating rifampicin and isoniazid

By a News Reporter-Staff News Editor at Biotech Week – Investigators publish new report on Pharmaceutical Research. According to news reporting originating from Fort Collins, Colorado, by NewsRx correspondents, research stated, “Poly-(DL-lactic-co-glycolic) acid (PLGA) nanoparticles were prepared by a double emulsion solvent evaporation spray-drying technique and coated with polyethylene glycol (PEG 1% v/v). The PLGA nanoparticles had a small size (229 +/- 7.6 to 382 +/- 23.9 nm), uniform size distribution and positive zeta potential (+12.45 +/- 4.53 mV).”

Our news editors obtained a quote from the research from the Department of Pharmacology, “In vitro/in vivo assays were performed to evaluate the pharmacokinetic (PK) and pharmacodynamic (PD) performance of these nanoparticles following nanoencapsulation of the anti-tuberculosis drugs rifampicin (RIF) and isoniazid (INH). The results demonstrated the potential for the reduction in protein binding of these drugs by protection in the polymer core. Furthermore, in vitro efficacy was demonstrated using Mycobacterium tuberculosis (M. tb.) (strain H(37)Rv). Sustained drug release over seven days were observed for these drugs following once-off oral administration in mice with subsequent drug distribution of up to 10 days in the liver and lungs for RIF and INH, respectively.”

According to the news editors, the research concluded: “It was concluded by these studies combined with our previous reports that spray-dried PLGA nanoparticles demonstrate potential for the improvement of tuberculosis chemotherapy by nanoencapsulation of anti-tuberculosis drugs.”


The news editors report that additional information may be obtained by contacting L. Booysen, CSU Anim Canc Center, Dept. of Pharmacol, Fort Collins, CO 80523, United States. (2013 Apr 03)
ISF College of Pharmacy, Moga: Development and characterization of ligand-appended liposomes for multiple drug therapy for pulmonary tuberculosis

By a News Reporter-Staff News Editor at Biotech Week – Data detailed on Mycobacterium Infections have been presented. According to news reporting originating in Moga, India, by NewsRx journalists, research stated, “Tuberculosis (TB) remains one of the oldest and deadliest diseases in the current scenario. The intracellular organism *Mycobacterium tuberculosis*, which mainly resides in mononuclear phagocytes, is responsible for tuberculosis in humans.”

The news reporters obtained a quote from the research from the ISF College of Pharmacy, “A few therapies are available for the treatment of tuberculosis but they have many hurdles. To overcome these hurdles, a combination of chemotherapeutic agent-loaded vesicular systems have been prepared to overcome tuberculosis. To investigate the role of novel drug delivery systems for the treatment of pulmonary tuberculosis, ligand appended liposomals have been developed. In the present study, drug-loaded, ligand-appended liposomes and their DPI (Dry Powder Inhaler) forms have been prepared and characterized using various in vitro and in vivo parameters. The prepared ligand-appended liposomal formulation showed good entrapment efficiency, prolonged drug release, improved recovery of drugs from the target site, and proved to be more suitable for use as DPI, justifying their potential for improved drug delivery.”

According to the news reporters, the research concluded: “Thus we tried our best by our project to reduce the national burden of tuberculosis, which is still a global health challenge.”


Our news correspondents report that additional information may be obtained by contacting A. Bhardwaj, Nanomedicine Research Center, Dept. of Pharmaceutics, ISF College of Pharmacy, Moga, India. (2013 Apr 03)
University Hospital, London: Rifampicin pharmacokinetics in extreme prematurity to treat congenital tuberculosis

By a News Reporter-Staff News Editor at Biotech Week – Investigators publish new report on Drug Research. According to news reporting from London, United Kingdom, by NewsRx journalists, research stated, “Little evidence is available on the pharmacokinetics of antituberculous medication in premature infants. We report rifampicin (RMP) pharmacokinetics in an extremely premature, low-birthweight female infant born to a mother with known miliary tuberculosis.”

The news correspondents obtained a quote from the research from University Hospital, “Intravenous RMP, isoniazid (INH), ciprofloxacin and amikacin were used, as the enteral route was not possible. Area under the curve calculations revealed low average RMP concentrations at doses of 5-10 mg/kg. We review the literature with regard to the dosing regimen and therapeutic drug levels of RMP and INH in premature infants and discuss issues of management.”

According to the news reporters, the research concluded: “Evidence from this case suggests 10 mg/kg/day is the minimum dose required.”

For more information on this research see: Rifampicin pharmacokinetics in extreme prematurity to treat congenital tuberculosis. Bmj Case Reports, 2013;2013():. (BMJ Publishing Group - http://group.bmj.com/; Bmj Case Reports - http://casereports.bmj.com/)

Our news journalists report that additional information may be obtained by contacting K. Le Doare, Dept. of Paediatrics, Croydon University Hospital, London, UK. (2013 Apr 03)

Boston University: Initiating antiretroviral therapy when presenting with higher CD4 cell counts results in reduced loss to follow-up in a resource-limited setting

By a News Reporter-Staff News Editor at AIDS Weekly – Current study results on AIDS/HIV Research have been published. According to news reporting out of Boston, Massachusetts, by NewsRx editors, research stated, “In August 2011, South Africa expanded its adult antiretroviral therapy (ART) guidelines to allow treatment initiation at CD4 cell values 350 cells/mu l or less. Mortality and morbidity are known to be reduced when initiating at higher CD4 levels; we explored the impact on patient loss to follow-up.”

Our news journalists obtained a quote from the research from Boston University, “An observational cohort study. We analyzed routine data of 1430 adult patients initiating ART from April to December 2010 from a Johannesburg primary healthcare clinic offering ART initiation at CD4 cell count 350 cells/ml or less since 2010. We compared loss to follow-up (≥ 3 months late for the last scheduled visit), death, and incident
tuberculosis within 1 year of ART initiation for those initiating at CD4 cell values 200 or less versus 201-350 cells/μl. Half (52.0%) of patients presented in the lower CD4 cell group [200 cells/μl, median: 105 cells/μl, interquartile range (IQR): 55-154] and initiated ART, and 48.0% in the higher group (CD4 cell count 201-350 cells/μl, median: 268 cells/μl, IQR: 239-307). The proportion of women and pregnant women was greater in the high CD4 cell group; the lower CD4 cell group included more patients with prevalent tuberculosis. Among men and nonpregnant women, initiating at 201-350 cells/μl was associated with 26-42% reduced loss to follow-up compared to those initiating 200 cells/ml or less. We found no CD4 cell effect among pregnant women. Risk of mortality [adjusted hazard ratio (aHR) 0.34, 95% confidence interval (CI) 0.13-0.84] and incident tuberculosis (aHR 0.44, 95% CI 0.23-0.85) was lower among the higher CD4 cell group.”

According to the news editors, the research concluded: “This is one of the first studies from a routine clinical setting to demonstrate South Africa’s 2011 expansion of ART treatment guidelines can be enacted without increasing program attrition.”

For more information on this research see: Initiating antiretroviral therapy when presenting with higher CD4 cell counts results in reduced loss to follow-up in a resource-limited setting. *Aids*, 2013;27(4):645-650. *Aids* can be contacted at: Lippincott Williams & Wilkins, 530 Walnut St, Philadelphia, PA 19106-3621, USA. (Lippincott Williams and Wilkins - www.lww.com; Aids - http://journals.lww.com/aidsonline/pages/default.aspx)

Our news journalists report that additional information may be obtained by contacting K. Clouse, Boston University, Dept. of Epidemiol, Sch Public Hlth, Boston, MA 02215, United States. (2013 Apr 01)

**University of KwaZulu-Natal, Durban: Tuberculosis in medical doctors - a study of personal experiences and attitudes**

By a News Reporter-Staff News Editor at Tuberculosis Week – Fresh data on Mycobacterium Infections are presented in a new report. According to news reporting originating in Durban, South Africa, by NewsRx journalists, research stated, “Background. The concurrent TB and HIV epidemics in sub-Saharan Africa place all health care workers (HCWs) at increased risk of exposure to Mycobacterium tuberculosis. This study explores personal experiences, attitudes and perceptions of medical doctors following treatment for TB within the healthcare system.”

The news reporters obtained a quote from the research from the University of KwaZulu-Natal, “Sixty-two medical doctors who were diagnosed and treated for TB during 2007 - 2009 agreed to participate
and complete a semi-structured questionnaire. Results. The response rate was 64.5% (N=40). Mean age ±SD of participants was 33.7±10.6 years. A correct diagnosis of TB was made within 7 days of clinical presentation in 20% of participants, and was delayed beyond 3 weeks in 52.5%. Non-routine special investigations and procedures were performed in 26 participants. Complications following invasive procedures were reported by 8 participants. Multi-drug resistant TB (MDR-TB) was diagnosed in 4 participants. Nineteen considered defaulting on their treatment because of drug side-effects. The majority (n=36) expressed concerns regarding lack of infection control at the workplace, delays in TB diagnosis and negative attitudes of senior medical colleagues and administrators. Ninety per cent of participants indicated that their personal illness experiences had positively changed their professional approach to patients in their current practice. The inappropriate delays in diagnosis in a large number of participants, coupled with a number of negative personal perceptions towards their treatment, are cause for concern.”

According to the news reporters, the research concluded: “The results further amplify the need for improved educational and awareness programmes among all healthcare personnel (including hospital administrators), adherence to national health guidelines, effective infection control measures, pre-and post-employment screening in all HCWs, and changes in attitudes on the part of senior medical colleagues and administrators.”


Our news correspondents report that additional information may be obtained by contacting A. Naidoo, Dept. of Family Medicine, Nelson R Mandela School of Medicine, University of KwaZulu-Natal, Durban, South Africa.

The publisher of the *South African Medical Journal Suid-afrikaanse Tydskrif Vir Geneeskunde* can be contacted at: Med Assoc S Africa, Med House Central Sq 7430 Pinelands Priv Bag X1, Johannesburg, South Africa. (2013 Apr 01)
Postgraduate Institute of Medical Education and Research, Chandigarh: Pleural tuberculosis following lung cancer chemotherapy: a report of two cases proven pathologically by pleural biopsy

By a News Reporter-Staff News Editor at Biotech Week – Researchers detail new data in Lung Cancer. According to news reporting originating from Chandigarh, India, by NewsRx correspondents, research stated, “Malignancy per se and cytotoxic chemotherapy given for its treatment both are recognised risk factors for the development of tuberculosis (TB). However, individual case descriptions of pleural tuberculosis (TB-PE) following chemotherapy for lung cancer (LC) have not been published previously.”

Our news editors obtained a quote from the research from the Postgraduate Institute of Medical Education and Research, “We herein report the first two cases of histopathologically proven TB-PE following LC chemotherapy. The first patient was a 38-year-old man with stage IV non-small cell LC (adenocarcinoma) who developed TB-PE following four cycles of chemotherapy (pemetrexed-cisplatin). The second patient was a 49-year-old man with extensive disease small cell LC who developed TB-PE after six cycles of chemotherapy (irinotecan-cisplatin). In both patients, diagnosis of TB-PE was established by demonstration of granulomatous inflammation, caseous necrosis and positive stain for acid-fast bacilli in pleural biopsy specimens. Both cases responded to standard four-drug antitubercular therapy. These cases highlight the importance of carrying out an extensive evaluation for exudative pleural effusions in LC patients receiving chemotherapy, especially in countries with high TB prevalence.”

According to the news editors, the research concluded: “Attributing such pleural effusions to disease progression, without histopathological confirmation, may be associated with disastrous consequences.”

For more information on this research see: Pleural tuberculosis following lung cancer chemotherapy: a report of two cases proven pathologically by pleural biopsy. Bmj Case Reports, 2013;2013():. (BMJ Publishing Group - http://group.bmj.com/; Bmj Case Reports - http://casereports.bmj.com/)

The news editors report that additional information may be obtained by contacting K. Madan, Dept. of Pulmonary Medicine, Postgraduate Institute of Medical Education & Research, Chandigarh, India. (2013 Mar 27)
The changing landscape of diagnostic services for tuberculosis

By a News Reporter-Staff News Editor at Biotech Week – Current study results on Critical Care Medicine have been published. According to news reporting originating from Geneva, Switzerland, by NewsRx correspondents, research stated, “During the last decade there has been a dramatic change in the laboratory approach to tuberculosis (TB) diagnosis in the developing world. This change began with the realization that acid-fast bacillus smear microscopy alone was totally inadequate to deal with the dual problems of human immunodeficiency virus (HIV)-associated TB and drug-resistant TB that threaten to undermine global progress in TB control.”

Our news editors obtained a quote from the research, “Subsequently, increased financial resources for TB laboratory services and the establishment of a systematic process for endorsement of new TB diagnostic tools and approaches by the World Health Organization (WHO) have led to rapid expansion of TB laboratory services and the availability of several new diagnostic tests that have been introduced. These include both commercial automated and noncommercial systems for phenotypic mycobacterial liquid culture and drug susceptibility testing, a simple and inexpensive test for mycobacterial species identification in culture isolates, light-emitting diode fluorescence microscopy, and rapid molecular methods for TB case detection and the diagnosis of drug-resistant TB. The latter methodologies that include line probe assays and an automated cartridge-based real-time polymerase chain reaction (PCR)-based test are being scaled up at an unprecedented pace and are truly revolutionizing the diagnosis of drug-resistant TB. On the other hand, little progress has been made in the quest for a true point-of-care test for TB.”

According to the news editors, the research concluded: “Fortunately, this is being addressed in several discovery initiatives that hopefully will provide impetus for the development of rapid, accurate TB diagnostics for the lowest level of the health system.”

For more information on this research see: The changing landscape of diagnostic services for tuberculosis. Seminars In Respiratory and Critical Care Medicine, 2013;34(1):17-31. (Thieme - www.thieme.com)

The news editors report that additional information may be obtained by contacting C.C. Boehme, Foundation for New Innovative Diagnostics (FIND), Geneva, Switzerland. (2013 Mar 27)
Cooper University Hospital, Camden: Tuberculous myopericarditis: a rare presentation in an immunocompetent host

By a News Reporter-Staff News Editor at Life Science Weekly – Research findings on Tuberculosis are discussed in a new report. According to news reporting originating from Camden, New Jersey, by NewsRx correspondents, research stated, “Tuberculosis is a common cause of pericardial disease in India. Myocardial involvement, although well described in the literature, is a rare manifestation of tuberculosis.”

Our news editors obtained a quote from the research from Cooper University Hospital, “We report a patient with disseminated tuberculosis and myopericarditis manifesting as cardiogenic shock. The patient gradually improved on antituberculosis drug therapy, steroids and an evidence-based guideline driven therapy for heart failure.”

According to the news editors, the research concluded: “Follow-up imaging showed calcification of the pericardium and improvement of his left ventricular systolic function.”

For more information on this research see: Tuberculous myopericarditis: a rare presentation in an immunocompetent host. *Bmj Case Reports*, 2013;2013(): (BMJ Publishing Group - http://group.bmj.com; *Bmj Case Reports* - http://casereports.bmj.com/)

The news editors report that additional information may be obtained by contacting N. Desai, Dept. of Medicine, Cooper University Hospital, Camden, New Jersey, United States. *(2013 Mar 26)*

University of Sao Paulo: Case Report: Leprosy and Tuberculosis Co-Infection: Clinical and Immunological Report of Two Cases and Review of the Literature

By a News Reporter-Staff News Editor at Malaria Weekly – A new study on Tropical Medicine and Public Health is now available. According to news reporting originating in Sao Paulo, Brazil, by NewsRx journalists, research stated, “A review of the records of patients seen between 2004 and 2011 at the Dermatology Clinic of the Sao Paulo University Medical School showed that only two leprosy patients had been co-infected with tuberculosis (TB). One patient showed a type 1 leprosy reaction during the first 3 months of treatment of pleural TB and in the other patient, pulmonary TB was diagnosed during the first 3 months of treatment of a type 1 leprosy reaction.”

The news reporters obtained a quote from the research from the University of Sao Paulo, “Both patients showed normal cellular immune response tests, including those of the interferon-gamma (IFN-gamma)/interleukin 12 (IL-12) axis. Although both mycobacterial infections are endemic in developing countries like Brazil, the co-infection
has hardly been reported in the last decade. There is no suitable explanation for this observation.”

According to the news reporters, the research concluded: “The reports on the interaction between the two mycobacteria are highly speculative: some studies suggest that leprosy, especially the anergic form, would predispose to TB, whereas other investigations suggested an antagonism between the two diseases.”


Our news correspondents report that additional information may be obtained by contacting M.A.B. Trindade, University of Sao Paulo, Medical Mycol Lab, Inst Trop Med, BR-05403000 Sao Paulo, Brazil. (2013 Mar 18)

Case Western Reserve University, Cleveland: Smoking and 2-month culture conversion during anti-tuberculosis treatment

By a News Reporter-Staff News Editor at Life Science Weekly – Current study results on Tuberculosis and Lung Disease have been published. According to news originating from Cleveland, Ohio, by NewsRx correspondents, research stated, “To investigate risk factors for delayed sputum culture conversion to negative during anti-tuberculosis treatment, with an emphasis on smoking. Nested case-control study of adults with non-cavitary, culture-confirmed pulmonary tuberculosis (TB) participating in an anti-tuberculosis treatment trial in Brazil.”

Our news journalists obtained a quote from the research from Case Western Reserve University, “A case of delayed culture conversion was a patient who remained culture-positive after 2 months of treatment. Odds ratios with 95% confidence intervals were calculated. Fifty-three cases and 240 control patients were analyzed. Smokers had three-fold greater odds of remaining culture-positive after 2 months of treatment (P = 0.007) than non-smokers, while smokers and ex-smokers who smoked &gt;20 cigarettes a day had two-fold greater odds of remaining culture-positive after 2 months of treatment (P = 0.045). Cigarette smoking adversely affects culture conversion during anti-tuberculosis treatment.”

According to the news editors, the research concluded: “Support for smoking cessation should be considered to improve outcomes in TB control programs.”

The news correspondents report that additional information may be obtained from E.L. Maciel, Case Western Reserve University, Dept. of Med, Div Infect Dis, TB Res Unit, Cleveland, OH 44106, United States. (2013 Mar 12)

**Department of Health, Hong Kong: A pilot external quality assurance programme for line-probe assay detection of anti-tuberculosis drug resistance**

By a News Reporter-Staff News Editor at Life Science Weekly – Fresh data on Tuberculosis and Lung Disease are presented in a new report. According to news reporting from Hong Kong, People’s Republic of China, by NewsRx journalists, research stated, “Multidrug-resistant tuberculosis (MDR-TB; resistance to isoniazid and rifampicin) is difficult to detect and control. Line-probe assays (LiPA) are widely used for the rapid detection of MDR-TB.”

The news correspondents obtained a quote from the research from the Department of Health, “To ensure the quality of the test, a pilot external quality assurance (EQA) programme was initiated to assess the feasibility of running such a programme and the possibility of improving the proficiency of TB laboratories in performing the test. Prepared filter-paper-based Mycobacterium tuberculosis DNA samples were shipped to participant laboratories for LiPA EQA. The tests were performed blind, and the results were returned to the organising laboratory for comparison and analysis. A total of four rounds of EQA samples were dispatched to five laboratories in four countries. Overall inter- and intra-laboratory reproducibility was respectively 97% and 96%. The strengths and weaknesses of the participant laboratories in performing the test were discussed. A LiPA EQA programme can ensure quality and improve the performance of TB laboratories.”

According to the news reporters, the research concluded: “This is a critical step during the initial stages at the time of setting up this method of testing.”

For more information on this research see: A pilot external quality assurance programme for line-probe assay detection of anti-tuberculosis drug resistance. *International Journal of Tuberculosis and Lung Disease*, 2013;17(2):262-266. *International Journal of Tuberculosis and Lung Disease* can be contacted at: Int Union Against
Ningxia Medical University: Ultra-short-course chemotherapy for spinal tuberculosis: five years of observation

By a News Reporter-Staff News Editor at Life Science Weekly – Fresh data on Spinal Research are presented in a new report. According to news originating from Ningxia, People’s Republic of China, by NewsRx correspondents, research stated, “This study aimed to explore the feasibility of ultra-short-course chemotherapy in the treatment of spinal tuberculosis. One hundred and eighty-five patients with confirmed spinal tuberculosis and surgical indication were included.”

Our news journalists obtained a quote from the research from Ningxia Medical University, “The chemotherapy regimen was 2SHRZ/XHRZ. According to the duration of the chemotherapy, the patients were divided into two groups, the ultra-short-course chemotherapy group with an average duration of 4.5 months, and the standard chemotherapy group with an average duration of 9 months. The same surgery was performed for patients in the two groups. The duration of the follow-up ranged from 61 to 87 months, with an average of 69.1 months. Erythrocyte sedimentation rate and C-reactive protein, kyphosis and nerve function, recovery of work, and activities of daily living were not significantly different between the two groups before or after treatment; however, the aforementioned indices were significantly different before and after treatment within groups. There was no significant difference in postoperative bone graft healing between the two groups. The drug side effects were significantly different between the two groups. With thorough focus debridement, bone grafting, and internal fixation, the efficacy of ultra-short chemotherapy was similar to that of standard chemotherapy for the treatment of spinal tuberculosis.”

According to the news editors, the research concluded: “The ultra-short-course chemotherapy can shorten the course of treatment and reduce drug side effects.”

For more information on this research see: Ultra-short-course chemotherapy for spinal tuberculosis: five years of observation. European Spine Journal, 2013;22(2):274-281. European Spine Journal can be contacted at: Springer, 233 Spring St, New York, NY 10013,

By a News Reporter-Staff News Editor at Life Science Weekly – Current study results on General Medicine have been published. According to news originating from Vancouver, Canada, by NewsRx correspondents, research stated, “We undertook a quantitative benefit-risk analysis of a targeted isoniazid (INH) therapy for latent tuberculosis (TB) infection for different groups of contacts of active TB cases. We developed a decision-analytic model to compare the treatment of latent TB infection in subgroups of contacts to no treatment over a 6-year time horizon in a Canadian setting.”

Our news journalists obtained a quote from the research from the University of British Columbia, “Contacts were stratified into 32 groups on the basis of five binary variables: type of contact (close or casual), tuberculin skin test (TST) results (positive or negative at 5 mm cutoff), Bacillus Calmette-Guerin vaccination status, place of birth (foreign- or Canadian-born), and age group (cutoff 35 years). Risk of TB reactivation was calculated for each subgroup from a longitudinal registry of contacts, adjusted for several potential confounders and comorbid conditions. We calculated the quality-adjusted life-years gained because of delayed or prevention of active TB via treatment of latent TB infection versus quality-adjusted life-years lost because of the adverse events to INH. A targeted policy based on adopting INH therapy only in subgroups with positive expected incremental net health benefit resulted in a different treatment decision than the current guidelines in five subgroups comprising 3.9% of the contacts. Namely, the targeted policy comprised no INH therapy in casual contacts with a positive vaccination history even with a positive TST result and INH therapy in foreign-born close contacts younger than 35 years even with a negative TST result.”

According to the news editors, the research concluded: “From a benefit-risk viewpoint, INH treatment of contacts should be tailored on the basis of risk assessment algorithms that consider a range of factors at the time of screening.”

For more information on this research see: A Quantitative Benefit-Risk Analysis of Isoniazid for Treatment of Latent Tuberculosis Infection Using Incremental Benefit Framework. Value in Health,
Ben-Gurion University of the Negev, Beer Sheva: Epidemiology of extra-pulmonary tuberculosis in Israel, 1999-2010

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – A new study on Tuberculosis and Lung Disease is now available. According to news reporting out of Beer Sheva, Israel, by NewsRx editors, research stated, “The Israeli national tuberculosis (TB) surveillance system. To describe the epidemiology of extra-pulmonary tuberculosis (EPTB) in Israel between 1999 and 2010 and identify more susceptible populations.”

Our news journalists obtained a quote from the research from the Ben-Gurion University of the Negev, “Data were retrieved from the National Tuberculosis Registry and the Israeli Bureau of Statistics. During the study period, 995 EPTB patients were notified, corresponding to 19.6% of all TB cases. The average annual male:female ratio was 0.8, and the human immunodeficiency virus (HIV) infection rate was 5%. Most EPTB affected the lymph nodes (39.8%), pleura (16.9%) and urinary system (11.1%). Most EPTB patients (81.8%) were non-Israeli born. The estimated average annual incidence in Israeli-born citizens, non-Israeli-born citizens and migrant workers was respectively 0.23, 2.2 and 7.5 per 100000 population. The ratio of non-Israeli-born migrant workers to non-Israeli-born citizens with EPTB decreased from 1:6.3 in 1999 to 1:0.78 in 2010. Culture results were obtained for 624 (62.9%) of all cases. Of these, 41 (6.6%) were resistant to at least one first-line anti-tuberculosis drug and 8 (1.3%) were multidrug-resistant. Treatment success was achieved in 86.5%. Physicians should be aware of the possibility of EPTB in older patients, especially in the non-Israeli-born.”

According to the news editors, the research concluded: “Innovative screening procedures should be implemented for migrants from high-burden countries.”

For more information on this research see: Epidemiology of extra-pulmonary tuberculosis in Israel, 1999-2010. International Journal of Tuberculosis and Lung Disease, 2013;17(2):229-233. International Journal of Tuberculosis and Lung Disease can be contacted at: Int
John Innes Center, Norwich: The naphthoquinone diospyrin is an inhibitor of DNA gyrase with a novel mechanism of action

By a News Reporter-Staff News Editor at Tuberculosis Week – Data detailed on Mycobacterium Infections have been presented. According to news reporting originating from Norwich, United Kingdom, by NewsRx correspondents, research stated, “Tuberculosis and other bacterial diseases represent a significant threat to human health. The DNA topoisomerases are excellent targets for chemotherapy, and DNA gyrase in particular is a well-validated target for antibacterial agents. Naphthoquinones (e.g. diospyrin and 7-methyljuglone) have been shown to have therapeutic potential, particularly against Mycobacterium tuberculosis.”

Our news editors obtained a quote from the research from John Innes Center, “We have found that these compounds are inhibitors of the supercoiling reaction catalyzed by M. tuberculosis gyrase and other gyrases. Our evidence strongly suggests that the compounds bind to the N-terminal domain of GyrB, which contains the ATPase active site, but are not competitive inhibitors of the ATPase reaction. We propose that naphthoquinones bind to GyrB at a novel site close to the ATPase site.”

According to the news editors, the research concluded: “This novel mode of action could be exploited to develop new antibacterial agents.”


The news editors report that additional information may be obtained by contacting S. Karkare, From the Dept. of Biological Chemistry, John Innes Centre, Norwich Research Park, Norwich, NR4 7UH, UK. (2013 Mar 11)
Ghent University: Is repositioning of drugs a viable alternative in the treatment of tuberculosis?

By a News Reporter-Staff News Editor at Health & Medicine Week – A new study on Mycobacterium Infections is now available. According to news reporting originating in Ghent, Belgium, by NewsRx journalists, research stated, "Antimicrobial resistance is a serious problem because of the scarcity of new antibiotics effective against pathogens such as methicillin-resistant Staphylococcus aureus, -lactamase-producing Gram-negative bacteria and multidrug-resistant Mycobacterium tuberculosis. Extensively drug resistance is particularly worrying in tuberculosis (TB), since the causative bacteria have become resistant to almost all available first- and second-line drugs and resistance is a threat to achieving control of the disease."

The news reporters obtained a quote from the research from Ghent University, "Development of new drugs is a lengthy and costly endeavour. This is a particular problem for antibiotics, usage of which is likely to be of limited duration, and is even more true of antibiotics whose use is restricted to the treatment of a disease, such as TB, that is considered to be poverty related’, and for which the return on the investment is seen as non-attractive. In spite of this, there is an emerging pipeline of new drugs under development that hopefully will bring new anti-TB drugs to the market in the near future. The strategy of drug repurposing, finding new uses for existing approved medicines, has seen unexpected success in other medical areas. More than one blockbuster drug has originated from this strategy. And in the field of TB, there have been several examples in recent years of this approach leading to the use of drugs for which there is undeniable evidence of efficacy in the treatment of the disease, the best example being the fluoroquinolones, which were not developed originally to treat TB."

According to the news reporters, the research concluded: "This article reviews some examples of repurposing of drugs in the treatment of TB, newer candidates for repurposing for which there is already preliminary evidence of activity and possible new options that merit further investigation."


Our news correspondents report that additional information may be obtained by contacting J.C. Palomino, University of Ghent, Microbiol Lab, Dept. of Biochem & Microbiol, B-9000 Ghent, Belgium. (2013 Mar 08)
University of Cape Town, Rondebosch: Outcomes of clofazimine for the treatment of drug-resistant tuberculosis: a systematic review and meta-analysis

By a News Reporter-Staff News Editor at Biotech Week – Researchers detail new data in Mycobacterium Infections. According to news originating from Rondebosch, South Africa, by NewsRx correspondents, research stated, “Current anti-tuberculosis therapeutics are not sufficiently effective against drug-resistant tuberculosis (DR-TB), and there is a need for new drugs and therapeutic approaches. It has been proposed that repurposing clofazimine for DR-TB treatment might be one way to increase therapeutic options.”

Our news journalists obtained a quote from the research from the University of Cape Town, “We conducted a systematic review of studies reporting on the efficacy and safety of clofazimine as part of combination therapy for DR-TB. Six databases and six conference abstract sites were searched from inception until April 2012. All studies involving the use of clofazimine in the treatment of DR-TB were included. Twelve studies, comprising 3489 patients across 10 countries, were included in this review. Treatment success ranged from 16.5 (95 CI 2.738.7) to 87.8 (95 CI 76.895.6), with an overall pooled proportion of 61.96 achieving treatment success (95 CI 52.7971.12) (TAU(2) 0.07). Mortality, treatment interruptions, defaulting and adverse events were all in line with DR-TB treatment outcomes overall. The most commonly reported adverse events were gastrointestinal disturbances and skin pigmentation. The available evidence to date suggests that clofazimine could be considered as an additional therapeutic option in the treatment of DR-TB.”

According to the news editors, the research concluded: “The optimal dose of clofazimine and duration of use require further investigation.”


The news correspondents report that additional information may be obtained from T. Dey, University of Cape Town, Center Infect Dis Epidemiol & Res, ZA-7701 Rondebosch, South Africa. (2013 Mar 06)
Centers for Disease Control and Prevention, Atlanta: Epidemiology of recurrent tuberculosis in the United States, 1993-2010 [Short communication]

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators discuss new findings in Tuberculosis and Lung Disease. According to news reporting originating from Atlanta, Georgia, by NewsRx correspondents, research stated, “Recurrent tuberculosis (TB) can result from reactivation of a previous TB episode or reinfection with a new Mycobacterium tuberculosis strain. A retrospective analysis of all recurrent TB cases reported in the United States during 1993-2010 was conducted.”

Our news editors obtained a quote from the research from Centers for Disease Control and Prevention, “The proportion of recurrent cases remained stable during the study period (annual range 4.2-5.7%). Compared with persons without a previous diagnosis of TB, persons with recurrent TB experienced lower treatment completion within 12 months and higher mortality during the recurrent episode.”

According to the news editors, the research concluded: “Persons with recurrent TB have poorer outcomes, suggesting the need for targeted interventions to ensure treatment completion.”

For more information on this research see: Epidemiology of recurrent tuberculosis in the United States, 1993-2010 [Short communication]. _The International Journal of Tuberculosis and Lung Disease_, 2013;17(3):357-60.

The news editors report that additional information may be obtained by contacting L. Kim, Epidemic Intelligence Service and Division of Tuberculosis Elimination, Centers for Disease Control and Prevention, Atlanta, Georgia, United States. (*2013 Mar 05*)

Sri Krishnadevaraya University, Andhra Pradesh: Synthesis and Antitubercular Activity of 2-(substituted phenyl/benzyl-amino)-6-(4-chlorophenyl)-5-(methoxycarbonyl)-4-methyl-3,6-dihydropyrimidin-1-ium Chlorides

By a News Reporter-Staff News Editor at Chemicals & Chemistry – Researchers detail new data in Drug Design. According to news reporting out of Andhra Pradesh, India, by VerticalNews editors, research stated, “A series of 2-(substituted phenyl/benzyl-amino)-6-(4-chlorophenyl)-5-(methoxycarbonyl)-4-methyl-3,6-dihydropyrimidin-1-ium chlorides 713 and 15 was synthesized in their hydrochloride salt form. The title compounds were characterized by FT-IR, NMR (1H and 13C) and elemental analysis.”
Our news journalists obtained a quote from the research from Sri Krishnadevaraya University, “They were evaluated for their in vitro antitubercular activity against Mycobacterium tuberculosis H37Rv, multidrug resistance tuberculosis and extensively drug resistance tuberculosis by agar diffusion method and tested for the cytotoxic action on peripheral blood mononuclear cells by MTT assay. Among all the tested compounds in the series, compounds 7 and 11 emerged as promising antitubercular agents at 16 μg/mL against multidrug resistance tuberculosis and over 64 μg/mL against extensively drug resistance tuberculosis.”

According to the news editors, the research concluded: “The conformational features and supramolecular assembly of the promising compounds 7 and 11 were determined by single crystal X-ray study.”


Our news journalists report that additional information may be obtained by contacting V.K. Narayanaswamy, Sri Krishnadevaraya Univ, Dept. of Polymer Sci & Technol, Anantapur 515055, Andhra Pradesh, India. (2013 Mar 01)

UCMS and GTB Hospital, New Delhi: Instrumented stabilization in spinal tuberculosis

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators discuss new findings in Musculoskeletal Diseases and Conditions. According to news reporting from New Delhi, India, by NewsRx journalists, research stated, “Spinal tuberculosis (TB) produces neurological complications and grotesque spinal deformity, which in children increases even with treatment and after achieving healing. Long-standing, severe deformity leads to painful costo-pelvic impingement, respiratory distress, risk of developing late-onset paraplegia and consequent reduction in quality and longevity of life.”

The news correspondents obtained a quote from the research from UCMS and GTB Hospital, “The treatment objective is to avoid the sequelae of neural complications and achieve the healed status with a near-normal spine. In TB, the spine may become unstable if all three columns are diseased. Pathological fracture/dislocation of a diseased
vertebral body may occur secondary to mechanical insult. Surgical decompression adds further instability, as part of the diseased vertebral body is excised. The insertion of a metallic implant is to provide mechanical stability and the use of an implant in tubercular infection is safe. Indications for instrumented stabilisation can be categorised as: (a) pan vertebral disease, in which all three columns are diseased; (b) long-segment disease, in which after surgical decompression a bone graft >5 cm is inserted with instrumentation to prevent graft-related complications and consequent progression of kyphosis and neural complications and; (c) when surgical correction of a kyphosis is performed when both anterior decompression and posterior column shortening is required. The implant choice should be individualised according to the case. Pedicle screw fixation in kyphus correction in healed disease is a most suitable implant.”

According to the news reporters, the research concluded: “Hartshill sublaminar wiring stabilisation in active disease is a suitable implant to stabilise the spine, taking purchase against healthy posterior complex of the vertebral body to save a segment.”


Our news journalists report that additional information may be obtained by contacting A.K. Jain, UCMS and GTB Hospital, Orthopaedics, New Delhi, India.

Publisher contact information for the journal *International Orthopaedics* is: Springer, 233 Spring Street, New York, NY 10013, USA. (2013 Feb 26)

**Central South University, Changsha: One-stage surgical management for tuberculosis of the upper cervical spine by posterior debridement, short-segment fusion, and posterior instrumentation in children**

suffered from tuberculosis of the upper cervical spine were admitted to our hospital between June 2005 and December 2010.”

Our news journalists obtained a quote from the research from Central South University, “All of them were treated by one-stage posterior debridement, short-segment fusion, and posterior instrumentation. Then, the clinical efficacy was evaluated using statistical analysis based on the materials about the visual analogue scale (VAS) scores of pain, JOA scores of nerve function and erythrocyte sedimentation rate (ESR), which were collected at certain time. The average follow-up period was 28.1 +/- A 10.5 months (13-42 months). In the 11 cases, no postoperative complications related to instrumentation occurred and neurologic function was improved in various degrees. The average pretreatment ESR was 58.4 +/- A 4.9 mm/h (53-69 mm/h), which got normal (8.9 +/- A 6.5 mm/h) within 3 months in all patients. The average preoperative VAS was 7.4 +/- A 2.2, which decreased to 1.6 +/- A 1.8 postoperatively. Mean preoperative JOA was 11.2 +/- A 3.8, and the JOA at the last visit was 16.3 +/- A 1.0. All patients got bony fusion within 3-8 months after surgery.”

According to the news editors, the research concluded: “One-stage posterior debridement, short-segment fusion, and posterior instrumentation can be an effective treatment method for the treatment of tuberculosis of the upper cervical spine in children.”


The news correspondents report that additional information may be obtained from H.Q. Zhang, Central South University, Xiangya Hosp, Dept. of Spine Surg, Changsha 410008, Hunan, People’s Republic of China. (2013 Feb 23)

**University of Ulsan, Seoul: GenoType ® MTBDRplus assay detection of drug-resistant tuberculosis in routine practice in Korea**

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators publish new report on Tuberculosis and Lung Disease. According to news reporting from Seoul, South Korea, by NewsRx journalists, research stated, “Korea is an intermediate-burden country with high rates of tuberculosis (TB) drug resistance. To evaluate the performance of the GenoType ® MTBDRplus (MTBDR) assay in diagnosing drug-resistant TB in routine practice in Korea.”
The news correspondents obtained a quote from the research from the University of Ulsan, “The MTBDR assay was performed on 428 samples, and the results were retrospectively compared with the results of conventional drug susceptibility testing (DST). The interval between treatment and diagnosis of drug resistance was also compared. The sensitivity, specificity and positive and negative predictive values of the MTBDR assay were respectively 96.6%, 98.9%, 93.4% and 99.5% for the detection of rifampicin (RMP) resistance; 93.8%, 98.3%, 92.7% and 98.6% for isoniazid (INH) resistance; and 91.1%, 99.2%, 99.4% and 98.7% for multidrug-resistant TB (MDR-TB). The median interval between the start of anti-tuberculosis chemotherapy and the reporting of results was 88.9 days for conventional DST and 19.8 days for MTBDR using clinical specimens. The specificity of the MTBDR assay in detecting MDR-TB was very high, although the sensitivity in detecting INH resistance and MDR-TB was not optimal (<95%).”

According to the news reporters, the research concluded: “Although the turnaround time in detecting drug resistance was dramatically reduced with MTBDR compared to conventional DST, more effort is needed to shorten the turnaround time.”


Our news journalists report that additional information may be obtained by contacting J. Lyu, University of Ulsan, Div Pulm & Crit Care Med, Coll Med, Asan Med Center, Seoul 138736, South Korea. (2013 Feb 19)

University of Zurich: Changes in body weight and tuberculosis treatment outcome in Viet Nam

By a News Reporter-Staff News Editor at Life Science Weekly – New research on Tuberculosis and Lung Disease is the subject of a report. According to news originating from Zurich, Switzerland, by NewsRx correspondents, research stated, “National Tuberculosis Programme, Viet Nam, 2008. To assess the relationship between changes in body weight and tuberculosis (TB) treatment outcome.”

Our news journalists obtained a quote from the research from the University of Zurich, “All treatment cards of patients from a sample of 30 randomly selected treatment units in the country were analysed. Of 2609 patients, 2506 (96.1%) had a successful treatment outcome. The median body weight of all patients at diagnosis was 46.0 kg (25th and 75th percentiles 41-51). New sputum smear-positive TB patients with a
successful treatment outcome gained an average of 2.6 kg during treatment. Patients with weight loss during the first 2 months of treatment were more likely to have an unsuccessful outcome than patients without (OR 4.9, 95%CI 3.0-7.9). Patients weighing <40 kg at treatment start who gained more than 5% of their body weight after 2 months of treatment had a significantly smaller risk of an unsuccessful treatment outcome than patients who did not (OR 0.2, 95%CI 0.05-0.96).

According to the news editors, the research concluded: “Patients failing to gain weight or losing weight, particularly during the first 2 months of treatment, require particular attention, as they appear to be at an increased risk of unsuccessful treatment outcome.”


The news correspondents report that additional information may be obtained from N.B. Hoa, University of Zurich, Inst Social & Prevent Med, CH-8006 Zurich, Switzerland. (2013 Feb 19)

**University of Cape Town: A Time-to-Event Pharmacodynamic Model Describing Treatment Response in Patients with Pulmonary Tuberculosis Using Days to Positivity in Automated Liquid Mycobacterial Culture**

By a News Reporter-Staff News Editor at Biotech Week – Current study results on Mycobacterium Infections have been published. According to news reporting originating from Cape Town, South Africa, by NewsRx correspondents, research stated, “Days to positivity in automated liquid mycobacterial culture have been shown to correlate with mycobacterial load and have been proposed as a useful biomarker for treatment responses in tuberculosis. However, there is currently no quantitative method or model to analyze the change in days to positivity with time on treatment.”

Our news editors obtained a quote from the research from the University of Cape Town, “The objectives of this study were to describe the decline in numbers of mycobacteria in sputum collected once weekly for 8 weeks from patients on treatment for tuberculosis using days to positivity in liquid culture. One hundred forty-four patients with smear-positive pulmonary tuberculosis were recruited from a tuberculosis clinic in Cape Town, South Africa. A nonlinear mixed-effects repeated-time-to-event modeling approach was used to analyze the time-to-positivity data. A biexponential model described the decline in
the estimated number of bacteria in patients’ sputum samples, while a logistic model with a lag time described the growth of the bacteria in liquid culture. At baseline, the estimated number of rapidly killed bacteria is typically 41 times higher than that of those that are killed slowly. The time to kill half of the rapidly killed bacteria was about 1.8 days, while it was 39 days for slowly killed bacteria. Patients with lung cavitation had higher bacterial loads than patients without lung cavitation. The model successfully described the increase in days to positivity as treatment progressed, differentiating between bacteria that are killed rapidly and those that are killed slowly.”

According to the news editors, the research concluded: “Our model can be used to analyze similar data from studies testing new drug regimens.”


The news editors report that additional information may be obtained by contacting E. Chigutsa, Division of Clinical Pharmacology, Dept. of Medicine, University of Cape Town, Cape Town, South Africa. (2013 Feb 13)

Costs of inpatient treatment for multi-drug-resistant tuberculosis in South Africa

By a News Reporter-Staff News Editor at Tuberculosis Week – Fresh data on Global Health Research are presented in a new report. According to news reporting from Klerksdorp, South Africa, by NewsRx journalists, research stated, “In South Africa, patients with multi-drug-resistant tuberculosis (MDR-TB) are hospitalised from MDR-TB treatment initiation until culture conversion. Although MDR-TB accounts for &lt;3% of incident TB in South Africa, 55% of the public sector TB budget is spent on MDR-TB.”

The news correspondents obtained a quote from the research, “To inform new strategies for MDR-TB management, we estimated the per-patient cost (USD 2011) of inpatient MDR-TB treatment. All resources used by patients admitted to the MDR-TB hospital with confirmed MDR-TB from March 2009 to February 2010 were abstracted from patient records for up to 12 months after initial admission or until the earliest of final discharge, abscondment or death. Costs of hospital stay/day were estimated from hospital expenditure records and costs for drugs, laboratory tests, radiography and surgery from public sector sources. 133 patients met study inclusion criteria of whom 121 had
complete cost records. By 12 months, 86% were discharged with culture conversion, 8% died in hospital, 2% were still admitted, and 3% had absconded. The mean hospital stay was 105 days. The mean total cost per patient was $17,164, of which 95% were hospitalisation costs (buildings, staff, etc.) and = 2% each for MDR-TB drugs ($380); TB laboratory tests, including drug susceptibility testing ($236); and other costs. The inpatient cost per patient treated for MDR-TB is more than 40 times the cost of treating drug-susceptible TB in South Africa.”

According to the news reporters, the research concluded: “There is potential for substantial cost savings from improved management of drug-susceptible TB and shifting to a model of decentralised, outpatient MDR-treatment.”


Our news journalists report that additional information may be obtained by contacting K. Schnippel, Klerksdorp Tshepong Hosp Complex, NW Dept. of Hlth, Klerksdorp, South Africa. (2013 Feb 11)

**Xiangya Hospital, Changsha: Application of an antibiotic crescent-shaped polymethylmethacrylate strut in thoracic vertebral tuberculosis**

By a News Reporter-Staff News Editor at Pain & Central Nervous System Week – New research on Neurosurgery is the subject of a report. According to news reporting originating from Changsha, People’s Republic of China, by NewsRx correspondents, research stated, “Spinal tuberculosis accounts for up to 50% of all cases with musculoskeletal tuberculosis. In patients needing surgical treatment, the use of anterior instrumentation offers the theoretical advantage of more complete debridement and decompression, safer mobilization and reliable deformity correction.”

Our news editors obtained a quote from the research from Xiangya Hospital, “However, the placement of instrumentation in an infected area remains a matter of debate. We present a patient with thoracic vertebral tuberculosis using an antibiotic crescent-shaped PMMA strut for spinal reconstruction and fusion. The patient recovered satisfactory and no complication was observed in the follow-up. The antibiotic crescent-shaped PMMA strut can be used as a carrier for antibiotic drug and an ideal alternative for anterior spinal reconstruction.”
According to the news editors, the research concluded: “However, long-term outcome in this case requires further evaluation.”


The news editors report that additional information may be obtained by contacting W. Jun, Xiangya Hospital Central South University, Dept. of Orthopedics, Changsha, People’s Taiwan. (2013 Feb 11)

University of Amsterdam: Adverse Events in Healthy Individuals and MDR-TB Contacts Treated with Anti-Tuberculosis Drugs Potentially Effective for Preventing Development of MDR-TB: A Systematic Review

By a News Reporter-Staff News Editor at Biotech Week – New research on Mycobacterium Infections is the subject of a report. According to news originating from Amsterdam, Netherlands, by NewsRx correspondents, research stated, “A recent systematic review concluded that there is insufficient evidence on the effectiveness to support or reject preventive therapy for treatment of contacts of patients with multidrug resistant tuberculosis (MDR-TB). Whether preventive therapy is favorable depends both on the effectiveness and the adverse events of the drugs used.”

Our news journalists obtained a quote from the research from the University of Amsterdam, “We performed a systematic review to assess adverse events in healthy individuals and MDR-TB contacts treated with anti-tuberculosis drugs potentially effective for preventing development of MDR-TB. We searched MEDLINE, EMBASE, and other databases (August 2011). Record selection, data extraction, and study quality assessment were done in duplicate. The quality of evidence was assessed using the GRADE approach. Of 6,901 identified references, 20 studies were eligible. Among the 16 studies in healthy volunteers (a total of 87 persons on either levofloxacin, moxifloxacin, ofloxacin, or rifabutin, mostly for 1 week), serious adverse events and treatment discontinuation due to adverse events were rare (&lt;1 and &lt;5%, respectively), but mild adverse events frequently occurred. Due to small sample sizes of the levofloxacin and ofloxacin studies an increased frequency of mild adverse events compared to placebo could not be demonstrated or excluded. For moxifloxacin the comparative results were inconsistent. In four studies describing preventive therapy of MDR-TB contacts, therapy was stopped for 58-100% of the included persons because of the occurrence of adverse events ranging from mild adverse
events such as nausea and dizziness to serious events requiring treatment. The quality of the evidence was very low. Although the number of publications and quality of evidence are low, the available evidence suggests that shortly after starting treatment the occurrence of serious adverse events is rare.”

According to the news editors, the research concluded: “Mild adverse events occur more frequently and may be of importance because these may provoke treatment interruption.”

For more information on this research see: Adverse Events in Healthy Individuals and MDR-TB Contacts Treated with Anti-Tuberculosis Drugs Potentially Effective for Preventing Development of MDR-TB: A Systematic Review. Plos One, 2013;8(1):e53599. (Public Library of Science - www.plos.org; Plos One - www.plosone.org)

The news correspondents report that additional information may be obtained from M.W. Langendam, Dutch Cochrane Centre, Academic Medical Center, University of Amsterdam, Amsterdam, Netherlands. (2013 Feb 06)

Department of Obstetrics and Gynaecology, Kuala Lumpur: Genitourinary tuberculosis: an atypical clinical presentation

By a News Reporter-Staff News Editor at Life Science Weekly – New research on Tuberculosis is the subject of a report. According to news reporting from Kuala Lumpur, Malaysia, by NewsRx journalists, research stated, “Genitourinary tuberculosis is one of the common forms of extrapulmonary tuberculosis. We report a case of atypical genitourinary tuberculosis: massive uterovaginal prolapse with cervical lesion mimicking cervical carcinoma.”

The news correspondents obtained a quote from the research from the Department of Obstetrics and Gynaecology, “This particular case highlights the problem of healthcare in most of the developing countries. Lack of patient education, awareness, and access to a healthcare system resulted in a complicated situation. In an endemic area or in an immunocompromised individual, a higher index of suspicion would allow early recognition and treatment institution to minimise its late consequences as well as spreading of the disease.”

According to the news reporters, the research concluded: “Though anti-TB is the mainstay of treatment, surgical intervention might be needed in selected cases.”

For more information on this research see: Genitourinary tuberculosis: an atypical clinical presentation. Case Reports In Obstetrics and Gynecology, 2012;2012():727146. (Hindawi Publishing - www.hindawi.com; Case Reports In Obstetrics and Gynecology - http://www.hindawi.com/crim/obgyn/)
Our news journalists report that additional information may be obtained by contacting P.S. Lim, Dept. of Obstetrics & Gynaecology, Pusat Perubatan UKM, Jalan Yaakob Latif, 56000 Cheras, Kuala Lumpur, Malaysia. (2013 Feb 05)

**University of Camerino: Antibacterial activities of the extracts, fractions and compounds from Dioscorea bulbifera**

By a News Reporter-Staff News Editor at Tuberculosis Week – Investigators discuss new findings in Mycobacterium Infections. According to news reporting from Camerino, Italy, by NewsRx journalists, research stated, “Dioscorea bulbifera is an African medicinal plant used to treat microbial infections. In the present study, the methanol extract, fractions (DBB1 and DBB2) and six compounds isolated from the bulbils of D. bulbifera, namely bafoudiosbulbins A (1), B (2), C (3), F (4), G (5) and 2,7-dihydroxy-4-methoxyphenanthrene (6), were tested for their antimicrobial activities against Mycobacteria and Gram-negative bacteria involving multidrug resistant (MDR) phenotypes expressing active efflux pumps.”

The news correspondents obtained a quote from the research from the University of Camerino, “The microplate alamar blue assay (MABA) and the broth microdilution methods were used to determine the minimal inhibitory concentration (MIC) and minimal bactericidal concentration (MBC) of the above samples. The results of the MIC determinations indicated that when tested alone, the crude extract, fractions DBB1 and DBB2 as well as compounds 2 to 5 were able to prevent the growth of all the fifteen studied microorganisms, within the concentration range of 8 to 256 µg/mL. The lowest MIC value for the methanol extract and fractions (16 µg/mL) was obtained with DBB1 and DBB2 on E. coli AG100A and DBB2 on Mycobacterium tuberculosis MTCS2. The lowest value for individual compounds (8 µg/mL) was recorded with compound 3 on M. smegmatis and M. tuberculosis ATCC and MTCS2 strains respectively. The activity of the samples on many MDR bacteria such as Enterobacter aerogenes EA289, CM64, Klebsiella pneumoniae KP63 and Pseudomonas aeruginosa PA124 was better than that of chloramphenicol. When tested in the presence of the efflux pump inhibitor against MDR Gram-negative bacteria, the activity of most of the samples increased.”

According to the news reporters, the research concluded: “MBC values not greater than 512 µg/mL were recorded on all studied microorganisms with fraction DBB2 and compounds 2 to 5. The overall results of the present investigation provided evidence that the crude extract D. bulbifera as well as some of the compounds and mostly compounds 3 could be considered as potential antimicrobial drugs to fight against MDR bacteria.”
CHAPTER 7 THERAPIES AND TREATMENTS


Our news journalists report that additional information may be obtained by contacting V. Kuete, University of Camerino, Sch Sci & Technol, Div Chem, I-62032 Camerino, Italy. (2013 Feb 04)

**Chongqing Medical University: Phage in the diagnosis and treatment of tuberculosis**

By a News Reporter-Staff News Editor at Life Science Weekly – Researchers detail new data in Biology. According to news reporting from Chongqing, People’s Republic of China, by NewsRx journalists, research stated, “The serious global TB epidemic coupled with limited diagnostic and therapeutic technologies necessitate the study of the role phage in TB treatment. Mycobacterium phage have been used for TB diagnosis, but the accuracy of such methods needs to be improved.”

The news correspondents obtained a quote from the research from Chongqing Medical University, “Phage have various advantages in treating many kinds of bacterial infection, and coupled with the abuse and misuse of antibiotics, and the increasing prevalence of drug-resistant bacteria, they have been studied as a novel therapy to support antibiotics. The study of phage in TB therapy has developed from the selection of appropriate phage to the simultaneous use of multiple phage and even the use of purified lyase proteins.”

According to the news reporters, the research concluded: “Though phage have great potential in TB therapy, the technology is still in the in vitro and animal experiment stages, and needs further study.”


Our news journalists report that additional information may be obtained by contacting S.L. Guo, Chongqing Med Univ, Affiliated Hosp 1, Dept. of Resp & Crit Care Med, Chongqing 400016, People’s Republic of China. (2013 Jan 29)
Research Hospital, Istanbul: The outcome of tuberculosis cases with persistent smear positivity at the end of extended initial phase

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – Research findings on Respiratory Medicine are discussed in a new report. According to news reporting originating from Istanbul, Turkey, by NewsRx correspondents, research stated, “To present the treatment outcome in tuberculosis patients with sputum smear positivity in the third month of category 1 treatment regimes. A total of 1024 patients with tuberculosis treated in Ministry of Health Sureyyapasa Chest Diseases and Chest Surgery Training and Research Hospital from January 2004 to December 2005 were included in this retrospective cohort study.”

Our news editors obtained a quote from the research from Research Hospital, “Categorization and appropriate treatment of tuberculosis was performed according the World Health Organization guidelines. Of overall 1024 patients, 655 (64%) were determined to receive category 1 treatment while sputum smear positivity was identified in 11 of them [2%; mean (SD) age: 46 (17.9) years] in the third month. Continuation phase treatment was initiated in these 11 patients. Sputum conversion was evident in six of 10 cases in the 4th month, in three cases in the 5th month and in one case in the 6th month. None had culture positivity after the 3rd month. Of 11 cases, 10 completed therapy with major drugs in six months and treatment outcome was cure. No relapse was identified after five years later.”

According to the news editors, the research concluded: “Based on our data we recommend that the continuing phase should be started in cases with positive sputum smear at the end of the extended initial phase.”

For more information on this research see: The outcome of tuberculosis cases with persistent smear positivity at the end of extended initial phase. *Tuberkuloz Ve Toraks*, 2012;60(4):344-9.

The news editors report that additional information may be obtained by contacting A. Babalik, Clinic of Chest Diseases, Sureyyapasa Chest Diseases and Chest Surgery Training and Research Hospital, Istanbul, Turkey. (2013 Jan 28)
Ben-Gurion University of the Negev, Beer Sheva: Adult tuberculosis in Israel and migration: trends and challenges between 1999 and 2010

By a News Reporter-Staff News Editor at Life Science Weekly – Researchers detail new data in Tuberculosis and Lung Disease. According to news originating from Beer Sheva, Israel, by NewsRx correspondents, research stated, “Israel absorbs many migrants from countries with a high prevalence of tuberculosis (TB). To describe the epidemiology of TB among adults in Israel between 1999 and 2010 and identify populations with a high TB burden.”

Our news journalists obtained a quote from the research from the Ben-Gurion University of the Negev, “Data were retrieved from the National Tuberculosis Registry and the Israeli Bureau of Statistics. A total of 4652 adult TB patients were notified during the study period, with rates decreasing annually from 7.5 per 100 000 population in 1999 to 4.3 in 2010. Most (n = 3745, 80.5%) had pulmonary TB, the average female:male ratio was 1:1.4, and 227 (5.1%) were infected with the human immunodeficiency virus. Of all TB patients, 4079 (87.6%) were born outside Israel; of these, 3338 were citizens and 741 non-citizen migrant workers (MWs). The average annual rates of TB among Israeli-born citizens, foreign-born citizens and MWs were respectively 0.86, 11.9 and 27/100000. The ratio of MWs to foreign-born citizens fell from 1:11.7 in 1999 to 1:1.5 in 2010. TB was diagnosed 13.9 +/- 7.5 years following entry to Israel, mostly during the first year. Of 3551 isolates, 222 (4.5%) were multidrug-resistant; most (95.6%) were from foreign-born patients. The average treatment success rate for smear-positive pulmonary TB was 84.3%. TB rates have decreased, while the proportion of foreign-born subjects, particularly MWs, has increased.”

According to the news editors, the research concluded: “Adherence to preventive treatment can prevent TB in these cases.”


The news correspondents report that additional information may be obtained from Z. Mor, Ben Gurion University of the Negev, Fac Med, IL-84105 Beer Sheva, Israel. (2013 Jan 22)
APHP, Bobigny: Ileal leiomyosarcoma and lymph node granuloma. Relevance of a rare association

By a News Reporter-Staff News Editor at Tuberculosis Week – Research findings on Mycobacterium Infections are discussed in a new report. According to news originating from Bobigny, France, by NewsRx correspondents, research stated, “Leiomyosarcoma is rare in ileal location. We report the case of a 61 years old female patient presenting with ileal leiomyosarcoma occurring at 14 years after a uterine carcinoma treated by radiotherapy.”

Our news journalists obtained a quote from the research from APHP, “The ileal tumor was treated by surgical resection. This tumor was peculiar by the macroscopic polypoid appearance and by expression of PDGFRA protein together with muscle differentiation proteins: smooth muscle actin, desmin and h-caldesmon. Lymph node necrotizing granuloma diagnosis on the surgical resection specimen lead to the diagnosis of tuberculosis and the patient was treated accordingly. At 3 years after the diagnosis, the patient was well, without recurrence or metastases.”

According to the news editors, the research concluded: “We report the case of a patient diagnosed with ileal leiomyosarcoma occurring 14 years after adjuvant radiotherapy for uterine carcinoma. Analysis of the intestinal resection specimen lead to the diagnosis of associated tuberculosis. Moreover, the leiomyosarcoma was peculiar by PDGFRA expression, feature which might be of clinical relevance since the treatment options in radioinduced tumors associated with other conditions are limited.”


The news correspondents report that additional information may be obtained from A. Badescu, Service d’Anatomie Pathologique, Hopitaux Universitaires Paris Seine Saint-Denis, AP-HP, Bobigny, France. (2013 Jan 21)
Case Western Reserve University, Cleveland: Prolonged positivity of sputum smears with negative cultures during treatment for pulmonary tuberculosis

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – Research findings on Tuberculosis and Lung Disease are discussed in a new report. According to news originating from Cleveland, Ohio, by NewsRx correspondents, research stated, “Acid-fast bacilli (AFB) microscopy of sputum smears is the most widely used tool for both diagnosing pulmonary tuberculosis (PTB) and monitoring treatment response. It is not uncommon for patients who show clinical improvement to have prolonged positivity of sputum smears (i.e., &gt;= 60 days after initiation of treatment) with corresponding negative cultures.”

Our news journalists obtained a quote from the research from Case Western Reserve University, “To assess treatment outcomes and characteristics associated with prolonged smear-positive, culture-negative status. A retrospective review was performed of all patients seen by the Cuyahoga County TB Program in Cleveland from 2000 to 2009. There were 159 consecutive smear-positive, drug-susceptible PTB cases with sufficient analyzable bacteriologic, clinical and radiographic data for study. A smear-positive, culture-negative pattern was seen in 51 patients (32.1%) &gt;= 2 months after initiation of treatment. Age &gt;= 46 years and extent of baseline chest X-ray abnormality were both significantly associated with a prolonged smear-positive, culture-negative pattern. No patients were culture-positive for Mycobacterium tuberculosis after &gt;= 2 months. There was no increased risk of death in the prolonged smear-positive, culture-negative group, and no confirmed relapses.”

According to the news editors, the research concluded: “In our population of patients, in the absence of clinical or radiographic evidence of deterioration, late smear positivity usually has no clinical significance and requires no specific action.”

For more information on this research see: Prolonged positivity of sputum smears with negative cultures during treatment for pulmonary tuberculosis. International Journal of Tuberculosis and Lung Disease, 2012;16(12):1663-1667. International Journal of Tuberculosis and Lung Disease can be contacted at: Int Union Against Tuberculosis Lung Disease (I U A T L D), 68 Boulevard Saint-Michel, 75006 Paris, France.

The news correspondents report that additional information may be obtained from F. van der Kuyp, Case Western Reserve University, Metrohlth Med Center, Dept. of Med, Cuyahoga Cty TB ProgramDiv Infect Dis, Cleveland, OH 44109, United States. (2013 Jan 21)
Joint Clinical Research Center, Kampala: Socio-demographic determinants and prevalence of Tuberculosis knowledge in three slum populations of Uganda

By a News Reporter-Staff News Editor at AIDS Weekly – Data detailed on Public Health have been presented. According to news reporting originating in Kampala, Uganda, by NewsRx journalists, research stated, “Knowledge of tuberculosis has been shown to influence health seeking behaviour; and urban slum dwellers are at a higher risk of acquiring tuberculosis than the general population. The study aim was to assess knowledge of tuberculosis and identify the associated socio-demographic determinants, in order to inform tailored interventions for advocacy, communication and social mobilisation in three urban-slum communities of Uganda.”

The news reporters obtained a quote from the research from Joint Clinical Research Center, “A cross-sectional survey of 1361 adults between April and October 2011. Data was analyzed by descriptive statistics. Adjusted odds ratios (aOR) and 95% confidence intervals (95% CI) of potential determinants of tuberculosis (TB) knowledge were estimated by multivariable ordinal logistic regression using Stata 11.2 software. We found low knowledge of TB cause (26.7%); symptoms (46.8%), transmission (54.3%), prevention (34%) and free treatment (35%). Knowledge about TB treatment (69.4) and cure (85.1) was relatively high. Independent determinants of poor knowledge of TB in the multivariable analysis included (aOR, 95% CI) lack of formal education (0.56; 0.38 - 0.83, P = 0.004), unemployment (0.67; 0.49 - 0.90, P = 0.010) and never testing for HIV (0.69; 0.51 - 0.92, P<0.012). Whilst, older age (1.73; 1.30 - 2.29, P<0.001) and residing in Lira (2.02; 1.50 - 2.72, P<0.001) were independent determinants of higher knowledge of TB. This study revealed deficiencies in the public health knowledge about TB symptoms, diagnosis and treatment among urban-slum dwellers in Uganda.”

According to the news reporters, the research concluded: “Tuberculosis control programmes in similar settings should consider innovative strategies for TB education, advocacy, communication and social mobilisation to reach the youth, unemployed and less-educated; as well as those who have never tested for HIV.”

University of Manchester: Drug therapy for children with tuberculosis

By a News Reporter-Staff News Editor at Pediatrics Week – New research on Mycobacterium Infections is the subject of a report. According to news reporting originating in Manchester, United Kingdom, by VerticalNews editors, the research stated, “The scientific basis of drug treatment for both active tuberculosis (TB) disease and TB infection, has been established, with treatment in children being largely extrapolated from adult active disease trials. It is essential that active TB disease is excluded before asymptomatic TB infection is diagnosed and treated.”

The news reporters obtained a quote from the research from the University of Manchester, “Nearly half of all children with active TB disease are found as asymptomatic tuberculin, or interferon gamma release assay (IGRA), positive contacts on screening by local TB services, usually of sputum TB microscopy positive adult relatives or other index cases, but with evidence of lung infiltrate or mediastinal lymphadenopathy on the child’s chest x-ray. New drug regimens for both active disease and latent infection are in development, and also some novel drugs. However, none of these have yet been tested in children, and so again data will need to be extrapolated from adult results.”

According to the news reporters, the research concluded: “In addition, there are issues regarding pharmacokinetics and dosing for current drugs, particularly isoniazid.”


Our news correspondents report that additional information may be obtained by contacting L.P. Ormerod, University of Manchester, Manchester, Lancs, United Kingdom. (2013 Jan 19)
University of Stellenbosch, Cape Town: Caring for Children with Drug-Resistant Tuberculosis Practice-based Recommendations

By a News Reporter-Staff News Editor at Pediatrics Week – New research on Mycobacterium Infections is the subject of a report. According to news reporting out of Cape Town, South Africa, by VerticalNews editors, research stated, “The management of children with drug-resistant tuberculosis (DR-TB) is challenging, and it is likely that in many places, the roll-out of molecular diagnostic testing will lead to more children being diagnosed. There is a limited evidence base to guide optimal treatment and follow-up in the pediatric population; in existing DR-TB guidelines, the care of children is often relegated to small ‘special populations’ sections.”

Our news journalists obtained a quote from the research from the University of Stellenbosch, “This article seeks to address this gap by providing clinicians with practical advice and guidance. This is achieved through review of the available literature on pediatric DR-TB, including research studies and international guidelines, combined with consensus opinion from a team of experts who have extensive experience in the care of children with DR-TB in a wide variety of contexts and with varying resources.”

According to the news editors, the research concluded: “The review covers treatment initiation, regimen design and treatment duration, management of comorbid conditions, treatment monitoring, adverse events, adherence promotion, and infection control, all within a multidisciplinary environment.”


Our news journalists report that additional information may be obtained by contacting J.A. Seddon, University of Stellenbosch, Fac Med & Hlth Sci, Dept. of Paediat & Child Hlth, Desmond Tutu TB Center, Cape Town, South Africa. (2013 Jan 19)
University of Sao Paulo: Relationship of NAT2, CYP2E1 and GSTM1/GSTT1 polymorphisms with mild elevation of liver enzymes in Brazilian individuals under anti-tuberculosis drug therapy

By a News Reporter-Staff News Editor at Tuberculosis Week – Current study results on Chemistry and Laboratory Medicine have been published. According to news reporting originating from Sao Paulo, Brazil, by NewsRx correspondents, research stated, “The relationship of NAT2, CYP2E1 and GSTM1/GSTT1 polymorphisms with mild elevation of liver biomarkers was investigated in individuals under anti-tuberculosis drug therapy. Tuberculosis outpatients (18-70y) with (n=59) and without (n=40) mild increase of liver enzymes (MILE) at two-month treatment were selected.”

Our news editors obtained a quote from the research from the University of Sao Paulo, “Blood samples were obtained for DNA extraction and evaluation of serum markers of liver function. NAT2, CYP2E1 and GSTM1/GSTT1 polymorphisms were detected by DNA sequencing, PCR-RFLP, and PCR multiplex. Frequency of NAT2*5/*5 genotype was higher in MILE than in non-MILE group (p=0.04). Patients carrying NAT2*5/*5 genotype had increased susceptibility to MILE (OR: 9.00, 95CI: 1.46-55.48, p=0.018). CYP2E1*5B allele (*1A/*5B plus *5B/*5B genotypes) carriers had a trend for reduced risk for MILE (OR: 0.34, 95CI: 0.11-1.03, p=0.056) that was confirmed by lower levels of liver markers than CYP2E1*1A/*1A carriers after treatment (p <0.05). Moreover, increased post-treatment ALT, AST and total bilirubin were associated with GSTM1*1/GSTT1*1 genotypes (p <0.05). Patients taking CYP2E1 inhibitors had increased susceptibility to MILE (OR: 7.39, 95CI: 1.93-28.29, p=0.003), which was independent of the studied polymorphisms.”

According to the news editors, the research concluded: “These results are suggestive that NAT2, CYP2E1 and GSTM1/GSTT1 polymorphisms and concomitant use of CYP2E1 inhibitors contribute to the susceptibility to mild alterations in liver enzymes in patients under anti-tuberculosis drug therapy.”


The news editors report that additional information may be obtained by contacting F.J. Forestiero, Dept. of Clinical and Toxicological Analysis, School of Pharmaceutical Sciences, University of Sao Paulo, Sao Paulo, SP, Brazil. (2013 Jan 14)
**Zhejiang Cancer Hospital, Hangzhou: Application Of Nanotechnology In The Control Of Lung Tuberculosis**

By a News Reporter-Staff News Editor at Tuberculosis Week – A new study on Drug Development is now available. According to news reporting out of Hangzhou, People’s Republic of China, by NewsRx editors, research stated, “Tuberculosis is a serious disease which has to be treated effectively on time. Currently, many patients suffer from poor diagnosis and limited treatment due to the multidrug resistance of pathogens.”

Our news journalists obtained a quote from the research from Zhejiang Cancer Hospital, “In recent years, nanotechnology has been employed in an effort to control tuberculosis. Diverse applications of nanomaterials have been developed.”

According to the news editors, the research concluded: “This review summarizes the advances in nanotechnology in the control of tuberculosis.”


Our news journalists report that additional information may be obtained by contacting X. Cai, Zhejiang Canc Hosp, Dept. of Pharm, Hangzhou, Zhejiang, People’s Republic of China. (2013 Jan 14)

**Cukurova University, Adana: Detection of latent tuberculosis infection in rheumatologic diseases before anti-TNF alpha therapy: tuberculin skin test versus IFN-gamma assay**

By a News Reporter-Staff News Editor at Tuberculosis Week – Current study results on Rheumatology have been published. According to news reporting originating from Adana, Turkey, by NewsRx correspondents, research stated, “We aimed to evaluate tuberculin skin test (TST) and interferon-gamma (IFN-gamma) test results for latent tuberculosis infection (LTBI) in patients with rheumatologic diseases prior to anti-TNF alpha therapy. Ninety patients were evaluated in the study at the Departments of Chest Diseases and Rheumatology for anti-TNF alpha therapy for their rheumatologic diseases.”

Our news editors obtained a quote from the research from Cukurova University, “Tuberculin skin test was performed (Mantoux method) and peripheral blood samples were collected for IFN-gamma assay (Quantiferon TB-Gold In Tube) before the anti-TNF alpha therapy. Of 90 patients, TST positivity was detected in 56 (62.2%) patients, while IFN-gamma positivity was detected in 34 (37.8%) patients. Among 56 TST
positive patients, IFN-gamma positivity was detected in 24 (42.9%) patients, and among 34 TST negative patients, IFN-gamma positivity was detected in 10 (29.4%) patients. There was no significant agreement between TST and IFN-gamma assay results (Kappa = 0.12, P = 0.2). Forty-three (47.8%) patients were using immunosuppressive drugs owing to their rheumatologic diseases. In this group, TST and IFN-gamma positivity is significantly lower than in those who did not receive immunosuppressive treatment (P < 0.05).

According to the news editors, the research concluded: “We conclude that the IFN-gamma assay may not be preferred to TST as a diagnostic test in patients with rheumatologic diseases prior to anti-TNF alpha treatment.”


The news editors report that additional information may be obtained by contacting I. Hanta, Cukurova University, Fac Med, Dept. of Biostat, TR-01330 Adana, Turkey. (2013 Jan 07)

Health Protection Agency, Leeds: What really happens to tuberculosis patients classified as lost to follow-up in West Yorkshire?

By a News Reporter-Staff News Editor at Tuberculosis Week – Investigators discuss new findings in Mycobacterium Infections. According to news reporting originating in Leeds, United Kingdom, by NewsRx journalists, research stated, “Tuberculosis (TB) patients who do not complete treatment pose a potential public health risk. In West Yorkshire, local clinicians suspected that this risk was overestimated by the national Enhanced Tuberculosis Surveillance system.”

The news reporters obtained a quote from the research from Health Protection Agency, “We audited patients who failed to complete treatment and were categorised as lost-to-follow-up (LTFU) between 2004 and 2008, using a combination of hand searching existing records and obtaining additional information from clinicians. In the study period 2,031 TB cases with reported outcome were notified in West Yorkshire, 23% (n=474) did not complete treatment, and 199 (42%) of those were categorised as LTFU 12 months after notification. Of these 199, 49% (n=98) remained LTFU after the audit, 51% (n=101) were re-classified to the following categories: 24% (n=47) transferred abroad, 16% (n=31)
recommenced and completed treatment, 6% (n=13) transferred to another clinic in the United Kingdom (UK), and 5% (n=10) died. These patients therefore no-longer posed a public health risk. Further training for clinicians to improve accuracy of outcome reporting has been initiated.”

According to the news reporters, the research concluded: “Nationally, the collection of treatment outcome data needs to be strengthened and extending the follow-up for treatment outcome monitoring should be considered.”

For more information on this research see: What really happens to tuberculosis patients classified as lost to follow-up in West Yorkshire? *Euro Surveillance*, 2012;17(38):.

Our news correspondents report that additional information may be obtained by contacting M. Day, Health Protection Agency, Yorkshire and the Humber, Leeds, UK. (2013 Jan 07)

**University Hospital, Barcelona: Clinical Features and Outcomes of Tuberculosis in Solid Organ Transplant Recipients**

By a News Reporter-Staff News Editor at Tuberculosis Week – Investigators publish new report on Transplantation. According to news reporting originating in Barcelona, Spain, by NewsRx journalists, research stated, “Tuberculosis (TB) remains a significant opportunistic infection in solid organ transplant (SOT) recipients. Moreover, its optimal treatment in SOT recipients is challenging due to the toxicity and potential drug-drug interactions of antituberculous drugs.”

The news reporters obtained a quote from the research from University Hospital, “We sought to assess the frequency, clinical characteristics, treatments, and outcomes of TB among SOT recipients. We reviewed retrospectively the medical charts of all TB cases occurring among SOT recipients from January 2000 to December 2011, retrieving data regarding baseline and clinical features, as well as treatment and outcomes. Eighteen of 2005 SOT recipients developed TB (0.9%). The frequency according to the type of allograft was 0.9% (10 of 1120) for kidney, 1% (7 of 701) for liver, and 0.5% (1 of 184) for heart recipients. Six patients (33%) had prior exposure to TB: a positive tuberculin test (n = 3), a positive quantiferon-TB (n = 1) for a prior history of TB (n = 3). None of them received antituberculous prophylaxis. The mean time after transplantation to TB diagnosis was 64 months (range 2-169). Five patients (28%) developed TB within the first year post-transplantation. The mean duration of symptoms before diagnosis was 30 days (range 1-180). Nine patients (50%) displayed pulmonary TB; 7 (39%) had disseminated infections, and 2 (11%) had lymph node involvement. None of the Mycobacterium tuberculosis isolates were resistant
to first-line antituberculous drugs. All patients were given isoniazide. Most of them received a 3-drug regimen. Rifampin was prescribed in 11 cases. Seven patients (5 liver and 2 kidney recipients) developed hepatotoxicity. One patient developed rejection without allograft loss. Mortality during antituberculous treatment was 17% (3/18). In this study, 0.9% of SOT recipients developed TB, which frequently presented with extrapulmonary involvement, causing considerable mortality.”

According to the news reporters, the research concluded: “Hepatotoxicity mainly among liver transplant recipients was a significant therapeutic drawback.”


Our news correspondents report that additional information may be obtained by contacting M. Bodro, Hosp Univ Bellvitge, Dept. of Cardiol, Barcelona, Spain. (2013 Jan 07)

**Johns Hopkins University, Baltimore: Unrecognised tuberculosis at antiretroviral therapy initiation is associated with lower CD4+ T cell recovery**

By a News Reporter-Staff News Editor at Biotech Week – New research on Global Health Research is the subject of a report. According to news reporting from Baltimore, Maryland, by NewsRx journalists, research stated, “To investigate whether an unrecognised diagnosis of tuberculosis (TB) at the start of antiretroviral therapy (ART) influences subsequent CD4+ T cell (CD4) count recovery in an urban HIV clinic in Uganda. In a retrospective cohort study, a multivariable polynomial mixed effects model was used to estimate CD4 recovery in the first 96 weeks of ART in two groups of patients: prevalent TB (started ART while on TB treatment), unrecognised TB (developed TB within 6 months after start ART).”

The news correspondents obtained a quote from the research from Johns Hopkins University, “Included were 511 patients with a median baseline CD4 count of 57 cells/mm3 (interquartile range: 22130), of whom 368 (72%) had prevalent TB and 143 (28%) had unrecognised TB. Compared with prevalent TB, unrecognised TB was associated with lower CD4 count recovery at 96 weeks: -22.3 cells/mm3 (95% confidence interval -43.2 to -1.5, P = 0.036). These estimates were adjusted for gender, age, baseline CD4 count and the use of zidovudine-based regimen.
Unrecognised TB at the time of ART initiation resulted in impaired CD4 recovery compared with TB treated before ART initiation.”

According to the news reporters, the research concluded: “More vigilant screening with more sensitive and rapid TB diagnostics prior to ART initiation is needed to decrease the risk of ART-associated TB and sub-optimal immune reconstitution.”

For more information on this research see: Unrecognised tuberculosis at antiretroviral therapy initiation is associated with lower CD4+ T cell recovery. Tropical Medicine & International Health, 2012;17(12):1527-1533. Tropical Medicine & International Health can be contacted at: Wiley-Blackwell, 111 River St, Hoboken 07030-5774, NJ, USA. (Wiley-Blackwell - http://www.wiley.com/; Tropical Medicine & International Health - http://onlinelibrary.wiley.com/journal/10.1111/(ISSN)1365-3156)

Our news journalists report that additional information may be obtained by contacting S.M. Hermans, Johns Hopkins University, Sch Med, Dept. of Med, Div Infect Dis, Baltimore, MD 21205, United States. (2013 Jan 02)

Radboud University, Nijmegen: Pharmacokinetics of anti-tuberculosis drugs in Venezuelan children younger than 16 years of age: supportive evidence for the implementation of revised WHO dosing recommendations

By a News Reporter-Staff News Editor at Biotech Week – Research findings on Mycobacterium Infections are discussed in a new report. According to news reporting originating from Nijmegen, Netherlands, by NewsRx correspondents, research stated, “The World Health Organization (WHO) recently issued revised first-line antituberculosis (anti-TB) drug dose recommendations for children, with dose increases proposed for each drug. No pharmacokinetic data are available from South American children.”

Our news editors obtained a quote from the research from Radboud University, “We examined the need for implementation of these revised guidelines in Venezuela. Plasma isoniazid, rifampicin, pyrazinamide and ethambutol concentrations were assessed prior to and at 2, 4 and 8 h after intake of TB drugs by 30 TB patients aged 115 years. The effects of dose in mg/kg, age, sex, body weight, malnutrition and acetylator phenotype on maximum plasma drug concentrations (Cmax) and exposure (AUC0-24) were determined. Results 25 patients (83%) had an isoniazid Cmax below 3 mg/l and 23 patients (77%) had a rifampicin Cmax below 8 mg/l. One patient (3%) had a pyrazinamide Cmax below 20 mg/l. The low number of patients on ethambutol (n = 5) precluded
firm conclusions. Cmax and AUC0-24 of all four drugs were significantly and positively correlated with age and body weight. Patients aged 14 years had significantly lower Cmax and AUC0-24 values for isoniazid and rifampicin and a trend to lower values for pyrazinamide compared to those aged 515 years. The geometric mean AUC0-24 for isoniazid was much lower in fast acetylators than in slow acetylators (5.2 vs. 12.0, P< 0.01). We provide supportive evidence for the implementation of the revised WHO pediatric TB drug dose recommendations in Venezuela.”

According to the news editors, the research concluded: “Follow-up studies are needed to describe the corresponding plasma levels that are achieved by the recommended increased doses of TB drugs.”

For more information on this research see: Pharmacokinetics of anti-tuberculosis drugs in Venezuelan children younger than 16 years of age: supportive evidence for the implementation of revised WHO dosing recommendations. Tropical Medicine & International Health, 2012;17(12):1449-1456. Tropical Medicine & International Health can be contacted at: Wiley-Blackwell, 111 River St, Hoboken 07030-5774, NJ, USA. (Wiley-Blackwell - http://www.wiley.com/; Tropical Medicine & International Health - http://onlinelibrary.wiley.com/journal/10.1111/(ISSN)1365-3156)

The news editors report that additional information may be obtained by contacting L.M. Verhagen, Radboud University, Dept. of Pharm, Nijmegen, Netherlands. (2013 Jan 02)

University of London: Prevention of drug resistance by combined drug treatment of tuberculosis

By a News Reporter-Staff News Editor at Biotech Week – Fresh data on Mycobacterium Infections are presented in a new report. According to news reporting originating from London, United Kingdom, by NewsRx editors, the research stated, “Treatment with a combination of anti-tuberculosis drugs is thought to work by the first drug killing mutants resistant to the second drug, while the second drug kills those resistant to the first drug. Combined treatment has been remarkably successful in preventing the emergence of resistance during the treatment of tuberculosis.”

Our news editors obtained a quote from the research from the University of London, “This success has led to the introduction of multi-drug treatment for leprosy, HIV infections and cancer. Its success in tuberculosis depends on a number of conditions such as the chromosomal nature of drug resistance in Mycobacterium tuberculosis and the absence of plasmids carrying resistance factors as well as the manner in which the bacterial population in tuberculosis does not come into
contact with other potentially resistant bacteria. For multi-drug treatment to be effective in preventing resistance, the drugs must be sufficiently active so that each can inhibit all the bacteria in lesions. There must also be effective post-antibiotic lags in growth restarting to prevent growth between doses.”

According to the news editors, the research concluded: “Special bacterial populations that are drug tolerant or survive drug action unusually successfully are also a potential source of resistance.”


The news editors report that additional information may be obtained by contacting D.A. Mitchison, St George’s University of London, London, SW17 0RE, UK. (*2013 Jan 02*)

University of Stellenbosch, Tygerberg: Sulfamethoxazole enhances the antimycobacterial activity of rifampicin

By a News Reporter-Staff News Editor at Biotech Week – New research on Mycobacterium Infections is the subject of a report. According to news reporting originating in Tygerberg, South Africa, by NewsRx journalists, research stated, “To investigate the effect of trimethoprim/sulfamethoxazole on the survival of Mycobacterium tuberculosis and trimethoprim and sulfamethoxazole individually and combined with the first-line tuberculosis drugs (isoniazid, rifampicin and ethambutol). M. tuberculosis strains were exposed to either trimethoprim/sulfamethoxazole combination or sulfamethoxazole and trimethoprim alone at various concentrations. The strains were also exposed to sulfamethoxazole in combination with existing antibiotics to assess the combined effect on the growth of M. tuberculosis in the BACTEC 460TB system.”

The news reporters obtained a quote from the research from the University of Stellenbosch, “The effect of the drugs was compared with vehicle-treated controls. Drug interactions were interpreted using quotient values obtained from the growth index of cultures treated with a single drug or the combination. Trimethoprim showed a negligible effect on the growth of M. tuberculosis while sulfamethoxazole inhibited 80 of the growth of M. tuberculosis at 4.75 mg/L. There was no synergistic activity between sulfamethoxazole and trimethoprim, although an additive effect was observed. A statistically significant synergistic effect was observed between sulfamethoxazole and rifampicin. Sulfamethoxazole also had an additive effect with ethambutol, but there was no interaction with isoniazid. Sulfamethoxazole is the main active compound against M. tuberculosis in the combination trimethoprim/sulfamethoxazole and has a synergistic effect with rifampicin.”
According to the news reporters, the research concluded: “These findings suggest that sulfamethoxazole has potential in the multidrug regimen against M. tuberculosis.”


Our news correspondents report that additional information may be obtained by contacting L. Macingwana, University of Stellenbosch, Fac Med & Hlth Sci, Dept. of Paediat & Child Hlth, ZA-7505 Tygerberg, South Africa. (2013 Jan 02)

**Medical College, Chennai: Expenditure Pattern for TB Treatment among Patients Registered in an Urban Government DOTS Program in Chennai City, South India**

By a News Reporter-Staff News Editor at Journal of India – Investigators discuss new findings in Mycobacterium Infections. According to news reporting from Chennai, India, by VerticalNews journalists, research stated, “Tuberculosis (TB) patients registered in the government clinics under the DOTS (Directly Observed Treatment, Short Course) program in Chennai city catering to about 4.3 million population. To estimate the pattern and overall costs incurred by the new patients (who have never had treatment for tuberculosis or have taken antituberculosis drugs for less than one month) registered under DOTS program in the treatment of tuberculosis in Chennai city.”

The news correspondents obtained a quote from the research from Medical College, “A cross-sectional survey among new TB patients, who had completed intensive phase of antituberculosis treatment, was done using a precoded semi-structured questionnaire between March and June 2007. Information was collected on demographic, socioeconomic characteristics and expenditure for before and during treatment. Mean costs were used for comparison. Among the 300 TB patients, most economically productive age group and 186 (62%) were males. The overall estimated total costs incurred right from the onset of symptoms until treatment completion was found to be Rs. 3211 (3.8% of annual family income) under DOTS program, which is less compared to previous studies. The overall mean total cost was significantly high among male (Rs. 3270; p<0.01), employed (Rs. 3945; p<0.01), and extrapulmonary patients (Rs. 3915; p<0.01). The study has reiterated the fact that DOTS helps in reducing out-of-pocket expenses to patients with tuberculosis and hence is a cost-effective health intervention.”
According to the news reporters, the research concluded: “This cost reduction may help to increase the access to the poor people which would help in achieving universal access to TB care services.”

For more information on this research see: Expenditure Pattern for TB Treatment among Patients Registered in an Urban Government DOTS Program in Chennai City, South India. *Tuberculosis Research and Treatment*, 2012;2012():747924. (Hindawi Publishing - www.hindawi.com; Tuberculosis Research and Treatment - http://www.hindawi.com/journals/trt/)

Our news journalists report that additional information may be obtained by contacting R. Ananthakrishnan, Dept. of Community Medicine, Sree Balaji Medical College and Hospital, Chennai 600044, India. (2013 Jan 01)

**Medical College, Navi Mumbai: Retropharyngeal cold abscess without Pott’s spine**

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators publish new report on General Surgery. According to news originating from Navi Mumbai, India, by NewsRx correspondents, research stated, “Retropharyngeal abscesses are infections deep in the neck space that can pose an immediate life-threatening emergency, with potential for airway compromise and other catastrophic complications. In adults these abscesses can develop as a result of vertebral pyogenic osteomyelitis, tuberculosis of the spine, or external injuries caused by endoscopes or foreign bodies (e.g. fish bones).”

Our news journalists obtained a quote from the research from Medical College, “Tuberculosis of the retropharyngeal space is one of the rare forms of extrapulmonary tuberculosis. Early diagnosis and treatment are necessary to prevent the serious complications of the disease.”

According to the news editors, the research concluded: “We present a case of tuberculous retropharyngeal abscess in an adult woman without tuberculosis of the cervical spine who was managed surgically by aspirating the retropharyngeal abscess transorally, together with antituberculosis treatment.”


The news correspondents report that additional information may be obtained from J. Singh, Dept. of ENT, Padmashree Dr D Y Patil Medical College, Sector 5, Nerul, Navi Mumbai, India, India.
Indian Institute of Technology, Guwahati: Targeting essential cell wall lipase Rv3802c for potential therapeutics against tuberculosis

By a News Reporter-Staff News Editor at Computer Weekly News – Current study results on Molecular Graphics and Modelling have been published. According to news reporting out of Guwahati, India, by VerticalNews editors, research stated, “Cell wall and lipid metabolism plays a vital role in the survival and infection of Mycobacterium tuberculosis. Increase in the incidences of life-threatening multidrug-resistant (MDR) and extreme drug-resistant (XDR) tuberculosis worsens the existing scenario and urge the need of new druggable targets and new drugs.”

Our news journalists obtained a quote from the research from the Indian Institute of Technology, “Targeting Rv3802c, an essential cell wall lipase, can open up a new arsenal to fight the dreadful opportunistic pathogen. Our current study highlights the essentiality of Rv3802c. Its 3D structure is predicted for the first time which provides insight in identifying the ligand binding sites. Our analysis showed Rv3802c is highly conserved throughout mycobacterial species with no significant sequence homolog found in human proteome. Virtual screening followed by comparative docking studies of Rv3802c with its closest human structural homolog has been carried out to identify potential inhibitors effective towards mycobacterial proteins. Two diverse molecules from ZINC database, ZINC26726377 and ZINC43866786 have been identified as potential inhibitors effective towards Rv3802c based on the difference in predicted binding free energy of -3.99 and -3.28kcal/mol respectively.”

According to the news editors, the research concluded: “Rv3802c is a promising drug target and also a step towards understanding and targeting the pathogen’s cell wall and lipid metabolism simultaneously to combat tuberculosis.”

CHAPTER 7  THERAPIES AND TREATMENTS

Our news journalists report that additional information may be obtained by contacting P. Saravanan, Dept. of Biotechnology, Indian Institute of Technology Guwahati, Guwahati 781039, Assam, India. (2012 Dec 27)

College of Medicine, Kolkata: Cerebral tuberculoma as a manifestation of paradoxical reaction in patients with pulmonary and extrapulmonary tuberculosis

By a News Reporter-Staff News Editor at Life Science Weekly – Data detailed on Neuroscience have been presented. According to news reporting out of Kolkata, India, by NewsRx editors, research stated, “Expansion of cerebral tuberculomas or their new appearance as a manifestation of paradoxical reaction in patients under antituberculous chemotherapy is well documented. Distinguishing paradoxical reaction from disease progression or treatment failure is an important issue in tuberculosis management.”

Our news journalists obtained a quote from the research from the College of Medicine, “Five cases of cerebral tuberculomas are reported here as manifestations of paradoxical reaction in patients with pulmonary and extrapulmonary tuberculosis on antituberculous treatment. Case 1 and 2 had tuberculous meningitis, Case 3 had miliary tuberculosis, Case 4 had miliary tuberculosis and destructive vertebral lesions, and Case 5 had pulmonary tuberculosis.”

According to the news editors, the research concluded: “Continuation of antituberculous drugs and addition of steroids led to full recovery of all patients.”

For more information on this research see: Cerebral tuberculoma as a manifestation of paradoxical reaction in patients with pulmonary and extrapulmonary tuberculosis. Journal of Neurosciences In Rural Practice, 2012;3(3):350-4.

Our news journalists report that additional information may be obtained by contacting A. Das, Dept. of Respiratory Medicine, Medical College, Kolkata, India. (2012 Dec 25)
World Health Organization, Phnom Penh: Early detection of tuberculosis through community-based active case finding in Cambodia

By a News Reporter-Staff News Editor at Life Science Weekly – Current study results on Public Health have been published. According to news reporting originating in Phnom Penh, Cambodia, by NewsRx journalists, research stated, “Since 2005, Cambodia’s national tuberculosis programme has been conducting active case finding (ACF) with mobile radiography units, targeting household contacts of TB patients in poor and vulnerable communities in addition to routine passive case finding (PCF). This paper examines the differences in the demographic characteristics, smear grades, and treatment outcomes of pulmonary TB cases detected through both active and passive case finding to determine if ACF could contribute to early case finding, considering associated project costs for ACF.”

The news reporters obtained a quote from the research from World Health Organization, “Demographic characteristics, smear grades, and treatment outcomes were compared between actively (n = 405) and passively (n = 602) detected patients by reviewing the existing programme records (including TB registers) of 2009 and 2010. Additional analyses were performed for PCF cases detected after the ACF sessions (n = 91). The overall cost per case detected through ACF was US$108. The ACF approach detected patients from older populations (median age of 55 years) compared to PCF (median age of 48 years; p<0.001). The percentage of smear-negative TB cases detected through ACF was significantly higher (71.4%) than that of PCF (40.5%). Among smear-positive patients, lower smear grades were observed in the ACF group compared to the PCF group (p = 0.002). A fairly low initial defaulter rate (21 patients, 5.2%) was observed in the ACF group. Once treatment was initiated, high treatment success rates were achieved with 96.4% in ACF and with 95.2% in PCF. After the ACF session, the smear grade of TB patients detected through routine PCF continued to be low, suggesting increased awareness and early case detection. The community-based ACF in Cambodia was found to be a cost-effective activity that is likely to have additional benefits such as contribution to early case finding and detection of patients from a vulnerable age group, possibly with an extended benefit for reducing secondary cases in the community.”

According to the news reporters, the research concluded: “Further investigations are required to clarify the primary benefits of ACF in early and increased case detection and to assess its secondary impact on reducing on-going transmission.”

For more information on this research see: Early detection of tuberculosis through community-based active case finding in Cambodia. *BMC Public Health*, 2012;12():2-10. *BMC Public Health*
Impact of community tracer teams on treatment outcomes among tuberculosis patients in South Africa

By a News Reporter-Staff News Editor at Tuberculosis Week – Investigators publish new report on Public Health. According to news reporting from Pretoria, South Africa, by NewsRx journalists, research stated, “Tuberculosis (TB) indicators in South Africa currently remain well below global targets. In 2008, the National Tuberculosis Program (NTP) implemented a community mobilization program in all nine provinces to trace TB patients that had missed a treatment or clinic visit.”

The news correspondents obtained a quote from the research, “Implementation sites were selected by TB program managers and teams liaised with health facilities to identify patients for tracing activities. The objective of this analysis was to assess the impact of the TB Tracer Project on treatment outcomes among TB patients. The study population included all smear positive TB patients registered in the Electronic TB Registry from Quarter 1 2007-Quarter 1 2009 in South Africa. Subdistricts were used as the unit of analysis, with each designated as either tracer (standard TB program plus tracer project) or non-tracer (standard TB program only). Mixed linear regression models were utilized to calculate the percent quarterly change in treatment outcomes and to compare changes in treatment outcomes from Quarter 1 2007 to Quarter 1 2009 between tracer and non-tracer subdistricts. For all provinces combined, the percent quarterly change decreased significantly for default treatment outcomes among tracer subdistricts (-0.031%; p< 0.001) and increased significantly for successful treatment outcomes among tracer subdistricts (0.003%; p = 0.03). A significant decrease in the proportion of patient default was observed for all provinces combined over the time period comparing tracer and non-tracer subdistricts (p = 0.02). Examination in stratified models revealed the results were not consistent across all provinces; significant differences were observed between tracer and non-tracer subdistricts over time in five of nine provinces for treatment default. Community mobilization of teams to trace TB patients that missed a clinic appointment or treatment dose may be an effective strategy to mitigate default rates and improve treatment outcomes.”
According to the news reporters, the research concluded: “Additional information is necessary to identify best practices and elucidate discrepancies across provinces; these findings will help guide the NTP in optimizing the adoption of tracing activities for TB control.”


Our news journalists report that additional information may be obtained by contacting L.E. Bronner, Republ S Africa Natl Dept. of Hlth, ZA-0001 Pretoria, South Africa. *(2012 Dec 24)*

**University of London Imperial College: Detection and treatment of subclinical tuberculosis**

By a News Reporter-Staff News Editor at Tuberculosis Week – Investigators publish new report on Tuberculosis and Lung Disease. According to news reporting out of London, United Kingdom, by NewsRx editors, research stated, “Reduction of active disease by preventive therapy has the potential to make an important contribution towards the goal of tuberculosis (TB) elimination.”

Our news journalists obtained a quote from the research from the University of London Imperial College, “This report summarises discussions amongst a Working Group convened to consider areas of research that will be important in optimising the design and delivery of preventative therapies.”

According to the news editors, the research concluded: “The Working Group met in Cape Town on 26th February 2012, following presentation of results from the GC11 Grand Challenges in Global Health project to discover drugs for latent TB.”


Our news journalists report that additional information may be obtained by contacting B.D. Robertson, University of London Imperial College, MRC Natl Inst Med Res, London SW7 2AZ, United Kingdom. *(2012 Dec 24)*
University of Barcelona: A predictive scoring instrument for tuberculosis lost to follow-up outcome

By a News Reporter-Staff News Editor at Life Science Weekly – New research on Respiratory Research is the subject of a report. According to news reporting from Barcelona, Spain, by NewsRx journalists, research stated, “Adherence to tuberculosis (TB) treatment is troublesome, due to long therapy duration, quick therapeutic response which allows the patient to disregard about the rest of their treatment and the lack of motivation on behalf of the patient for improved. The objective of this study was to develop and validate a scoring system to predict the probability of lost to follow-up outcome in TB patients as a way to identify patients suitable for directly observed treatments (DOT) and other interventions to improve adherence.”

The news correspondents obtained a quote from the research from the University of Barcelona, “Two prospective cohorts, were used to develop and validate a logistic regression model. A scoring system was constructed, based on the coefficients of factors associated with a lost to follow-up outcome. The probability of lost to follow-up outcome associated with each score was calculated. Predictions in both cohorts were tested using receiver operating characteristic curves (ROC). The best model to predict lost to follow-up outcome included the following characteristics: immigration (1 point value), living alone (1 point) or in an institution (2 points), previous anti-TB treatment (2 points), poor patient understanding (2 points), intravenous drugs use (IDU) (4 points) or unknown IDU status (1 point). Scores of 0, 1, 2, 3, 4 and 5 points were associated with a lost to follow-up probability of 2.2% 5.4% 9.9%, 16.4%, 15%, and 28%, respectively. The ROC curve for the validation group demonstrated a good fit (AUC: 0.67 [95% CI; 0.65-0.70]). This model has a good capacity to predict a lost to follow-up outcome.”

According to the news reporters, the research concluded: “Its use could help TB Programs to determine which patients are good candidates for DOT and other strategies to improve TB treatment adherence.”


Our news journalists report that additional information may be obtained by contacting T. Rodrigo, University of Barcelona, Dept. of Salut Public, Barcelona, Spain. (2012 Dec 18)
Guru Jambheshwar University of Science and Technology, Haryana: Isoniazid: the magic molecule

By a News Reporter-Staff News Editor at Health & Medicine Week – Research findings on Medicinal Chemistry are discussed in a new report. According to news reporting from Haryana, India, by NewsRx journalists, research stated, “The resurgence of tuberculosis and emergence of multidrug resistant isolates has focused attention on the need for an improved understanding of molecular aspects of the disease, and for elucidation of the factors responsible for drug action and resistance.”

The news correspondents obtained a quote from the research from the Guru Jambheshwar University of Science and Technology, “Isoniazid is the frontline drug employed in the treatment of tuberculosis. Recent research has probed the mechanism of action of isoniazid (INH), a key drug in the chemotherapy of tuberculosis and also the antitubercular potential of derivatives of isoniazid has been evaluated.”

According to the news reporters, the research concluded: “We have made an attempt to compile an account of various derivatives of isoniazid reported for their diverse biological activities like antitubercular, -bacterial, -fungal and -viral activities.”

For more information on this research see: Isoniazid: the magic molecule. Medicinal Chemistry Research, 2012;21(12):3940-3957. Medicinal Chemistry Research can be contacted at: Springer, 233 Spring St, New York, NY 10013, USA. (Springer - www.springer.com; Medicinal Chemistry Research - http://www.springerlink.com/content/1054-2523/)

Our news journalists report that additional information may be obtained by contacting V. Judge, Guru Jambheshwar Univ Sci & Technol, Dept. of Pharmaceut Sci, Hisar 125001, Haryana, India. (2012 Dec 14)

Saarland University, Homburg: Tuberculosis in transplantation: diagnosis, prevention, and treatment

By a News Reporter-Staff News Editor at Disease Prevention Week – Investigators publish new report on Science. According to news reporting out of Homburg, Germany, by NewsRx editors, research stated, “Tuberculosis should always be taken into consideration as a possible infectious complication in transplant recipients. It is more frequent and fatal, and its diagnosis, prevention, and treatment are more challenging, in transplanted patients, as compared with the general population.”
Our news journalists obtained a quote from the research from Saarland University, “Latent infection with *M. tuberculosis* is indirectly diagnosed by assessing the presence of a specific adaptive immune response, but depending on the assay used, the informative value of immunodiagnostic assays may be limited by the inhibitory action of immunosuppressive medication, and the positive predictive value for progression toward active tuberculosis is generally low. Diagnosis of active tuberculosis is challenging, since symptoms in immunocompromised patients are frequently less pronounced and atypical. Finally, treatment of tuberculosis is complicated by unpredictable drug interactions, drug-related organ toxicities, and development of drug resistance.”

According to the news editors, the research concluded: “This review provides an overview of the epidemiological characteristics of posttransplant tuberculosis and summarizes current knowledge on the prevention, diagnosis, and treatment of tuberculosis in transplant recipients.”

For more information on this research see: Tuberculosis in transplantation: diagnosis, prevention, and treatment. *Current Infectious Disease Reports*, 2012;14(6):650-7. *Current Infectious Disease Reports* can be contacted at: Springer, 233 Spring Street, New York, NY 10013, USA. (Springer - www.springer.com; Current Infectious Disease Reports - http://www.springerlink.com/content/1523-3847/)

Our news journalists report that additional information may be obtained by contacting S. Kirsch, Dept. of Internal Medicine IV, Saarland University, Homburg, Germany.

Publisher contact information for the journal *Current Infectious Disease Reports* is: Springer, 233 Spring Street, New York, NY 10013, USA. (2012 Dec 11)

**University of Stellenbosch, Cape Town: Evaluation of lay health workers’ needs to effectively support anti-tuberculosis treatment adherence in Malawi**

By a News Reporter-Staff News Editor at Life Science Weekly – New research on Tuberculosis and Lung Disease is the subject of a report. According to news originating from Cape Town, South Africa, by NewsRx correspondents, research stated, “To identify barriers and facilitators to efforts by lay health workers (LHWs) to support anti-tuberculosis treatment adherence in Malawi to inform the design of a knowledge translation intervention for improving adherence. Qualitative study utilizing focus groups and interviews conducted with LHWs providing tuberculosis (TB) care in Zomba District, Malawi.”

Our news journalists obtained a quote from the research from the University of Stellenbosch, “Participants identified lack of knowledge, both general (understanding of TB and its treatment) and job-specific (understanding of tasks such as completion of treatment forms), as the
key barrier to LHWs in their role as adherence supporters. Lack of knowledge among LHWs providing TB care was reported to lead to a lack of confidence, conflicting messages given to patients, poor interactions with patients and errors in documentation. In addition to lack of knowledge, a number of system barriers were identified as limiting LHWs’ ability to function optimally, including a lack of physical resources, workload, communication delays and ineffective guardians. Our findings suggest a gap between LHW knowledge and their responsibilities as adherence supporters.”

According to the news editors, the research concluded: “The results have informed the development of an educational outreach intervention and point-of-care tool, to be evaluated in a randomized trial in Zomba District.”

For more information on this research see: Evaluation of lay health workers’ needs to effectively support anti-tuberculosis treatment adherence in Malawi. *International Journal of Tuberculosis and Lung Disease*, 2012;16(11):1492-1497. *International Journal of Tuberculosis and Lung Disease* can be contacted at: Int Union Against Tuberculosis Lung Disease (I U A T L D), 68 Boulevard Saint-Michel, 75006 Paris, France.

The news correspondents report that additional information may be obtained from L.M.P. Ritchie, University of Stellenbosch, Fac Hlth Sci, Cape Town, South Africa. (2012 Dec 11)

**University of Witwatersrand, Johannesburg: Quantifying errors in the estimation of tuberculosis mortality in a population of South African miners**

By a News Reporter-Staff News Editor at Life Science Weekly – Current study results on Tuberculosis and Lung Disease have been published. According to news originating from Johannesburg, South Africa, by NewsRx correspondents, research stated, “All-cause mortality, based on national tuberculosis programme (NTP) register deaths, may under- or overestimate tuberculosis (TB) specific mortality in the population. To assess the factors influencing this measurement in a single large population with high TB prevalence and mortality.”

Our news journalists obtained a quote from the research from the University of Witwatersrand, “Routinely collected data on TB cases and treatment outcomes were linked to population data from a cohort of South African miners from 1995 to 2008. Vital status and cause of death were determined from multiple sources, including the TB programme, death register and autopsy. The TB mortality rate, based on 430 deaths on the TB register, was 192/100000 person-years (py). Many of these deaths (57%) were not caused by TB, and 483 TB deaths were identified outside the programme. Overall, there were 674 TB-specific deaths; the TB-specific mortality rate was 302/100000 py. These deaths included

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191 (28%) on the TB register, 23 (3%) among defaulters/transfers, 153 (23%) after anti-tuberculosis treatment and 307 (46%) in men who had never been on the programme. This study highlights methodological issues in estimating TB mortality. In this population, a method using the product of TB incidence and case fatality consistently underestimated TB mortality."

According to the news editors, the research concluded: “Accurate estimates of TB-specific mortality are crucial for the proper evaluation of TB control programmes.”


The news correspondents report that additional information may be obtained from P. Sonnenberg, University of Witwatersrand, Sch Public Hlth, Johannesburg, South Africa. (2012 Dec 11)

**Albert Einstein College of Medicine, Bronx: Stability, denaturation and refolding of Mycobacterium tuberculosis MfpA, a DNA mimicking protein that confers antibiotic resistance**

By a News Reporter-Staff News Editor at Health & Medicine Week – Current study results on Biophysical Chemistry have been published. According to news reporting from Bronx, New York, by NewsRx journalists, research stated, “MfpA from *Mycobacterium tuberculosis* is a founding member of the pentapeptide repeat class of proteins (PRP) that is believed to confer bacterial resistance to the drug fluoroquinolone by mimicking the size, shape and surface charge of duplex DNA. We show that phenylalanine side chain stacking stabilizes the N-terminus of MfpA’s pentapeptide thus extending the DNA mimicry analogy.”

The news correspondents obtained a quote from the research from the Albert Einstein College of Medicine, “The Lumry-Eyring model was applied to multiple spectral measures of MfpA denaturation revealing that the MfpA dimer dissociates to monomers which undergo a structural transition that leads to aggregation. MfpA retains high secondary and tertiary structure content under denaturing conditions. Dimerization stabilizes MfpA’s pentapeptide repeat fold. The high Arrhenius activation energy of the barrier to aggregate formation rationalizes its stability.”
According to the news reporters, the research concluded: “The mechanism of MfpA denaturation and refolding is a ‘double funnel’ energy landscape where the ‘native’ and ‘aggregate’ funnels are separated by the high barrier that is not overcome during in vitro refolding.”


Our news journalists report that additional information may be obtained by contacting S. Khrapunov, Dept. of Biochemistry, Albert Einstein College of Medicine, Bronx, NY 10461, United States. *(2012 Dec 07)*

**Research Institute, Kolkata: Adjunct therapy of Ayurvedic medicine with anti tubercular drugs on the therapeutic management of pulmonary tuberculosis**

By a News Reporter-Staff News Editor at Biotech Week – Investigators discuss new findings in Mycobacterium Infections. According to news originating from Kolkata, India, by NewsRx correspondents, research stated, ‘Pulmonary tuberculosis (PTB) is an age old disease described in Vedic Medicine as ‘Yakshma’. Later on, in Ayurveda it earned a prefix and found way into mythology as ‘Rajayakshma’.”

Our news journalists obtained a quote from the research from Research Institute, “After the discovery of streptomycin, the therapeutic management of PTB received a major breakthrough. The treatment module changed remarkably with the formulation of newer anti-tubercular drugs (ATD) with appreciable success. Recent resurgence of PTB in developed countries like United States posed a threat to the medical community due to resistant strains. Consequently, WHO looked toward traditional medicine. Literature reveals that Ayurvedic treatment of PTB was in vogue in India before the introduction of ATD with limited success.”

According to the news editors, the research concluded: “Records show that 2766 patients of PTB were treated with Ayurvedic drugs in a tertiary care hospital in Kolkata in the year 1933-1947.”

For more information on this research see: Adjunct therapy of Ayurvedic medicine with anti tubercular drugs on the therapeutic management of pulmonary tuberculosis. *Journal of Ayurveda and Integrative Medicine*, 2012;3(3):141-9.

The news correspondents report that additional information may be obtained from P.K. Debnath, National Research Institute of Ayurvedic Drug Development, Kolkata, India. *(2012 Dec 05)*
CHAPTER 7 THERAPIES AND TREATMENTS

University of Michigan, Ann Arbor: Cosubstrate Tolerance of the Aminoglycoside Resistance Enzyme Eis from Mycobacterium tuberculosis

By a News Reporter-Staff News Editor at Biotech Week – Fresh data on Chemotherapy are presented in a new report. According to news reporting from Ann Arbor, Michigan, by NewsRx journalists, research stated, “We previously demonstrated that aminoglycoside acetyltransferases (AACs) display expanded cosubstrate promiscuity. The enhanced intracellular survival (Eis) protein of Mycobacterium tuberculosis is responsible for the resistance of this pathogen to kanamycin A in a large fraction of clinical isolates.”

The news correspondents obtained a quote from the research from the University of Michigan, “Recently, we discovered that Eis is a unique AAC capable of acetylating multiple amine groups on a large pool of aminoglycoside (AG) antibiotics, an unprecedented property among AAC enzymes. Here, we report a detailed study of the acyl-coenzyme A (CoA) cosubstrate profile of Eis. We show that, in contrast to other AACs, Eis efficiently uses only 3 out of 15 tested acyl-CoA derivatives to modify a variety of AGs. We establish that for almost all acyl-CoAs, the number of sites acylated by Eis is smaller than the number of sites acetylated. We demonstrate that the order of n-propionylation of the AG neamine by Eis is the same as the order of its acetylation. We also show that the 6’ position is the first to be n-propionylated on amikacin and netilmicin. By sequential acylation reactions, we show that AGs can be acetylated after the maximum possible n-propionylation of their scaffolds by Eis.”

According to the news reporters, the research concluded: “The information reported herein will advance our understanding of the multiacetylation mechanism of inactivation of AGs by Eis, which is responsible for M. tuberculosis resistance to some AGs.”

For more information on this research see: Cosubstrate Tolerance of the Aminoglycoside Resistance Enzyme Eis from Mycobacterium tuberculosis. Antimicrobial Agents and Chemotherapy, 2012;56(11):5831-5838. Antimicrobial Agents and Chemotherapy can be contacted at: Amer Soc Microbiology, 1752 N St NW, Washington, DC 20036-2904, USA. (American Society for Microbiology - www.asm.org; Antimicrobial Agents and Chemotherapy - aac.asm.org)

Our news journalists report that additional information may be obtained by contacting W.J. Chen, University of Michigan, Inst Life Sci, Ann Arbor, MI 48109, United States. (2012 Dec 05)
Brigham and Women’s Hospital, Boston: The impact of new tuberculosis diagnostics on transmission: why context matters

By a News Reporter-Staff News Editor at Tuberculosis Week – A new study on World Health Organization is now available. According to news reporting originating in Boston, Massachusetts, by NewsRx journalists, research stated, “To estimate the impact of new tuberculosis diagnostics on tuberculosis transmission given the complex contextual factors that can lead to patient loss before diagnosis or treatment. An epidemic model of tuberculosis specifying discrete steps along the tuberculosis diagnostic pathway was constructed.”

The news reporters obtained a quote from the research from Brigham and Women’s Hospital, “The model was calibrated to the epidemiology of tuberculosis and human immunodeficiency virus (HIV) infection in the United Republic of Tanzania and was used to assess the impact of a new diagnostic tool with 70% sensitivity for smear-negative pulmonary tuberculosis. The influence of contextual factors on the projected epidemic impact of the new diagnostic tool over the decade following introduction was explored. With the use of smear microscopy, the incidence of tuberculosis will decline by an average of 3.94% per year. If the new tool is added, incidence will decline by an annual 4.25%. This represents an absolute change of 0.31 percentage points (95% confidence interval: 0.04-0.42). However, the annual decline in transmission with use of the new tool is less when existing strategies for the diagnosis of smear-negative cases have high sensitivity and when symptomatic individuals delay in seeking care. Other influential contextual factors include access to tuberculosis care, patient loss before diagnosis, initial patient default after diagnosis and treatment success rate.”

According to the news reporters, the research concluded: “When implementing and scaling up the use of a new diagnostic tool, the operational context in which diagnosis and treatment take place needs to be considered.”


Our news correspondents report that additional information may be obtained by contacting H.H. Lin, Brigham & Women’s Hospital, Div Global Hlth Equ, Boston, MA 02115, United States. (2012 Dec 03)
Center for Disease Control and Prevention, Atlanta: Tuberculosis among Healthcare Workers, United States, 1995-2007

By a News Reporter-Staff News Editor at Tuberculosis Week – Research findings on Hospitals are discussed in a new report. According to news reporting out of Atlanta, Georgia, by NewsRx editors, research stated, “We examined surveillance data to describe the epidemiology of tuberculosis (TB) among healthcare workers (HCWs) in the United States during the period 1995-2007. Cross-sectional descriptive analysis of existing surveillance data.”

Our news journalists obtained a quote from the research from Center for Disease Control and Prevention, “TB cases reported to the Centers for Disease Control and Prevention from the 50 states and the District of Columbia from 1995 through 2007. Of the 200,744 reported TB cases in persons 18 years of age or older, 6,049 (3%) occurred in individuals who were classified as HCWs. HCWs with TB were more likely than other adults with TB to be women (unadjusted odds ratio [95% confidence interval], 4.1 [3.8-4.3]), be foreign born (1.3 [1.3-1.4]), have extrapulmonary TB (1.6 [1.5-1.7]), and complete TB treatment (2.5 [2.3-2.8]).”

According to the news editors, the research concluded: “Healthcare institutions may benefit from intensifying TB screening of HCWs upon hire, especially persons from countries with a high incidence of TB, and encouraging treatment for latent TB infection among HCWs to prevent progression to TB disease.”

For more information on this research see: Tuberculosis among Healthcare Workers, United States, 1995-2007. Infection Control and Hospital Epidemiology, 2012;33(11):1126-1131. Infection Control and Hospital Epidemiology can be contacted at: Univ Chicago Press, 1427 E 60TH St, Chicago, IL 60637-2954, USA. (University of Chicago Press - press.uchicago.edu; Infection Control and Hospital Epidemiology - /ucp/journals/journal/iche.html)

Our news journalists report that additional information may be obtained by contacting L.A. Lambert, Center Dis Control & Prevent, Div TB Eliminat, Atlanta, GA 30333, United States. (2012 Dec 03)
Pitie-Salpetriere Hospital, Paris: Influence of replacing tuberculin skin test with ex vivo interferon gamma release assays on decision to administer prophylactic antituberculosis antibiotics before anti-TNF therapy

By a News Reporter-Staff News Editor at Anti-Infectives Week – Research findings on Mycobacterium Infections are discussed in a new report. According to news reporting out of Paris, France, by NewsRx editors, research stated, “The recommendations for detecting latent tuberculosis infection (LTBI) before antitumour necrosis factor (anti-TNF) therapy are based on the tuberculin skin test (TST), which lacks both specificity and sensitivity and can lead to unnecessary treatment with antibiotics. A study was undertaken to investigate the effect of replacing TST with interferon gamma (IFN gamma) release assays (IGRA) in screening for LTBI and deciding to begin prophylactic antituberculosis (TB) antibiotics before anti-TNF therapy in immune-mediated inflammatory diseases.”

Our news journalists obtained a quote from the research from Pitie-Salpetriere Hospital, “In 15 tertiary care hospitals, consecutive patients with rheumatoid arthritis, spondylarthropathies or Crohn’s disease were screened for LTBI before anti-TNF therapy with TST, Quantiferon TB Gold in tube (QTF-Gold IT) and T-SPOT. TB at the same time. The potential diagnosis of LTBI and the effect on the decision to begin antibiotic prophylaxis were assessed. Among 429 patients, 392 had results for the three tests. The results for TST, T-SPOT. TB and QTF Gold IT were positive for 35.2%, 15.1% and 9.9% of patients, respectively (p <0.0001). Antibiotics were required for 177 patients (45.2%) if positive TST results were included in the LTBI definition, 107 patients (27.3%) if TST results were replaced with results from one of the IGRA tests and 84 patients (21.4%) if TST results were replaced with QTF-Gold IT results (p <0.0001). The decision on the use of antibiotic prophylaxis was changed for 113 patients (28.8%, 95% CI 24.4% to 33.6%) if TST results were replaced with QTF-Gold IT results.”

According to the news editors, the research concluded: “Replacing TST with IGRA for determining LTBI allowed the proportion of patients with immune-mediated inflammatory diseases needing prophylactic anti-TB antibiotics before beginning anti-TNF agents to be reduced by half.”

Chongqing Medical University: Posterior transpedicular debridement, decompression and instrumentation for thoracic tuberculosis in patients over the age of 60

By a News Reporter-Staff News Editor at Tuberculosis Week – A new study on Tuberculosis is now available. According to news reporting out of Chongqing, People’s Republic of China, by NewsRx editors, research stated, “Our aim was to evaluate the feasibility and efficiency of the application of posterior transpedicular debridement with instrumentation and fusion to the treatment of over 60-year-old patients with thoracic tuberculosis. Fifteen over 60-year-old patients with thoracic tuberculosis treated by posterior transpedicular debridement with instrumentation and fusion between August 2006 and November 2010, seven males and eight females in this study were reviewed, retrospectively.”

Our news journalists obtained a quote from the research from Chongqing Medical University, “Their age ranged from 61 to 75 (mean age 63.4). The follow-up period ranged from 12 to 51 months (mean 30 months). The patients were evaluated based on vertebral body loss, kyphotic angle, fusion status of affected segment, visual analog scale (VAS) pain score, and Frankel’s classification. A solid fusion was achieved in all 15 cases. No postoperative complications, chronic infection, sinus formation or significant loss of deformity correction was noted in these patients. Moreover, VAS score was reduced and Frankel’s grade was recovered in all patients and there was no recurrence of the tuberculous infection.”

According to the news editors, the research concluded: “Posterior transpedicular debridement with instrumentation and fusion is a feasible and effective procedure in the treatment for thoracic tuberculosis in patients over the age of 60.”

For more information on this research see: Posterior transpedicular debridement, decompression and instrumentation for thoracic tuberculosis in patients over the age of 60. Archives of Orthopaedic and Trauma Surgery, 2012;132(10):1407-1414. Archives of Orthopaedic and Trauma Surgery can be contacted at: Springer, 233 Spring St, New York, NY 10013, USA. (Springer - www.springer.com; Archives of Orthopaedic and Trauma Surgery - http://www.springerlink.com/content/0936-8051/)

Our news journalists report that additional information may be obtained by contacting B. He, Chongqing Med Univ, Affiliated Hosp 1,
Infections due to non-tuberculous mycobacteria (NTM)

By a News Reporter-Staff News Editor at Tuberculosis Week – Investigators discuss new findings in Medical Research. According to news reporting out of Uttar Pradesh, India, by NewsRx editors, the research stated, “The membership list of genus mycobacterium is ever expanding and it has grown to 95 in year 2003. While leprosy and tuberculosis are specific diseases caused by mycobacteria, other members are usually saprophytes but can be opportunistic and at times deadly pathogens.”

Our news journalists obtained a quote from the research, “These other mycobacteria are referred to as atypical mycobacteria, non-tuberculous mycobacteria (NTM) or mycobacteria other than tubercle bacilli (MOTT). These organisms can produce localized disease in the lungs, lymph glands, skin, wounds or bone. Occasionally they may produce disseminated disease. Of the more than 90 known species of NTM, about one third have been associated with disease in humans. The species causing human disease are: Mycobacterium avium, M. intracellulare, M. kansasii, M. paratuberculosis, M. scrofulaceum, M. simiae, M. habana, M. interjectum, M. xenopi, M. heckshornense, M. szulgai, M. fortuitum, M. immunogenum, M. chelonae, M. marinum, M. genavense, M. haemophilum, M. celatum, M. conspicuum, M. malmoense, M. ulcerans, M. smegmatis, M. wolinskyi, M. goodii, M. thermo resistible, M. neoaerum, M. vaccae, M. palustre, M. elephantis, M. bohemicam and M. septicum. Isolation of these mycobacteria from representative specimens and their rapid identification is very important as the treatment strategy for tuberculosis and other mycobacterioses is different. Several biochemical, chemical (lipid) and molecular techniques have been developed for rapid identification of these species. Along with suggestive clinical features, poor response to antitubercular treatment and repeated isolation of the organisms from the clinical specimens these techniques can help in establishing correct diagnosis.”

According to the news editors, the research concluded: “Further, many drugs like rifampicin, rifabutin, ethambutol, clofazimine, amikacin, new generation quinolones and macrolides effective against mycobacterial infections are available that can be used in appropriate combinations and dosage to treat these infections.”

For more information on this research see: Infections due to non-tuberculous mycobacteria (NTM). *Indian Journal of Medical Research, 2012;136(2):R290-R304. Indian Journal of Medical Research* can be contacted at: Indian Council Medical Res, PO Box 4911 Ansari Nagar, New Delhi 110029, India.
TB questions, East Kwaio answers: community-based participatory research in a remote area of Solomon Islands

By a News Reporter-Staff News Editor at Tuberculosis Week – Research findings on Rural Health are discussed in a new report. According to news originating from Tamworth, Australia, by NewsRx correspondents, research stated, “East Kwaio is a remote region on the island of Malaita, Solomon Islands. Atoifi Adventist Hospital (the Hospital) is the only hospital and tuberculosis (TB) services provider in the region.”

Our news journalists obtained a quote from the research, “If people come to the Hospital with TB, they are usually admitted for the two-month intensive phase of treatment as there are no community-based TB services. Most people walk or travel by canoe to the Hospital as there are no roads. East Kwaio is known to have high rates of TB; however, it has a low case detection rate and low treatment completion. The aims of this study were to explore why people with TB, especially from the mountain areas, present to the Hospital so late in their illness or do not present at all.”

According to the news editors, the research concluded: “The study was part of a larger project to strengthen the research capacity of local health workers and community leaders, supported by visiting researchers from Australia.”


The news correspondents report that additional information may be obtained from P.D. Massey, Health Protection, Hunter New England Population Health, Tamworth, New South Wales, Australia. (2012 Nov 19)
Yonsei University, Wonju: c-Jun N-terminal kinase (JNK) and p38 mitogen-activated protein kinase (p38 MAPK) are involved in Mycobacterium tuberculosis-induced expression of Leukotactin-1

By a News Reporter-Staff News Editor at Tuberculosis Week – Current study results on Mycobacterium Infections have been published. According to news reporting from Wonju, South Korea, by NewsRx journalists, research stated, “Leukotactin (Lkn)-1 is a CC chemokine and is upregulated in macrophages in response to Mycobacterium tuberculosis (MTB) infection. We investigated whether mitogen-activated protein kinases (MAPKs) are involved in MTB-induced expression of Lkn-1.”

The news correspondents obtained a quote from the research from Yonsei University, “The up-regulation of Lkn-1 by infection with MTB was inhibited in cells treated with inhibitors specific for JNK (SP600125) or p38 MAPK (SB202190). Since the up-regulation of Lkn-1 by MTB has been reported to be mediated by the PI3-K/PDK1/Akt signaling, we examined whether JNK and/or p38 MAPK are also involved in this signal pathway. MTB-induced Akt phosphorylation was blocked by treatment with JNK-or p38 MAPK-specific inhibitors implying that p38 and JNK are upstream of Akt. In addition, treatment with the PI3-K-specific inhibitor inhibited MTB-stimulated activation of JNK or p38 MAPK implying that PI3-K is upstream of JNK and p38 MAPK.”

According to the news reporters, the research concluded: “These results collectively suggest that JNK and p38 MAPK are involved in the signal pathway responsible for MTB-induced up-regulation of Lkn-1.”

For more information on this research see: c-Jun N-terminal kinase (JNK) and p38 mitogen-activated protein kinase (p38 MAPK) are involved in Mycobacterium tuberculosis-induced expression of Leukotactin-1. Bmb Reports, 2012;45(10):583-8.

Our news journalists report that additional information may be obtained by contacting J.E. Cho, Dept. of Biomedical Laboratory Science, College of Health Sciences, Yonsei University, Wonju 220-710, South Korea. (2012 Nov 19)

University Putra Malaysia, Selangor: Controlled-release approaches towards the chemotherapy of tuberculosis

By a News Reporter-Staff News Editor at Life Science Weekly – Current study results on Nanomedicine have been published. According to news reporting out of Selangor, Malaysia, by NewsRx editors, research stated, “Tuberculosis (TB), caused by the bacteria Mycobacterium tuberculosis, is notorious for its lethality to humans. Despite technological advances, the tubercle bacillus continues to threaten humans.”
Our news journalists obtained a quote from the research from University Putra Malaysia, “According to the World Health Organization’s 2011 global report on TB, 8.8 million cases of TB were reported in 2010, with a loss of 1.7 million human lives. As drug-susceptible TB requires long-term treatment of between 6 and 9 months, patient noncompliance remains the most important reason for treatment failure. For multidrug-resistant TB, patients must take second-line anti-TB drugs for 18-24 months and many adverse effects are associated with these drugs. Drug-delivery systems (DDSs) seem to be the most promising option for advancement in the treatment of TB. DDSs reduce the adverse effects of drugs and their dosing frequency as well as shorten the treatment period, and hence improve patient compliance. Further advantages of these systems are that they target the disease area, release the drugs in a sustained manner, and are biocompatible. In addition, targeted delivery systems may be useful in dealing with extensively drug-resistant TB because many side effects are associated with the drugs used to cure the disease.”

According to the news editors, the research concluded: “In this paper, we discuss the DDSs developed for the targeted and slow delivery of anti-TB drugs and their possible advantages and disadvantages.”

For more information on this research see: Controlled-release approaches towards the chemotherapy of tuberculosis. *International Journal of Nanomedicine*, 2012;7():5451-63.

Our news journalists report that additional information may be obtained by contacting B. Saifullah, Dept. of Chemistry, Faculty of Science, Universiti Putra Malaysia, Serdang, Selangor, Malaysia. (2012 Nov 13)

**Institute for Cancer Research and Treatment (IRCCS), Rome: A Twenty-year Retrospective Study of Pediatric Tuberculosis in Two Tertiary Hospitals in Rome**

By a News Reporter-Staff News Editor at Pediatrics Week – Current study results on Mycobacterium Infections have been published. According to news reporting from Rome, Italy, by VerticalNews journalists, research stated, “Tuberculosis (TB) is among the top 10 causes of child death worldwide. Nevertheless, childhood disease has been neglected by tuberculosis control programs.”

The news correspondents obtained a quote from the research from Institute for Cancer Research and Treatment (IRCCS), “This was a retrospective study of patients < 16 years of age diagnosed with active TB in 2 tertiary hospitals in Rome (Italy), between 1990 and 2009. Two hundred fourteen cases of active tuberculosis were identified (132 definite, 82 probable). Pulmonary involvement was the most common form
(75.5%), followed by lymphadenopathy (15.4%) and central nervous system TB (11%). Fever (51.86%) and cough (40%) were the most common presenting symptoms. A total of 23.4% of children were asymptomatic on admission. Sensitivities of the tuberculin skin test and the quantiferon test were 93.4% and 97%, respectively. Both tests performed in 52 children agreed in 49 cases (94%). Sensitivities for culture, Ziehl-Neelsen staining and polymerase chain reaction were 58%, 25% and 66.3%, respectively. The adult source case was identified in 28% of cases. History of contact with a patient with active TB was associated with pulmonary TB (P = 0.0014), whereas negative history of contact was associated with lymph node (P = 0.0064) and central nervous system TB (P = 0.05). Our study emphasizes the difficulty in managing children with suspected TB, because the absence of constitutional symptoms cannot exclude TB, and bacteriologic confirmation is the exception. Immunologic diagnosis can be a valuable tool to identify TB-infected children because the quantiferon test showed high sensitivity in all age groups.”

According to the news reporters, the research concluded: “This is of primary importance because early identification of children with latent tuberculous infection and appropriate chemoprophylaxis represent, to date, the most important tool to reduce the burden of TB.”

For more information on this research see: A Twenty-year Retrospective Study of Pediatric Tuberculosis in Two Tertiary Hospitals in Rome. *Pediatric Infectious Disease Journal*, 2012;31(10):1022-1026. *Pediatric Infectious Disease Journal* can be contacted at: Lippincott Williams & Wilkins, 530 Walnut St, Philadelphia, PA 19106-3621, USA. (Lippincott Williams and Wilkins - www.lww.com; Pediatric Infectious Disease Journal - http://journals.lww.com/pidj/pages/default.aspx)

Our news journalists report that additional information may be obtained by contacting D. Buonsenso, INMI IRCCS L Spallanzani, Dept. of Infect Dis, Div 1, Rome, Italy. (2012 Nov 10)

**Johns Hopkins University, Baltimore: Current tuberculosis diagnostic tools & role of urease breath test**

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators publish new report on Medical Research. According to news reporting out of Baltimore, Maryland, by NewsRx editors, research stated, “Tuberculosis (TB) remains a significant public health issue worldwide especially in developing countries, where the disease is endemic, and effective TB diagnostic as well as treatment-monitoring tools are serious barriers to defeating the disease. Detection of pathogen-specific metabolic pathways offers a potential alternative to
current methods, which focus on bacterial growth, bacterial nucleic acid amplification, or detection of host immune response to the pathogen.”

Our news journalists obtained a quote from the research from Johns Hopkins University, “Metabolic pathway detection may provide rapid and effective new tools for TB that can improve TB diagnostics for children and HIV infected patients. Metabolic breath tests are attractive because these are safe, and provide an opportunity for rapid point of care diagnostics and tool for drug efficacy evaluation during clinical trials. Our group has developed a rabbit urease breath test model to evaluate the sensitivity and the specificity of urease based detection of Mycobacterium tuberculosis. TB infected rabbits were given stable isotopically labelled urea as the substrate. The urea tracer was metabolized to C-13-CO2 and detected in exhaled breaths using portable infrared spectrometers. The signal correlated with bacterial load both for primary diagnostics and treatment monitoring. Clinical trials are currently ongoing to evaluate the value of the test in clinical management settings.”

According to the news editors, the research concluded: “Urea breath testing may provide a useful diagnostic and biomarker assay for tuberculosis and treatment response.”

For more information on this research see: Current tuberculosis diagnostic tools & role of urease breath test. Indian Journal of Medical Research, 2012;135(5):731-736. Indian Journal of Medical Research can be contacted at: Indian Council Medical Res, PO Box 4911 Ansari Nagar, New Delhi 110029, India.

Our news journalists report that additional information may be obtained by contacting M. Maiga, Johns Hopkins University, Dept. of Med, Johns Hopkins Sch Med, Center TB ResDiv Infect Dis, Baltimore, MD 21231, United States. (2012 Nov 06)

University of the Western Cape, Cape Town: Hazardous and Harmful Alcohol Use and Associated Factors in Tuberculosis Public Primary Care Patients in South Africa

By a News Reporter-Staff News Editor at Life Science Weekly – Research findings on Environmental Health are discussed in a new report. According to news reporting out of Cape Town, South Africa, by NewsRx editors, research stated, “The aim of this study was to assess the prevalence of hazardous and harmful alcohol use and associated factors among patients with tuberculosis in South Africa. In a cross-sectional survey new tuberculosis (TB) and TB retreatment patients were consecutively screened using the Alcohol Use Disorder Identification Test (AUDIT) within one month of anti-tuberculosis treatment.”

Our news journalists obtained a quote from the research from the University of the Western Cape, “The sample included 4,900 (54.5%
men and women 45.5%) tuberculosis patients from 42 primary care clinics in three districts. Overall 23.2% of the patients were hazardous or harmful alcohol drinkers, 31.8% of men and 13.0% of women were found to be hazardous drinkers, and 9.3% of men and 3.4% of women meet criteria for probable alcohol dependence (harmful drinking) as defined by the AUDIT. Men had significantly higher AUDIT scores than women. In multivariable analyses it was found that among men poor perceived health status, tobacco use, psychological distress, being a TB retreatment patient and not being on antiretroviral therapy (ART), and among women lower education, tobacco use and being a TB retreatment patient were associated with hazardous or harmful alcohol use. The study found a high prevalence of hazardous or harmful alcohol use among tuberculosis primary care patients.”

According to the news editors, the research concluded: “This calls for screening and brief intervention and a comprehensive alcohol treatment programme as a key component of TB management in South Africa.”

For more information on this research see: Hazardous and Harmful Alcohol Use and Associated Factors in Tuberculosis Public Primary Care Patients in South Africa. International Journal of Environmental Research and Public Health, 2012;9(9):3245-3257. International Journal of Environmental Research and Public Health can be contacted at: Mdp Ag, Postfach, Ch-4005 Basel, Switzerland.

Our news journalists report that additional information may be obtained by contacting K. Peltzer, Univ Western Cape, Dept. of Psychol, ZA-8000 Cape Town, South Africa. (2012 Nov 06)

Stellenbosch University, Tygerberg: Multidrug-resistant tuberculosis of the spine in children—characteristics from a high burden setting

By a News Reporter-Staff News Editor at Pediatrics Week – Investigators publish new report on Mycobacterium Infections. According to news reporting originating from Tygerberg, South Africa, by Vertical-News correspondents, research stated, “Few studies have described children with spinal multidrug-resistant tuberculosis (MDR-TB). Treatment involves surgery and medical care with long courses of drug therapy.”

Our news editors obtained a quote from the research from Stellenbosch University, “Hospital and laboratory records at Brooklyn Chest and Tygerberg Children’s Hospitals, Cape Town, South Africa, were analysed (January 2004 until December 2010) searching for children treated for MDR spinal TB. Of the 11 children identified, 4 were excluded. Of the 7 remaining, 5 were boys; median age: 8 years, median delay to treatment initiation: 36 weeks. Among them one child
died, five have completed treatment and one is near the end of therapy. Medications were well-tolerated and although two of the surviving children have spinal deformity, none have significant neurological deficit. The diagnosis of spinal MDR-TB is often delayed in children, frequently leading to advanced disease and severe vertebral damage.”

According to the news editors, the research concluded: “Children tolerate therapy well and, once identified, it is a condition that can be treated successfully.”


The news editors report that additional information may be obtained by contacting J.A. Seddon, Desmond Tutu TB Centre, Dept. of Paediatrics and Child Health, Faculty of Health Sciences, Stellenbosch University, Tygerberg, 7505, South Africa. (2012 Nov 03)

**Emory University School of Medicine, Atlanta:**

Imatinib-sensitive tyrosine kinases regulate mycobacterial pathogenesis and represent therapeutic targets against tuberculosis

By a News Reporter-Staff News Editor at Biotech Week – Data detailed on Drugs and Therapies have been presented. According to news originating from Atlanta, Georgia, by NewsRx correspondents, research stated, “The lengthy course of treatment with currently used antimycobacterial drugs and the resulting emergence of drug-resistant strains have intensified the need for alternative therapies against *Mycobacterium tuberculosis* (Mtb), the etiologic agent of tuberculosis. We show that Mtb and Mycobacterium marinum use ABL and related tyrosine kinases for entry and intracellular survival in macrophages.”

Our news journalists obtained a quote from the research from the Emory University School of Medicine, “In mice, the ABL family tyrosine kinase inhibitor, imatinib (Gleevec), when administered prophylactically or therapeutically, reduced both the number of granulomatous lesions and bacterial load in infected organs and was also effective against a rifampicin-resistant strain. Further, when coadministered with current first-line drugs, rifampicin or rifabutin, imatinib acted synergistically. These data implicate host tyrosine kinases in entry and intracellular survival of mycobacteria and suggest that imatinib may have therapeutic efficacy against Mtb.”

According to the news editors, the research concluded: “Because imatinib targets host, it is less likely to engender resistance compared
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to conventional antibiotics and may decrease the development of resis-
tance against coadministered drugs.”


The news correspondents report that additional information may be obtained from R.J. Napier, Graduate Program of Microbiology and Molecular Genetics, Emory University School of Medicine, Atlanta, GA 30322, United States. (2012 Oct 31)

**Centers for Disease Control and Prevention, Atlanta: Modelling tuberculosis trends in the USA**

By a News Reporter-Staff News Editor at Life Science Weekly – New research on Epidemiology is the subject of a report. According to news reporting from Atlanta, Georgia, by NewsRx journalists, research stated, “We present a mathematical transmission model of tuberculosis in the USA. The model is calibrated to recent trends of declining incidence in the US-born and foreign-born populations and is used in assessing relative impacts of treatment of latently infected individuals on elimi-
tation time, where elimination is defined as annual incidence <1 case/million.”

The news correspondents obtained a quote from the research from Centers for Disease Control and Prevention, “Provided current control efforts are maintained, elimination in the US-born population can be achieved before the end of this century. However, elimination in the foreign-born population is unlikely in this timeframe even with higher rates of targeted testing and treatment of residents of and immigrants to the USA with latent tuberculosis infection.”

According to the news reporters, the research concluded: “Cutting transmission of disease as an interim step would shorten the time to elimination in the US-born population but foreign-born rates would re-
main above the elimination target.”

For more information on this research see: Modelling tuberculosis trends in the USA. *Epidemiology and Infection*, 2012;140(10):1862-1872. *Epidemiology and Infection* can be contacted at: Cambridge Univ Press, 32 Avenue Of The Americas, New York, NY 10013-2473, USA. (Cambridge University Press - www.cambridge.org; Epidemiology and Infection - http://journals.cambridge.org/action/displayJournal?jid=HYG)

Our news journalists report that additional information may be ob-
Centers for Disease Control and Prevention, Chongqing:
Effect of scheduled monitoring of liver function during
anti-Tuberculosis treatment in a retrospective cohort in
China

By a News Reporter-Staff News Editor at Asia Business Newsweekly – Current study results on Mycobacterium Infections have been published. According to news reporting out of Chongqing, People’s Republic of China, by VerticalNews editors, research stated, “Data on effect of regular liver function monitoring during anti-TB treatment is limited in China. This study aimed to evaluate the effects of scheduled liver function monitoring on identification of asymptomatic liver damage and anti-TB treatment outcomes during anti-TB treatment.”

Our news journalists obtained a quote from the research from Centers for Disease Control and Prevention, “A retrospective analysis was performed based on a national-level cohort study. A total of 273 patients developing liver dysfunction were divided into two groups, 111 patients who were diagnosed through scheduled liver function test within two months after initiation of anti-TB treatment formed scheduled monitoring group, others who were diagnosed due to developing symptoms formed passive detection group (n = 162). The two groups were compared through clinical features, prognosis of liver dysfunction and impact on anti-TB treatment using propensity score weighting analysis. 33.3% of 273 patients did not have any clinical symptoms, including 8 with severe hepatotoxicity. 1.8% in scheduled monitoring group and 11.1% in passive detection group required hospitalization (P = 0.004). Regarding the prognosis of liver dysfunction, most patients recovered, no death happened in scheduled monitoring group while 3 died in passive detection group. In terms of impact on anti-TB treatment, 35.1% in scheduled monitoring group and 56.8% in passive detection group changed their anti-TB treatment (P = 0.001).”

According to the news editors, the research concluded: “Scheduled monitoring is effective in identifying asymptomatic liver damage, reducing hospitalization rate and improving compliance of anti-TB treatment.”


Our news journalists report that additional information may be obtained by contacting S.S. Wu, Center Dis Control & Prevent Chongqing Municipal, Chongqing, People’s Republic of China. (2012 Oct 30)
Clinical evaluation of Rasayana compound as an adjuvant in the management of tuberculosis with anti-Koch’s treatment

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators publish new report on Ayurveda Research. According to news originating from Ahmedabad, India, by NewsRx correspondents, research stated, “Tuberculosis (TB) continues to intimidate the human race since time immemorial not only due to its effects as a medical malady, but also by its impact as a social and economic tragedy. At the dawn of the new millennium, we are still mute witnesses to the silent yet efficient march of this sagacious disease, its myriad manifestations and above all its unequalled, vicious power.”

Our news journalists obtained a quote from the research, “Through the millennia, TB never ever disappeared from the developing world. In 1991, the World Health Assembly (WHA) resolution recognized TB as a major global public health problem. The DOTS strategy was launched in 1994, and became the global recommended strategy for TB control since then. The present study deals with clinical evaluation of Rasayana drugs considering of Amalaki (Emblica officinalis Gaertn.), Guduchi (Tinospora cordifolia willd.), Ashwagandha (Withania somnifera L.) Dunal, Yastimadhu (Glycyrrhiza glabra Linn.), Pippali (Piper longum Linn.), Sariva (Hemidesmus indicus R.Br.), Kustha (Saussurea lappa Falc.), Haridra (Curcuma longa Linn.) and Kulinjan (Alpinia galangal Linn.) as an adjuvant therapy with anti-Koch’s treatment.”

According to the news editors, the research concluded: “The results obtained revealed that Rasayana compound was found to decrease cough (83%), fever (93%), dyspnea (71.3%), hemoptysis (87%) and increase body weight (7.7%) with statistically highly significant (p <0.”

For more information on this research see: Clinical evaluation of Rasayana compound as an adjuvant in the management of tuberculosis with anti-Koch’s treatment. Ayu, 2012;33(1):38-43.

The news correspondents report that additional information may be obtained from P. Vyas, Ksharasutra Vaidya, Smt Maniben Govt Ayurvedic Hospital, Ahmedabad, India. (2012 Oct 30)
CHAPTER 7  THERAPIES AND TREATMENTS

Complutense University, Madrid: Susceptibility testing to second-line drugs and ethambutol by Genotype MTBDRsl and Bactec MGIT 960 comparing with agar proportion method

By a News Reporter-Staff News Editor at TB & Outbreaks Week – Current study results on Tuberculosis and Lung Disease have been published. According to news reporting out of Madrid, Spain, by NewsRx editors, research stated, “The incidence of multidrug-resistant tuberculosis (MDRTB) is increasing. Rapid detection of resistance to second-line drugs is essential for patient management and efficient control of tuberculosis.”

Our news journalists obtained a quote from the research from Complutense University, “The aim of the present study was to assess the ability of the GenoType MTBDRsl DNA strip and the Bactec MGIT 960 assay to detect resistance to second-line drugs and ethambutol in multidrug-resistant clinical isolates using the agar proportion method as a reference technique. Twenty-six Mycobacterium tuberculosis complex isolates identified as multidrug-resistant on the basis of conventional drug susceptibility testing were retrieved from our laboratory archive (1992-2010) for evaluation. The susceptibility of these strains to second-line drugs and ethambutol was tested prospectively using MGIT 960 and GenoType MTBDRsl. The turnaround time for agar proportion, MGIT 960, and GenoType MTBDRsl were, respectively, 21 days, 8 days, and 8 h. Sensitivity values for MGIT 960 and GenoType MTBDRsl were, respectively, ethambutol (85.7, 28.6%), amikacin (50, 75%), and ofloxacin (50, 83.3%). Specificity values were, respectively, ethambutol (73.7, 89.5%), amikacin (72.7, 95.5%), and ofloxacin (100, 100%). Our data show that both methods have significant limitations and cannot replace conventional drug susceptibility testing.”

According to the news editors, the research concluded: “The results of resistance testing should be interpreted with caution and confirmed using the reference method.”


Our news journalists report that additional information may be obtained by contacting P. Lopez-Roa, Univ Complutense, Dept. of Med, Fac Med, E-28040 Madrid, Spain. (2012 Oct 30)
University of Oslo: Diagnostic and treatment delay among Tuberculosis patients in Afar Region, Ethiopia: A cross-sectional study

By a News Reporter-Staff News Editor at Life Science Weekly – Research findings on Public Health are discussed in a new report. According to news reporting originating in Oslo, Norway, by NewsRx journalists, research stated, “TB is a major public health problem globally and Ethiopia is 8th among the 22 high burden countries. Early detection and effective treatment are pre-requisites for a successful TB control programme.”

The news reporters obtained a quote from the research from the University of Oslo, “In this regard, early health seeking action from patients’ side and prompt diagnosis as well as initiation of treatment from the health system’s side are essential steps. The aim of this study was to assess delay in the diagnosis and treatment of TB in a predominantly pastoralist area in Ethiopia. On a cross-sectional study, two hundred sixteen TB patients who visited DOTS clinics of two health facilities in Afar Region were included consecutively. Time from onset of symptoms till first consultation of formal health providers (patients’ delay) and time from first consultation till initiation of treatment (health system’s delay) were analyzed. The median patients’ and health system’s delay were 20 and 33.5 days, respectively. The median total delay was 70.5 days with a median treatment delay of 1 day. On multivariate logistic regression, self-treatment (aOR. 3.99, CI 1.50-10.59) and first visit to non-formal health providers (aOR. 6.18, CI 1.84-20.76) were observed to be independent predictors of patients’ delay. On the other hand, having extra-pulmonary TB (aOR. 2.08, CI 1.08-4.04), and a first visit to health posts/clinics (aOR. 19.70, CI 6.18-62.79), health centres (aOR. 4.83, CI 2.23-10.43) and private health facilities (aOR. 2.49, CI 1.07-5.84) were found to be independent predictors of health system’s delay. There is a long delay in the diagnosis and initiation of treatment and this was mainly attributable to the health system.”

According to the news reporters, the research concluded: “Health system strengthening towards improved diagnosis of TB could reduce the long health system’s delay in the management of TB in the study area.”

Osaka City University Graduate School of Medicine: A novel mechanism of growth phase-dependent tolerance to isoniazid in mycobacteria

By a News Reporter-Staff News Editor at Tuberculosis Week – Investigators publish new report on Biological Chemistry. According to news reporting originating from Osaka, Japan, by NewsRx correspondents, research stated, “Tuberculosis remains one of the most deadly infectious diseases worldwide and is a leading public health problem. Although isoniazid (INH) is a key drug for the treatment of tuberculosis, tolerance to INH necessitates prolonged treatment, which is a concern for effective tuberculosis chemotherapy.”

Our news editors obtained a quote from the research from the Osaka City University Graduate School of Medicine, “INH is a prodrug that is activated by the mycobacterial enzyme, KatG. Here, we show that mycobacterial DNA-binding protein 1 (MDP1), which is a histone-like protein conserved in mycobacteria, negatively regulates katG transcription and leads to phenotypic tolerance to INH in mycobacteria. Mycobacterium smegmatis deficient for MDP1 exhibited increased expression of KatG and showed enhanced INH activation compared with the wild-type strain. Expression of MDP1 was increased in the stationary phase and conferred growth phase-dependent tolerance to INH in M. smegmatis. Regulation of KatG expression is conserved between M. smegmatis and Mycobacterium tuberculosis complex. Artificial reduction of MDP1 in Mycobacterium bovis BCG was shown to lead to increased KatG expression and susceptibility to INH.”

According to the news editors, the research concluded: “These data suggest a mechanism by which phenotypic tolerance to INH is acquired in mycobacteria.”


The news editors report that additional information may be obtained by contacting M. Niki, Dept. of Bacteriology, Virology, Osaka City University Graduate School of Medicine, 1-4-3 Asahi-machi, Osaka 545-8585, Japan. (2012 Oct 29)
National Institutes of Health, Bethesda: Metronidazole prevents reactivation of latent Mycobacterium tuberculosis infection in macaques

By a News Reporter-Staff News Editor at Biotech Week – Current study results on Mycobacterium Infections have been published. According to news reporting originating in Bethesda, Maryland, by NewsRx journalists, research stated, “Targeting Mycobacterium tuberculosis bacilli in low-oxygen microenvironments, such as caseous granulomas, has been hypothesized to have the potential to shorten therapy for active tuberculosis (TB) and prevent reactivation of latent infection. We previously reported that upon low-dose M. tuberculosis infection, equal proportions of cynomolgus macaques develop active disease or latent infection and that latently infected animals reactivated upon neutralization of TNF.”

The news reporters obtained a quote from the research from the National Institutes of Health, “Using this model we now show that chemoprophylaxis of latently infected cynomolgus macaques with 6 mo of isoniazid (INH) effectively prevented anti-TNF antibody-induced reactivation. Similarly, 2-mo treatment of latent animals with a combination of INH and rifampicin (RIF) was highly effective at preventing reactivation disease in this model. Metronidazole (MTZ), which has activity only against anaerobic, nonreplicating bacteria, was as effective as either of these treatments in preventing reactivation of latent infection. Because hypoxic lesions also occur during active TB, we further showed that addition of MTZ to INH/RIF effectively treated animals with active TB within 2 mo. Healing lesions were associated with distinct changes in cellular pathology, with a shift toward increasingly fibrotic and calcified lesions.”

According to the news reporters, the research concluded: “Our data in the nonhuman primate model of active and latent TB supports targeting bacteria in hypoxic environments for preventing reactivation of latent infection and possibly shortening the duration of therapy in active TB.”

Columbia University, New York City: Substitution of Rifapentine for Rifampin During Intensive Phase Treatment of Pulmonary Tuberculosis: Study 29 of the Tuberculosis Trials Consortium

By a News Reporter-Staff News Editor at Ivy League Week – Investigators publish new report on Mycobacterium Infections. According to news reporting originating in New York City, New York, by NewsRx journalists, research stated, “In total, 531 adults with sputum smear-positive pulmonary tuberculosis were randomized to rifapentine 10 mg/kg/dose or rifampin 10 mg/kg/dose, administered 5 days per week for 8 weeks (intensive phase), with isoniazid, pyrazinamide, and ethambutol. Coprimary outcomes were negative sputum culture on liquid and on solid media at completion of intensive phase.”

The news reporters obtained a quote from the research from Columbia University, “Negative cultures on solid media occurred in 145 of 174 participants (83.3%) in the rifampin group and 171 of 198 participants (86.4%) in the rifapentine group (difference, 3.0%; 95% confidence interval [CI]: -4.3, 10.5); negative cultures in liquid media occurred in 110 of 169 (65.1%) in the rifampin group and 133 of 196 (67.9%) in the rifapentine group (difference, 2.8%; 95% CI: -6.9, 12.4). Among 529 participants who received study therapy, 40 of 254 participants (15.7%) in the rifampin group and 40 of 275 participants (14.5%) in the rifapentine group prematurely discontinued treatment (P = .79). The rifapentine regimen was safe but not significantly more active than a standard rifampin regimen, by the surrogate endpoint of culture status at completion of intensive phase.”

According to the news reporters, the research concluded: “Assessment of higher exposures to rifapentine for tuberculosis treatment is warranted. Clinical Trials registration. NCT00694629.”


Our news correspondents report that additional information may be obtained by contacting S.E. Dorman, Columbia University, Medical Center, New York, NY, United States. (2012 Oct 23)
St. Jude Children’s Research Hospital, Memphis: Antitubercular nitrofuran isoxazolines with improved pharmacokinetic properties

By a News Reporter-Staff News Editor at Pharma Business Week – Data detailed on Bioorganic and Medicinal Chemistry have been presented. According to news reporting originating in Memphis, Tennessee, by NewsRx journalists, research stated, “A series of tetracyclic nitrofuran isoxazoline anti-tuberculosis agents was designed and synthesized to improve the pharmacokinetic properties of an initial lead compound, which had potent anti-tuberculosis activity but suffered from poor solubility, high protein binding and rapid metabolism. In this study, structural modifications were carried on the outer phenyl and piperidine rings to introduce solubilizing and metabolically blocking functional groups.”

The news reporters obtained a quote from the research from St. Jude Children’s Research Hospital, “The compounds generated were evaluated for their in vitro antitubercular activity, bacterial spectrum of activity, solubility, permeability, microsomal stability and protein binding. Pharmacokinetic profiles for the most promising candidates were then determined. Compounds with phenyl morpholine and pyridyl morpholine outer rings were found to be the most potent anti-tuberculosis agents in the series. These compounds retained a narrow antibacterial spectrum of activity, with weak anti-Gram positive and no Gram negative activity, as well as good activity against non-replicating Mycobacterium tuberculosis in a low oxygen model. Overall, the addition of solubilizing and metabolically blocked outer rings did improve solubility and decrease protein binding as designed. However, the metabolic stability for compounds in this series was generally lower than desired.”

According to the news reporters, the research concluded: “The best three compounds selected for in vivo pharmacokinetic testing all showed high oral bioavailability, with one notable compound showing a significantly longer half-life and good tolerability supporting its further advancement.”


Our news correspondents report that additional information may be obtained by contacting R.a.k.e.s.h., Dept. of Chemical Biology and Therapeutics, St Jude Children’s Research Hospital, Memphis, TN, United States. (2012 Oct 22)
Department of Pulmonology, Istanbul: Serum CA-125: biomarker of pulmonary tuberculosis activity and evaluation of response to treatment

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – Investigators discuss new findings in Investigative Medicine. According to news reporting from Istanbul, Turkey, by NewsRx journalists, research stated, “CA-125 is a high molecular weight mucin-like glycoprotein and an ovarian cancer antigen. Elevated CA-125 levels are also seen with various other benign and malignant conditions.”

The news correspondents obtained a quote from the research from the Department of Pulmonology, “In this study, the ability of CA-125 to predict pulmonary tuberculosis activity was investigated. This analytical study included 42 cases with active tuberculosis (Group 1), 35 cases with inactive tuberculosis (Group 2) and 20 healthy subjects (Group 3). CA-125 measurements were taken in all three groups. Measurements in Group 1 were repeated after completing a two month anti-tuberculosis treatment in 38 of the 42 patients. Mean serum CA-125 level for Group 1 was 76.48 +/- 24.71 U/mL, which was significantly higher than levels in Group 2 (20.01 +/- 7.89 U/mL) and Group 3 (18.32 +/- 2.87 U/mL) (p <0.001). Of the 38 patients in Group 1 who were studied both pre- and post-treatment, CA-125 levels decreased significantly: from 78.88 +/- 24.72 U/mL before treatment to 22.78 +/- 8.02 U/mL after treatment (p <0.001). There was no statistically significant difference between the post-treatment values of Group 1 and either Group 2 and Group 3 values (p >0.05). Group 2 and Group 3 levels were not significantly different (p >0.05). The cut-off level for accurate determination of activity was 36.35 U/mL. The sensitivity at this level was 97.6% and specificity was 100%.”

According to the news reporters, the researchers concluded: “Our findings suggest that CA-125 can be a beneficial parameter in determination of pulmonary tuberculosis activity and the evaluation of response to treatment.”

For more information on this research see: Serum CA-125: biomarker of pulmonary tuberculosis activity and evaluation of response to treatment. *Clinical and Investigative Medicine, 2012;35(4):L223-L228. Clinical and Investigative Medicine* can be contacted at: Canadian Soc Clinical Investigation, Csci Head Office, 774 Echo Drive, Ottawa, On K1S 5N8, Canada.

University of Alexandria: Acute tuberculous abscess of the thyroid gland

By a News Reporter-Staff News Editor at Tuberculosis Week – Current study results on Tuberculosis have been published. According to news reporting originating from Alexandria, Egypt, by NewsRx correspondents, research stated, “The authors are presenting our experience of managing an interesting case of a 28-year-old woman who presented to our clinic with a midline neck swelling of 1-month duration. There was a rapid increase in the degree of swelling associated with erythema, pain and fever 7 days before seeking medical help.”

Our news editors obtained a quote from the research from the University of Alexandria, “Plain and contrast-enhanced CT scans of the neck were done. Diagnosis of acute suppurative abscess was made and the patient underwent emergency incision and drainage. Histopathological examination of the abscess wall showed epitheloid and Langhans’ giant cells. The findings were suggestive of tuberculosis. Subsequently, a positive culture for Mycobacterium tuberculosis was obtained on Lowenstein-Jenson medium. The patient was started on antituberculous chemotherapy for 6 months. On a 6-month clinical follow-up, the patient was asymptomatic and euthyroid.”

According to the news editors, the researchers concluded: “We discuss the clinical presentation, diagnosis and treatment of this case as well as a review of the literature.”

For more information on this research see: Acute tuberculous abscess of the thyroid gland. Bmj Case Reports, 2012;2012():. (BMJ Publishing Group - http://group.bmj.com/; Bmj Case Reports - http://casereports.bmj.com/)

The news editors report that additional information may be obtained by contacting M. Bahgat, Dept. of ENT and Head & Neck Surgery, Alexandria University Hospitals, Alexandria, Egypt. (2012 Oct 15)

University of Colorado, Denver: Successful Treatment of Pediatric Latent Tuberculosis Infection in a Community Health Center Clinic

By a News Reporter-Staff News Editor at Pediatrics Week – Research findings on Mycobacterium Infections are discussed in a new report. According to news originating from Denver, Colorado, by VerticalNews correspondents, research stated, “This study evaluates completion of treatment for latent tuberculosis infection (LTBI) in Mexican immigrant children aged 1-18 years in a Community Health Center (CHC). Children were screened for LTBI at a CHC.”

Our news journalists obtained a quote from the research from the University of Colorado, “All children with a tuberculin skin test (TST)
>= 10 mm had a chest radiograph (CXR). Those with negative CXR had nurse appointments to collect demographic information and to begin 9 months of INH treatment. A minimum 6 months of INH treatment defined completion. Between November 15, 2006 and March 15, 2009, 157 children had positive TSTs. Three never had a CXR, 2 had misdiagnosed LTBI and 2 had asymptomatic active tuberculosis. Of 150 with LTBI, 111 (74%) completed INH at CHC. Thirteen (9%) transferred care to school-based clinics or TB clinic (TBC) and 4 (3%) never started treatment. Twenty-two (15%) did not complete treatment at CHC. One developed INH hepatitis and 21 were lost to follow-up. Of 13 who transferred to school-based clinics/TBC, 10 completed therapy, with 121 (81%) completing treatment started at CHC. By logistic regression factors associated with not starting/incomplete LTBI treatment were older age, increased number of days between TST and CXR, and 0-1 well care visits versus >= 2 visits before TST placement. A visit co-pay >= $15.00 was associated with transfer of care to school-based clinics/TBC. Pediatric LTBI can be successfully treated by CHC nurses.”

According to the news editors, the researchers concluded: “Completion of treatment was associated with younger age, fewer days between TST reading and CXR, and being an established patient in the CHC.”

For more information on this research see: Successful Treatment of Pediatric Latent Tuberculosis Infection in a Community Health Center Clinic. Pediatric Infectious Disease Journal, 2012;31(9):E147-E151. Pediatric Infectious Disease Journal can be contacted at: Lippincott Williams & Wilkins, 530 Walnut St, Philadelphia, PA 19106-3621, USA. (Lippincott Williams and Wilkins - www.lww.com; Pediatric Infectious Disease Journal - http://journals.lww.com/pidj/pages/default.aspx)

The news correspondents report that additional information may be obtained from J. Young, University of Colorado, Sch Med, Denver, CO 80202, United States. (2012 Oct 13)

University of KwaZulu-Natal, Durban: Tuberculosis among adults starting antiretroviral therapy in South Africa: the need for routine case finding

By a News Reporter-Staff News Editor at Biotech Week – New research on Tuberculosis and Lung Disease is the subject of a report. According to news reporting out of Durban, South Africa, by NewsRx editors, research stated, “To investigate the prevalence of and evaluate screening modalities for undiagnosed tuberculosis (TB) in antiretroviral therapy (ART) eligible adults in South Africa. Individuals were screened for TB using symptoms, chest radiograph (CXR) and two sputum specimens for microscopy and culture, and were then followed for &lt;6 months to determine TB diagnoses.”
CHAPTER 7  THERAPIES AND TREATMENTS

Our news journalists obtained a quote from the research from the University of KwaZulu-Natal, “Among 361 participants (67% female, median age 38 years, median CD4 count 120 cells/mm(3)), 64 (18%) were sputum culture-positive; 114 (32%) fulfilled any TB case definition (culture- and/or smear-positive, or improvement on specific treatment). Symptom screening comprising any of cough, appetite loss or night sweats >2 weeks had a sensitivity and specificity of respectively 74.5% and 50.8%. Sensitivity was increased by CXR (to 96.1%), but not by smear microscopy. The World Health Organization symptom screen had a sensitivity and specificity of respectively 96.1% and 5.2% in our study population; the addition of CXR increased sensitivity to 100%. Median time to TB treatment was 8 days for diagnoses based on CXR (n = 72) vs. 37 days for diagnoses based only on sputum culture (n = 14). The very high prevalence of undiagnosed TB among patients presenting for ART mandates their routine investigation.”

According to the news editors, the researchers concluded: “CXR improved sensitivity substantially, allowed rapid treatment initiation and should be routine, where available, pending better point-of-care diagnostics.”

For more information on this research see: Tuberculosis among adults starting antiretroviral therapy in South Africa: the need for routine case finding. International Journal of Tuberculosis and Lung Disease, 2012;16(9):1252-1259. International Journal of Tuberculosis and Lung Disease can be contacted at: Int Union Against Tuberculosis Lung Disease (I U A T L D), 68 Boulevard Saint-Michel, 75006 Paris, France.

Our news journalists report that additional information may be obtained by contacting Y. Hanifa, University of KwaZulu Natal, Center AIDS Programme Res S Africa, Durban, South Africa. (2012 Oct 10)

Division of Rheumatology, Fortaleza: Tuberculosis infection in rheumatic patients with infliximab therapy: experience with 157 patients

By a News Reporter-Staff News Editor at Life Science Weekly – Current study results on Rheumatology have been published. According to news reporting originating in Fortaleza, Brazil, by NewsRx journalists, research stated, “It is recommended to evaluate the presence of latent tuberculosis infection (LTBI) prior to the use of antitumor necrosis factor alpha. The aim of this study is to assess the presence of LTBI in patients with rheumatic diseases undergoing treatment with infliximab in an endemic area for tuberculosis (TB).”

The news reporters obtained a quote from the research from the Division of Rheumatology, “LTBI was searched through the contact history, chest X-ray and tuberculin skin test with purified protein derivative (PPD) a parts per thousand yen5 mm. We studied 157 patients
in the period from May 2005 to October 2008, 99 (63.1%) were women with average age of 49 years and 58 (36.9%) were men with average age of 41 years. The group comprising 90 patients (57.3%) with rheumatoid arthritis (RA), 54 (34.4%) with ankylosing spondylitis (AS) and 13 (8.3%) with psoriatic arthritis (PsA) had PPD reactor 13.4% (21/157), being prevented by isoniazid (INH) in these patients. There are dissimilar responsiveness to the PPD between the three pathologies, and the reactivity was lower in RA (RA x AS: \( \chi^2(2) = 12; P = 0.0004 \); and RA x PsA: \( \chi^2(2) \) with Yates’ correction = 3.6; \( P = 0.05 \)). No significant difference between the reactivity of the PPD and the use of immunosuppressive drugs (\( P = 0.81 \)) is observed. The immunoprophylaxis with INH showed an efficacy of 95% (20/21); three (1.9%) patients developed active TB (spondylodiscitis, meningitis and lymphadenopathy) after the use of infliximab, reaffirming extrapulmonary involvement.”

According to the news reporters, the researchers concluded: “These results suggest that PPD has a low sensitivity for detection of LTBI in RA and that the previous use of immunosuppressive drugs does not affect the response to PPD.”


Our news correspondents report that additional information may be obtained by contacting C.A. Nobre, Hosp Geral Fortaleza, Div Rheumatol, Fortaleza, Ceara, Brazil. (2012 Oct 09)

**Ministry of Health, Rabat: Qualitative study of perceived causes of tuberculosis treatment default among health care workers in Morocco**

By a News Reporter-Staff News Editor at Life Science Weekly – A new study on Tuberculosis and Lung Disease is now available. According to news reporting from Rabat, Morocco, by NewsRx journalists, research stated, “In Morocco, tuberculosis (TB) treatment default is increasing in some urban areas. To provide a detailed description of factors that contribute to patient default and solutions from the point of view of health care professionals who participate in TB care.”

The news correspondents obtained a quote from the research from the Ministry of Health, “In-depth interviews were conducted with 62 physicians and nurses at nine regional public pulmonary clinics and local health clinics. Participants had a median of 24 years of experience in health care. Treatment default was seen as a result of multilevel
factors related to the patient (lack of means, being a migrant worker, distance to treatment site, poor understanding of treatment, drug use, mental illness), medical team (high patient load, low motivation, lack of resources for tracking defaulters), treatment organization (poor communication between treatment sites, no systematic strategy for patient education or tracking, incomplete record keeping), and health care system and society. Tailored recommendations for low- and higher-cost interventions are provided. Interventions to enhance TB treatment completion should take into account the local context and multilevel factors that contribute to default.”

According to the news reporters, the researchers concluded: “Qualitative studies involving health care workers directly involved in TB care can be powerful tools to identify contributing factors and define strategies to help reduce treatment default.”

For more information on this research see: Qualitative study of perceived causes of tuberculosis treatment default among health care workers in Morocco. International Journal of Tuberculosis and Lung Disease, 2012;16(9):1214-1220. International Journal of Tuberculosis and Lung Disease can be contacted at: Int Union Against Tuberculosis Lung Disease (I U A T L D), 68 Boulevard Saint-Michel, 75006 Paris, France.

Our news journalists report that additional information may be obtained by contacting D. Kizub, Minist Hlth, Directorate Epidemiol & Dis Control, Natl TB Control Programme, Rabat, Morocco. (2012 Oct 09)

School of Public Health, Gothenburg: Towards an empowerment approach in tuberculosis treatment in Cape Town, South Africa: a qualitative analysis of programmatic change

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators publish new report on Global Health. According to news reporting from Gothenburg, Sweden, by NewsRx journalists, research stated, “Tuberculosis rates in the world remain high, especially in low- and middle-income countries. International tuberculosis (TB) policy generally recommends the use of directly observed therapy (DOT) to ensure treatment adherence.”

The news correspondents obtained a quote from the research from the School of Public Health, “This article examines a change in TB treatment support that occurred in 2005 in South Africa, from DOT to the enhanced TB adherence programme (ETA). Seven key individuals representing academics, policy makers and service providers involved in the development of the ETA programme or knowledgeable about the
issue were purposively sampled and interviewed, and participant observation was conducted at ETA programme steering group meetings. Qualitative content analysis was used to analyse the data, drawing on the Kingdon model of agenda setting. This model suggests that three independent streams - problem, policy and politics - come together at a certain point, often facilitated by policy entrepreneurs, to provide an opportunity for an issue to enter the policy agenda. The results suggest the empowerment-oriented programme emerged through the presence of policy entrepreneurs with access to resources. Policy entrepreneurs were influenced by a number of simultaneously occurring challenges including problems within the existing programme; a perceived mismatch between patient needs and the existing TB treatment model; and the TB-HIV co-epidemic. Policy entrepreneurs saw the ART approach as a possible solution to these challenges. The Kingdon model contributed to describing the process of policy change.”

According to the news reporters, the researchers concluded: “Research evidence seemed to influence this change diffusely, through the interaction of policy entrepreneurs and academics.”


Our news journalists report that additional information may be obtained by contacting S. Atkins, Nord Sch Public Hlth, Hlth Promot Res Grp, Gothenburg, Sweden. *(2012 Oct 09)*


By a News Reporter-Staff News Editor at Tuberculosis Week – Data detailed on Mycobacterium Infections have been presented. According to news reporting from Orsay, France, by NewsRx journalists, research stated, “To evaluate the potential of F-18-fluorodeoxyglucose positron emission tomography/computed tomography (F-18-FDG PET/CT) for early therapeutic intervention in patients with probable or confirmed tuberculosis (TB). Twenty-one consecutive human immunodeficiency virus negative patients were prospectively included.”

The news correspondents obtained a quote from the research from Alternative Energies and Atomic Energy Commission, “All patients underwent F-18-FDG PET/CT before and after 1 month of anti-tuberculosis treatment. The maximum standardised uptake value (SU-Vmax) of the most F-18-FDG avid lesions was recorded. The median age of patients was 36 years (range 18-84); 33.3% were male, 80.9% were
born in endemic countries, and 23.8% had a past history of TB. TB was confirmed on culture in 8, on histology in 9 and on the basis of clinical symptoms in 4 patients. F-18-FDG PET/CT detected active pulmonary TB (n = 1), extra-pulmonary (n = 10) or both (n = 10). The second F-18-FDG PET/CT showed reduced radiotracer uptake intensity in 19 of 21 patients, with a median percentage decrease of SUVmax of 31% (range 2-84). Two patients showed no improvement. TB was ruled out in one patient during follow-up; the final diagnosis was a non-Hodgkin’s lymphoma. The other patient was smear-positive for 3 months.”

According to the news reporters, the researchers concluded: “F-18-FDG PET/CT allows an easy evaluation of early therapeutic response in patients with TB, particularly extra-pulmonary TB.”


Our news journalists report that additional information may be obtained by contacting V. Martinez, Center Hosp Frederic Jolliot, Commissariat Energie Atom & Energies Alternat Ors, Serv Med Nucl, Orsay, France. (2012 Oct 08)

Efficacy of serum chitotriosidase activity in early treatment of patients with active tuberculosis and a negative sputum smear

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – New research on Respiratory Therapeutics is the subject of a report. According to news reporting out of Istanbul, Turkey, by NewsRx editors, research stated, “The results of sputum culture for Mycobacterium tuberculosis must be awaited in most cases, which delays the start of treatment in patients with sputum smear-negative pulmonary tuberculosis. We investigated whether plasma chitotriosidase activity is a strong marker for early diagnosis of tuberculosis in patients for whom a bacillus smear is negative and tuberculosis culture is positive.”

Our news journalists obtained a quote from the research, “Clinical, radiological, and laboratory features were evaluated in 75 patients, 17 of whom were diagnosed as having active tuberculosis by negative acid-fast bacillus smear and positive culture, 38 as having sequel tuberculosis which was radiologically and microbiologically negative, and 20 who served as healthy controls. Serum chitotriosidase activity levels were measured in both cases and controls. The mean age of the cases with active pulmonary tuberculosis, cases with sequel lesions, and controls was 23 +/- 2.4 years, 22 +/- 1.7 years, and 24 +/-
2.1 years, respectively. Serum chitotriosidase levels were 68.05 +/- 72.61 nmol/hour/mL in smear-negative, culture-positive pulmonary tuberculosis cases (Group A) and 29.73 +/- 20.55 nmol/hour/mL in smear-negative, culture-negative sequel pulmonary tuberculosis cases (Group B). Serum chitotriosidase levels from patients in Group A were significantly higher than in Group B and Group C. There was no statistically significant difference in serum chitotriosidase levels between cases with sequel pulmonary tuberculosis (Group B, smear-negative, culture-negative) and healthy controls (Group C).

According to the news editors, the researchers concluded: “In patients with active tuberculosis and a negative sputum smear for acid-fast bacillus, plasma chitotriosidase activity seems to be a strong marker for diagnosis of active disease which can be used while awaiting culture results.”


Our news journalists report that additional information may be obtained by contacting C. Tasci, Istanbul Gulhane Med Fac, Dept. of Pulm Dis, Istanbul, Turkey. (2012 Oct 08)

**Government Medical College, Amritsar: Manifestations of tuberculosis in elderly versus young hospitalised patients in Amritsar, India**

By a News Reporter-Staff News Editor at Tuberculosis Week – Current study results on Mycobacterium Infections have been published. According to news reporting originating from Amritsar, India, by NewsRx correspondents, research stated, “Published literature on the clinical characteristics of tuberculosis (TB) among elderly patients in India is scarce, as the problem of geriatric TB has not received the attention it deserves. To compare the manifestations of TB among elderly and young patients.”

Our news editors obtained a quote from the research from Government Medical College, “Medical records of elderly and young TB patients were extracted and compared. Elderly patients had less frequent respiratory and constitutional symptoms, but a higher prevalence of comorbidities. The median duration of symptoms was also longer in the elderly. Both groups were similar on physical examination, except that the elderly had a higher frequency of development of jaundice following anti-tuberculosis chemotherapy. Human immunodeficiency virus positivity was only present among the younger group. Both groups had
significant proportions of alcoholics and drug abusers, but lesser percentage of smokers. Total admission analysis showed a male preponderance. The presentation of TB in elderly patients differs from that of younger patients in symptomatology.”

According to the news editors, the researchers concluded: “A high index of suspicion is therefore required to make a timely diagnosis of TB in the elderly.”

For more information on this research see: Manifestations of tuberculosis in elderly versus young hospitalised patients in Amritsar, India. *International Journal of Tuberculosis and Lung Disease*, 2012;16(9):1210-1213. *International Journal of Tuberculosis and Lung Disease* can be contacted at: Int Union Against Tuberculosis Lung Disease (I U A T L D), 68 Boulevard Saint-Michel, 75006 Paris, France.

The news editors report that additional information may be obtained by contacting B. Bhushan, Govt Med College, Dept. of TB & Chest Dis, Amritsar, Punjab, India. *(2012 Oct 08)*

University of Medicine and Dentistry of New Jersey (UMDNJ), Newark: A Ferritin Mutant of Mycobacterium tuberculosis Is Highly Susceptible to Killing by Antibiotics and Is Unable To Establish a Chronic Infection in Mice

By a News Reporter-Staff News Editor at Health & Medicine Week – A new study on Mycobacterium Infections is now available. According to news reporting from Newark, New Jersey, by NewsRx journalists, research stated, “Iron is an essential, elusive, and potentially toxic nutrient for most pathogens, including *Mycobacterium tuberculosis*. Due to the poor solubility of ferric iron under aerobic conditions, free iron is not found in the host. *M. tuberculosis* requires specialized iron acquisition systems to replicate and cause disease.”

The news correspondents obtained a quote from the research from the University of Medicine and Dentistry of New Jersey (UMDNJ), “It also depends on a strict control of iron metabolism and intracellular iron levels to prevent iron-mediated toxicity. Under conditions of iron sufficiency, *M. tuberculosis* represses iron acquisition and induces iron storage, suggesting an important role for iron storage proteins in iron homeostasis. *M. tuberculosis* synthesizes two iron storage proteins, a ferritin (BfrB) and a bacterioferritin (BfrA). The individual contributions of these proteins to the adaptive response of *M. tuberculosis* to changes in iron availability are not clear. By generating individual knockout strains of bfrA and bfrB, the contribution of each one of these proteins to the maintenance of iron homeostasis was determined. The effect of altered iron homeostasis, resulting from impaired iron storage, on the resistance of *M. tuberculosis* to in vitro and in vivo stresses was
examined. The results show that ferritin is required to maintain iron homeostasis, whereas bacterioferritin seems to be dispensable for this function. *M. tuberculosis* lacking ferritin suffers from iron-mediated toxicity, is unable to persist in mice, and, most importantly, is highly susceptible to killing by antibiotics, showing that endogenous oxidative stress can enhance the antibiotic killing of this important pathogen.”

According to the news reporters, the researchers concluded: “These results are relevant for the design of new therapeutic strategies against M.”

For more information on this research see: A Ferritin Mutant of Mycobacterium tuberculosis Is Highly Susceptible to Killing by Antibiotics and Is Unable To Establish a Chronic Infection in Mice. *Infection and Immunity*, 2012;80(10):3650-9. (American Society for Microbiology - www.asm.org; Infection and Immunity - iai.asm.org)

Our news journalists report that additional information may be obtained by contacting R. Pandey, Public Health Research Institute and Dept. of Medicine, University of Medicine and Dentistry of New Jersey, New Jersey Medical School, Newark, New Jersey, United States. (2012 Oct 05)

**University of Cape Town, Rondebosch: Approaches to target identification and validation for tuberculosis drug discovery: A University of Cape Town perspective**

By a News Reporter-Staff News Editor at Biotech Week – Investigators publish new report on Mycobacterium Infections. According to news reporting out of Rondebosch, South Africa, by NewsRx editors, research stated, “Tuberculosis (TB) disproportionately affects a few high-burden countries including South Africa. In these regions, basic TB research is rare, endemic countries being valued primarily as sites for drug trials and clinical studies.”

Our news journalists obtained a quote from the research from the University of Cape Town, “Our basic mycobacterial research focuses on current approaches to drug target identification and validation within the context of international trends in TB drug discovery. Increased funding for TB drug development globally prompted a significant shift in the composition of drug discovery consortia, with academic laboratories assuming a major role in collaboration with industrial partners. This hybrid model holds promise for the expansion of local programmes, especially where actively supported by government.”

According to the news editors, the researchers concluded: “However, the application of industry-standard business practices to research projects involving biology and chemistry expertise demands a
greater appreciation of the differences between a chemically, versus biologically, validated drug target, and of the factors informing these differences.”


Our news journalists report that additional information may be obtained by contacting D.F. Warner, University of Cape Town, Inst Infect Dis & Mol Med, DST NRF Center Excellence Biomed TB Res, MRC NHLS UCT Mol Mycobacteriol Res Unit, ZA-7700 Rondebosch, South Africa. (2012 Oct 03)

**Athens University School of Medicine: Breast tuberculosis: Diagnosis, management and treatment**

By a News Reporter-Staff News Editor at Life Science Weekly – A new study on Surgery Case Reports is now available. According to news reporting originating from Athens, Greece, by NewsRx correspondents, research stated, “Mammary (breast) tuberculosis is a rare manifestation of extra-pulmonary localization of the disease which accounts for less than 0.1% of breast conditions in developed countries, but reaches 3-4% in regions where the disease presents with high incidence (India, Africa). It appears mostly in women of reproductive age, multiparous, lactating.”

Our news editors obtained a quote from the research from the Athens University School of Medicine, “It has been scarcely reported to infect male patients, mainly before puberty, as well as women of older age. The most common presentation is that of a tumor in the middle or upper-outer quadrant of the breast, with multifocal involvement being rarely documented.”

According to the news editors, the researchers concluded: “The differential diagnosis includes breast cancer and abscess formation.”


The news editors report that additional information may be obtained by contacting S. Marinopoulos, Breast Unit, 1st Obstetrics and Gynecology Department, Athens University Medical School, Alexandra Hospital, Athens, Greece. (2012 Oct 02)
Center for Disease Control and Prevention, Atlanta: Predictors of failure in timely tuberculosis treatment completion, United States

By a News Reporter-Staff News Editor at Life Science Weekly – Fresh data on Tuberculosis and Lung Disease are presented in a new report. According to news reporting from Atlanta, Georgia, by NewsRx journalists, research stated, “The US tuberculosis (TB) surveillance system. To examine failure in timely TB treatment completion to identify interventions toward achieving the national goal of >= 93% treatment completion in <= 12 months among patients eligible for 6-9 month regimens.”

The news correspondents obtained a quote from the research from Center for Disease Control and Prevention, “We examined 1993-2006 trends in timely treatment completion; for 2006 cases, we used Poisson regression to assess predictors for failure in timely completion. Timely treatment completion improved from 64% in 1993 to 84% in 2006, with similar trends among foreign- and US-born persons and racial/ethnic subgroups. Annual increases in timely completion were <= 1 percentage point during 1998-2006. Subpopulations at highest risk for failure in timely completion were persons with combined pulmonary and extrapulmonary disease (foreign-born adjusted RR [aRR] 3.25, 95%CI 2.47-4.28; US-born aRR 2.75, 95%CI 1.98-3.83) or incarceration (foreign-born aRR 2.30, 95%CI 1.80-2.93; US-born aRR 1.71, 95%CI 1.36-2.14). Homelessness and human immunodeficiency virus infection were other risk factors. Particular attention to timely completion is needed for subpopulations requiring strong medical expertise in TB management and those at risk for treatment non-adherence, especially if foreign-born.”

According to the news reporters, the researchers concluded: “Understanding and addressing causes of delayed completion and improving documentation of treatment completion among all cases will be crucial to achieving the US goal.”

For more information on this research see: Predictors of failure in timely tuberculosis treatment completion, United States. International Journal of Tuberculosis and Lung Disease, 2012;16(8):1075-1082. International Journal of Tuberculosis and Lung Disease can be contacted at: Int Union Against Tuberculosis Lung Disease (I U A T L D), 68 Boulevard Saint-Michel, 75006 Paris, France.

Our news journalists report that additional information may be obtained by contacting K. Mitruka, Center Dis Control & Prevent, Surveillance Epidemiol & Outbreak Invest Branch, Div TB Eliminat, Atlanta, GA 30333, United States. (2012 Oct 02)
Emory University, Atlanta: Outcomes and follow-up of patients treated for multidrug-resistant tuberculosis in Orel, Russia, 2002-2005

By a News Reporter-Staff News Editor at Life Science Weekly – New research on Tuberculosis and Lung Disease is the subject of a report. According to news reporting originating from Atlanta, Georgia, by NewsRx correspondents, research stated, “Multidrug-resistant tuberculosis (MDR-TB) treatment facility, Orel Oblast, Russian Federation. To determine factors associated with poor outcome and to document status of patients after recording of TB outcomes.”

Our news editors obtained a quote from the research from Emory University, “Retrospective review of prospective single cohort. Among 192 patients, factors significantly associated with poor outcome in multivariate analysis include three or more treatment interruptions during the intensive phase of therapy and alcohol or drug addiction (adjusted OR [aOR] 2.1, 95%CI 1.0-4.3 and aOR 1.9, 95%CI 1.0-3.7). Previous treatment was associated with poor outcome, but only among smear-positive patients (aOR 3.1, 95%CI 1.3-7.3). Ten patients (5%) developed extensively drug-resistant TB (XDR-TB) during treatment; of 115 patients with at least 6 months of follow-up data after outcomes were recorded, 13 (11%) developed XDR-TB. Interventions focused on supporting patient adherence during the intensive phase of treatment; the management of drug and alcohol addiction should be developed and studied. A substantial proportion of patients developed XDR-TB during and after treatment.”

According to the news editors, the researchers concluded: “Longer term follow-up data of patients treated for MDR-TB are needed to better inform programmatic policy.”

For more information on this research see: Outcomes and follow-up of patients treated for multidrug-resistant tuberculosis in Orel, Russia, 2002-2005. International Journal of Tuberculosis and Lung Disease, 2012;16(8):1069-1074. International Journal of Tuberculosis and Lung Disease can be contacted at: Int Union Against Tuberculosis Lung Disease (I U A T L D), 68 Boulevard Saint-Michel, 75006 Paris, France.

The news editors report that additional information may be obtained by contacting J.S. Cavanaugh, Emory University, Div Infect Dis, Sch Med, Atlanta, GA 30322, United States. (2012 Oct 02)
Military Hospital, Rajasthan: Paradoxical reaction to antitubercular therapy in miliary tuberculosis

By a News Reporter-Staff News Editor at Tuberculosis Week – Data detailed on Tuberculosis have been presented. According to news originating from Rajasthan, India, by NewsRx correspondents, research stated, “An 18-year-old boy presented with fever, weight loss and loss of appetite for 6 &emsp; months duration. Investigation revealed raised erythrocyte sedimentation rate, negative sputum smear examination for acid-fast bacilli, x-ray and high-resolution CT chest showed bilateral, diffuse infiltration of lung parenchyma with miliary shadows.”

Our news journalists obtained a quote from the research from Military Hospital, “The patient was treated as a case of miliary tuberculosis with antitubercular therapy (ATT). On the 10th day of treatment the patient developed high-grade fever, cough and breathlessness. Chest x-ray showed an increased infiltration of lung parenchyma.”

According to the news editors, the researchers concluded: “The patient was diagnosed as a case of paradoxical reaction to ATT and was managed successfully with steroids.”

For more information on this research see: Paradoxical reaction to antitubercular therapy in miliary tuberculosis. Bmj Case Reports, 2012;2012(): (BMJ Publishing Group - http://group.bmj.com/; Bmj Case Reports - http://casereports.bmj.com/)

The news correspondents report that additional information may be obtained from A. Gupta, Dept. of Medical Division, Military Hospital Jodhpur, Jodhpur, Rajasthan, India. (2012 Sep 24)

University of Delhi, New Delhi: Activity of Trifluoperazine against Replicating, Non-Replicating and Drug Resistant M. tuberculosis

By a News Reporter-Staff News Editor at Tuberculosis Week – Data detailed on Mycobacterium Infections have been presented. According to news reporting from New Delhi, India, by NewsRx journalists, research stated, “Trifluoperazine, a known calmodulin antagonist, belongs to a class of phenothiazine compounds that have multiple sites of action in mycobacteria including lipid synthesis, DNA processes, protein synthesis and respiration. The objective of this study is to evaluate the potential of TFP to be used as a lead molecule for development of novel TB drugs by showing its efficacy on multiple drug resistant (MDR) Mycobacterium tuberculosis (M.tb) and non-replicating dormant M.tb.”

The news correspondents obtained a quote from the research from the University of Delhi, “Wild type and MDR M.tb were treated with TFP under different growth conditions of stress like low pH, starvation, presence of nitric oxide and in THP-1 infection model. Perturbation in
growth kinetics of bacilli at different concentrations of TFP was checked to determine the MIC of TFP for active as well as dormant bacilli. TFP is able to significantly reduce the actively replicating as well as non-replicating bacillary load. It has also shown inhibitory effect on the growth of MDR M.tb. TFP has shown enhanced activity against intracellular bacilli, presumably because phenothiazines are known to get accumulated in macrophages. This concentration was, otherwise, found to be non-toxic to macrophage in vitro. Our results show that TFP has the potential to be an effective killer of both actively growing and non-replicating bacilli including MDR TB.”

According to the news reporters, the researchers concluded: “Further evaluation and in vivo studies with Trifluoperazine can finally help us know the feasibility of this compound to be used as either a lead compound for development of new TB drugs or as an adjunct in the current TB chemotherapy.”

For more information on this research see: Activity of Trifluoperazine against Replicating, Non-Replicating and Drug Resistant M. tuberculosis. Plos One, 2012;7(8):e44245. (Public Library of Science - www.plos.org; Plos One - www.plosone.org)

Albert Einstein College of Medicine, Bronx: Old Drugs, New Purpose: Retooling Existing Drugs for Optimized Treatment of Resistant Tuberculosis

By a News Reporter-Staff News Editor at Politics & Government Week – A new study on Mycobacterium Infections is now available. According to news reporting from Bronx, New York, by VerticalNews journalists, research stated, “Treatment of drug-resistant tuberculosis is hindered by the high toxicity and poor efficacy of second-line drugs. New compounds must be used together with existing drugs, yet clinical trials to optimize combinations of drugs for drug-resistant tuberculosis are lacking.”

The news correspondents obtained a quote from the research from the Albert Einstein College of Medicine, “We conducted an extensive review of existing in vitro, animal, and clinical studies involving World Health Organization-defined group 1, 2, and 4 drugs used in drug-resistant tuberculosis regimens to inform clinical trials and identify critical research questions. Results suggest that optimizing the dosing of pyrazinamide, the injectables, and isoniazid for drug-resistant tuberculosis is a high priority. Additional pharmacokinetic, pharmacodynamic, and toxicodynamic studies are needed for pyrazinamide and
ethionamide. Clinical trials of the comparative efficacy and appropriate treatment duration of injectables are recommended. For isoniazid, rapid genotypic tests for Mycobacterium tuberculosis mutations should be nested in clinical trials.”

According to the news reporters, the researchers concluded: “Further research focusing on optimization of dose and duration of drugs with activity against drug-resistant tuberculosis is paramount.”


Our news journalists report that additional information may be obtained by contacting K.E. Dooley, Albert Einstein College of Medicine, Bronx, NY 10467, United States. (2012 Sep 20)

**World Health Organization, Geneva: Cost and cost-effectiveness of multidrug-resistant tuberculosis treatment in Estonia and Russia**

By a News Reporter-Staff News Editor at Politics & Government Week – Current study results on Multidrug Resistant Tuberculosis have been published. According to news reporting out of Geneva, Switzerland, by VerticalNews editors, research stated, “Evidence on the cost and cost-effectiveness of treatment of multidrug-resistant tuberculosis (MDR-TB) is limited, and no published data are available from former Soviet Union countries, where rates of MDR-TB are highest globally. We evaluated the cost and cost-effectiveness of MDR-TB treatment in Estonia and Russia (Tomsk Oblast), comparing cohorts enrolled on treatment according to World Health Organization (WHO) guidelines in 2001 and 2002 with cohorts treated in previous years.”

Our news journalists obtained a quote from the research from World Health Organization, “Costs were assessed from a health system perspective in 2003 US$; effects were measured as cures, deaths averted and disability-adjusted life-years (DALYs) averted. Cure rates when WHO guidelines were followed were 61% (90 out of 149) in Estonia and 76% (76 out of 100) in Tomsk Oblast, with a cost per patient treated of US$8,974 and US$10,088, respectively. Before WHO guidelines were followed, cure rates were 52% in Estonia and 15% in Tomsk Oblast; the cost per patient treated was US$4,729 and US$2,282, respectively. Drugs and hospitalisation accounted for 69-90% of total
costs. The cost per DALY averted by treatment following WHO guidelines was US$579 (range US$297-US$902) in Estonia and US$429 (range US$302-US$546) in Tomsk Oblast.”

According to the news editors, the researchers concluded: “Treatment of patients with MDR-TB can be cost-effective, but requires substantial additional investment in tuberculosis control in priority countries.”


Our news journalists report that additional information may be obtained by contacting K. Floyd, Stop TB Department, World Health Organization, 20 Avenue Appia, 1211 Geneva, Switzerland. (2012 Sep 20)

Maimonides Hospital, Brooklyn: Disseminated Tuberculosis Secondary to Adalimumab

By a News Reporter-Staff News Editor at Biotech Week – Investigators publish new report on Mycobacterium Infections. According to news reporting out of Brooklyn, New York, by NewsRx editors, research stated, “A 62-year-old woman with rheumatoid arthritis presented with fever (T-103.9 degrees F). Vital signs and physical examination were normal.”

Our news journalists obtained a quote from the research from Maimonides Hospital, “She was taking adalimumab, methotrexate, and prednisone for the past 9 months. Blood and urine cultures, human immunodeficiency virus, rapid plasma reagin, purified protein derivative, and cerebrospinal fluid test findings were negative. Computed tomography showed scattered 0.2-cm nodules in the lungs and innumerable subcentimeter lesions in the liver and spleen. Broad-spectrum antibiotics were started empirically. Liver biopsy findings revealed necrotizing granulomas and were negative for acid fast bacilli and fungi on staining. As the patient was persistently febrile despite antibiotics, the antibiotics were discontinued, and an antituberculous regimen including INH, ethambutol, and pyrazinamide was initiated empirically on day 40 of hospitalization. Fourteen days after liver biopsy, acid-fast bacilli grew in the tissue culture. Disseminated tuberculosis (TB) was diagnosed. Fever subsided after 1 week of anti-TB treatment. Antitumor necrosis factor alpha therapy in rheumatoid arthritis increases the risk of TB 5-fold. This is mostly as a result of reactivation of latent TB and commonly presents as disseminated TB. It usually occurs in the early stage of treatment. In our patient, the screening test results for TB before initiation of Adalimumab could have been falsely negative due to immunosuppression secondary to steroids. Our case emphasizes
that current screening tests can miss latent TB especially in immuno-suppressed patients. As it is difficult to diagnose TB with polymerase chain reaction and culture, histopathology should be sought early.”

According to the news editors, the researchers concluded: “Patients on antitumor necrosis factor alpha therapy presenting with fever of unknown origin should be considered for empirical anti-TB treatment regardless of microbiological and tissue diagnosis.”

For more information on this research see: Disseminated Tuberculosis Secondary to Adalimumab. *American Journal of Therapeutics*, 2012;19(4):E139-E140. *American Journal of Therapeutics* can be contacted at: Lippincott Williams & Wilkins, 530 Walnut St, Philadelphia, PA 19106-3621, USA. (Lippincott Williams and Wilkins - www.lww.com; American Journal of Therapeutics - http://journals.lww.com/americantherapeutics/pages/default.aspx)

Our news journalists report that additional information may be obtained by contacting M. Pednekar, Maimonides Hospital, Dept. of Internal Med, Brooklyn, NY 11219, United States. (*2012 Sep 19*)

### Research Center Borstel: Therapeutic targeting of interleukin-6 trans-signaling does not affect the outcome of experimental tuberculosis

By a News Reporter-Staff News Editor at Biotech Week – Data detailed on Joint Diseases and Conditions have been presented. According to news reporting originating in Borstel, Germany, by NewsRx journalists, research stated, “Treatment of autoreactive inflammatory diseases such as rheumatoid arthritis with anti-inflammatory drugs is associated with an increased rate of reactivation tuberculosis (TB). Interleukin-6 (IL-6) plays a pivotal role in inflammation and protection against various infectious diseases.”

The news reporters obtained a quote from the research from Research Center Borstel, “IL-6 signals by two mechanisms via the ubiquitous transmembrane protein gp130: ‘classic’ signaling using the membrane-bound IL-6 receptor (IL-6R), which is expressed mainly on hepatocytes and some leukocytes, and trans-signaling using soluble IL-6R (sIL-6R). Trans-signaling by the IL-6/sIL-6R complex is selectively inhibited by natural soluble gp130 (sgp130) and by sgp130 designer proteins. As specific blockade of IL-6 trans-signaling represents a promising approach for the therapy of inflammatory diseases, we evaluated the potential risk of interfering with this alternative pathway and analyzed the outcome of experimental TB after treatment with an IgG1-Fc fusion protein of soluble gp130 (sgp130Fc) and in sgp130Fc-overexpressing transgenic (sgp130Fc(tg)) mice. In contrast to treatment with antitumor necrosis factor (TNF) antibodies, administration of sgp130Fc did
not interfere with protective immune responses after infection with *Mycobacterium tuberculosis* (Mtb). Moreover, Mtb-infected sgp130Fc(tg) mice were capable of controlling mycobacterial growth.

According to the news reporters, the researchers concluded: “Our finding that IL-6 trans-signaling plays no role for protective immune responses against Mtb supports the superior safety of therapeutic targeting of IL-6 trans-signaling compared to anti-TNF treatment.”


Our news correspondents report that additional information may be obtained by contacting J. Sodenkamp, Infection Immunology, Research Center Borstel, Borstel, Germany. (2012 Sep 19)

**Centers for Disease Control and Prevention, Atlanta:**

*Predictors of poor outcomes among patients treated for multidrug-resistant tuberculosis at DOTS-plus projects*

By a News Reporter-Staff News Editor at AIDS Weekly – Research findings on Mycobacterium Infections are discussed in a new report. According to news reporting from Atlanta, Georgia, by NewsRx journalists, research stated, “The Objective of this analysis was to identify predictors of death, failure, and default among MDR-TB patients treated with second-line drugs in DOTS-plus projects in Estonia, Latvia, Philippines, Russia, and Peru, 2000-2004. Risk ratios (RR) with 95% confidence intervals (CI) were calculated using multivariable regression.”

The news correspondents obtained a quote from the research from Centers for Disease Control and Prevention, “Of 1768 patients, treatment outcomes were: cure/completed -1156 (65%), died -200 (11%), default -241 (14%), failure -118 (7%). Independent predictors of death included: age &gt;45 years (RR = 1.90 (95%CI 1.29-2.80), HIV infection (RR = 4.22 (2.65-6.72)), extrapulmonary disease (RR = 1.54 (1.04-2.26)), BMI &lt;18.5 (RR = 2.71 (1.91-3.85)), previous use of fluoroquinolones (RR = 1.91 (1.31-2.78)), resistance to any thioamide (RR = 1.59 (1.14-2.22)), baseline positive smear (RR = 2.22 (1.60-3.10)), no culture conversion by 3rd month of treatment (RR = 1.69 (1.19-2.41)); failure: cavitary disease (RR = 1.73 (1.07-2.80)), resistance to any fluoroquinolone (RR = 2.73 (1.71-4.37)) and any thioamide (RR = 1.62 (1.12-2.34)), and no culture conversion by 3rd month (RR = 5.84 (3.02-11.27)); default: unemployment (RR = 1.50 (1.12-2.01)), homelessness (RR = 1.52 (1.00-2.31)), imprisonment (RR = 1.86 (1.42-2.45)), alcohol abuse (RR = 1.60
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(1.18-2.16)), and baseline positive smear (RR = 1.35 (1.07-1.71)). Patients with biomedical risk factors for treatment failure or death should receive heightened medical attention.”

According to the news reporters, the researchers concluded: “To prevent treatment default, management of patients who are unemployed, homeless, alcoholic, or have a prison history requires extra measures to insure treatment completion.”


Our news journalists report that additional information may be obtained by contacting E.V. Kurbatova, US Centers for Disease Control and Prevention, Atlanta, GA, United States. (2012 Sep 17)

Oswaldo Cruz Foundation, Rio de Janeiro: Optochiasmatic Tuberculoma As The Sole Manifestation Of Late Recurrent Tuberculosis

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – Current study results on Mycobacterium Infections have been published. According to news reporting originating in Rio de Janeiro, Brazil, by NewsRx journalists, research stated, “Brain tuberculomas account for 10-20% of space occupying brain lesions in developing countries. Most lesions are observed at time of tuberculosis diagnosis or soon after starting treatment.”

The news reporters obtained a quote from the research from Oswaldo Cruz Foundation, “We herein describe a 32 year-old patient with a 14-month history of headache and progressive visual loss. Her past medical history revealed pulmonary tuberculosis treated eight years before. A brain MRI showed a T1- and T2-weighted isointense contrast-enhancing lesion in the optic chiasm. A presumptive diagnosis of optochiasmatic tuberculoma was made and isoniazid, rifampin, pyrazinamide, and ethambutol were started. Despite treatment, the patient evolved to blindness.”

According to the news reporters, the researchers concluded: “The prompt recognition of this condition is extremely important since the presence of optochiasmal enhancement is associated with blindness in patients with tuberculosis.”

For more information on this research see: Optochiasmatic Tuberculoma As The Sole Manifestation Of Late Recurrent Tuberculosis. Revista Do Instituto De Medicina Tropical De Sao Paulo, 2012;54(4):229-230. Revista Do Instituto De Medicina Tropical De Sao Paulo can be
Konyang University School of Medicine, Daejeon: Cecal fecaloma due to intestinal tuberculosis: endoscopic treatment

By a News Reporter-Staff News Editor at Gastroenterology Week – Researchers detail new data in Mycobacterium Infections. According to news reporting from Daejeon, South Korea, by NewsRx journalists, research stated, “Colorectal fecaloma is a mass of accumulated feces that is much harder in consistency than a fecal impaction. The rectosigmoid area is the common site for fecalomas and the cecum is the most unusual site.”

The news correspondents obtained a quote from the research from the Konyang University School of Medicine, “Diagnosis is usually made by distinctive radiographic findings of a mobile intraluminal mass with a smooth outline and no mucosal attachment. Most of the fecalomas are successfully treated by conservative methods such as laxatives, enemas and rectal evacuation. When conservative treatments have failed, endoscopic procedures or a surgical intervention may be needed.”

According to the news reporters, the researchers concluded: “We report here that a cecal fecaloma caused by intestinal tuberculosis scar was successfully removed by endoscopic procedures.”

For more information on this research see: Cecal fecaloma due to intestinal tuberculosis: endoscopic treatment. *Clinical Endoscopy*, 2012;45(2):174-6.

Our news journalists report that additional information may be obtained by contacting S.M. Kim, Dept. of Internal Medicine, Konyang University College of Medicine, Daejeon, South Korea. (2012 Aug 27)
Sao Paulo State University: DNA damage in peripheral blood mononuclear cells of patients undergoing anti-tuberculosis treatment

By a News Reporter-Staff News Editor at Tuberculosis Week – A new study on Mycobacterium Infections is now available. According to news originating from Sao Paulo, Brazil, by NewsRx correspondents, research stated, “Tuberculosis (TB), a chronic infectious disease, is a major cause of morbidity and mortality worldwide. Expression of iNOS and consequent production of NO during the inflammatory process is an important defense mechanism against TB bacteria.”

Our news journalists obtained a quote from the research from Sao Paulo State University, “We have tested whether pulmonary TB patients undergoing anti-tuberculosis treatment present DNA damage, and whether this damage is related to oxidative stress, by evaluating total hydrophilic antioxidant capacity and iNOS expression. DNA damage in peripheral blood mononuclear cells from patients and healthy tuberculin test (PPD) positive controls was evaluated by single-cell gel electrophoresis (comet assay), and iNOS expression was measured by qPCR. We also evaluated total hydrophilic antioxidant capacity in plasma from patients and controls. Compared to controls, pulmonary TB patients under treatment presented increased DNA damage, which diminished during treatment. Also, the antioxidant capacity of these individuals was increased at the start of treatment, and reduced during treatment. TB patients showed lower iNOS expression, but expression tended to increase during treatment. Our results indicate that pulmonary TB patients under anti-TB treatment exhibit elevated DNA damage in peripheral blood mononuclear cells.”

According to the news editors, the researchers concluded: “This damage was not related to nitric oxide but may be due to other free radicals.”

For more information on this research see: DNA damage in peripheral blood mononuclear cells of patients undergoing anti-tuberculosis treatment. Mutation Research-Genetic Toxicology and Environmental Mutagenesis, 2012;747(1):82-85. Mutation Research-Genetic Toxicology and Environmental Mutagenesis can be contacted at: Elsevier Science Bv, PO Box 211, 1000 Ae Amsterdam, Netherlands.

The news correspondents report that additional information may be obtained from L.R.C. de Oliveira, Sao Paulo State Univ, Botucatu Med Sch UNESP, Dept. of Internal Med, BR-18618000 Sao Paulo, Brazil. (2012 Aug 20)
National Institutes of Health, Bethesda: Infection Dynamics and Response to Chemotherapy in a Rabbit Model of Tuberculosis using [18F]2-Fluoro-Deoxy-D-Glucose Positron Emission Tomography and Computed Tomography

By a News Reporter-Staff News Editor at Life Science Weekly – Current study results on Mycobacterium Infections have been published. According to news originating from Bethesda, Maryland, by NewsRx correspondents, research stated, “With a host of new antitubercular chemotherapeutics in development, methods to assess the activity of these agents beyond mouse efficacy are needed to prioritize combinations for clinical trials. Lesions in Mycobacterium tuberculosis-infected rabbits are hypoxic, with histopathologic features that closely resemble those of human tuberculous lesions.”

Our news journalists obtained a quote from the research from the National Institutes of Health, “Using [(18)F]2-fluoro-deoxy-d-glucose [(18)F]FDG positron emission tomography-computed tomography (PET-CT) imaging, we studied the dynamics of tuberculosis infection in rabbits, revealing an initial inflammatory response followed by a consolidative chronic disease. Five weeks after infection, as much as 23% of total lung volume was abnormal, but this was contained and to some extent reversed naturally by 9 weeks. During development of this chronic state, individual lesions in the same animal had very different fates, ranging from complete resolution to significant progression. Lesions that remained through the initial stage showed an increase in volume and tissue density over time by CT. Initiation of chemotherapy using either isoniazid (INH) or rifampin (RIF) during chronic infection reduced bacterial load with quantitative changes in [(18)F]FDG uptake, lesion density and total lesion volume measured by CT. The [(18)F]FDG PET uptake in lesions was significantly reduced with as little as 1 week of treatment, while the volume and density of lesions changed more slowly.”

According to the news editors, the researchers concluded: “The results from this study suggest that rabbits may be a useful surrogate species for evaluating novel chemotherapies and understanding changes in both PET and CT scans in human clinical trials.”

Institute of Microbial Technology, Chandigarh: Redox biology of tuberculosis pathogenesis

By a News Reporter-Staff News Editor at Tuberculosis Week – Research findings on Mycobacterium Infections are discussed in a new report. According to news reporting originating from Chandigarh, India, by NewsRx correspondents, research stated, “Mycobacterium tuberculosis (Mtb) is one of the most successful human pathogens. Mtb is persistently exposed to numerous oxidoreductive stresses during its pathogenic cycle of infection and transmission.”

Our news editors obtained a quote from the research from the Institute of Microbial Technology, “The distinctive ability of Mtb, not only to survive the redox stress manifested by the host but also to use it for synchronizing the metabolic pathways and expression of virulence factors, is central to its success as a pathogen. This review describes the paradigmatic redox and hypoxia sensors employed by Mtb to continuously monitor variations in the intracellular redox state and the surrounding microenvironment. Two component proteins, namely, DosS and DosT, are employed by Mtb to sense changes in oxygen, nitric oxide, and carbon monoxide levels, while WhiB3 and anti-sigma factor RsrA are used to monitor changes in intracellular redox state. Using these and other unidentified redox sensors, Mtb orchestrates its metabolic pathways to survive in nutrient-deficient, acidic, oxidative, nitrosative, and hypoxic environments inside granulomas or infectious lesions. A number of these metabolic pathways are unique to mycobacteria and thus represent potential drug targets. In addition, Mtb employs versatile machinery of the mycothiol and thioredoxin systems to ensure a reductive intracellular environment for optimal functioning of its proteins even upon exposure to oxidative stress. Mtb also utilizes a battery of protective enzymes, such as superoxide dismutase (SOD), catalase (KatG), alkyl hydroperoxidase (AhpC), and peroxiredoxins, to neutralize the redox stress generated by the host immune system.”

According to the news editors, the researchers concluded: “This chapter reviews the current understanding of mechanisms employed by Mtb to sense and neutralize redox stress and their importance in TB pathogenesis and drug development.”

For more information on this research see: Redox biology of tuberculosis pathogenesis. Advances In Microbial Physiology, 2012;60():263-324.
University Hospital, Padua: Outbreak of transient conversions of the QuantiFERON-TB Gold In-Tube test in laboratory health care worker screenings

By a News Reporter-Staff News Editor at Tuberculosis Week – Researchers detail new data in Mycobacterium Infections. According to news reporting from Padua, Italy, by NewsRx journalists, research stated, “Gamma interferon release assays were recently introduced in health care worker (HCWs) screenings for tuberculosis surveillance. In longitudinal surveys, conversions and reversions are seen, and yet whether these changes are unspecific or are an expression of new infections and microbial clearance remains unclear.”

The news correspondents obtained a quote from the research from University Hospital, “In order to further elucidate these changes, we analyzed an outbreak of 15 transient conversions in 53 HCWs who operate in the same laboratory and handle specimens potentially containing Mycobacterium tuberculosis who underwent screening by the QuantiFERON-TB Gold In-Tube (QFT-GIT) test between 11 May and 30 June 2010: 15/46 (33%) negative HCWs showed a conversion and then reverted after 7 to 107 days. To validate these results, an evaluation of methodological procedures and test reliability, as well as an analysis of results obtained during the same period and processed by the same laboratory, was carried out. For the latter purpose, QFT-GIT results determined for 78 ward HCWs who underwent screening during the same period and were employed in departments with at least 3 infectious tuberculosis patients per year or had cared for an infectious patient without airborne precautions were analyzed with the following results: 6/63 (9%) HCWs with negative results in 3 different departments showed transient conversion (p=0.002; odds ratio, 4.60; 95% confidence interval, 1.62 to 13.04). A retrospective survey of in-house biosafety practices led to determination of a single exposure factor within the laboratory. These data emphasize the validity of the hypothesis that a transient conversion demonstrates the presence of a real tubercular infection and could be an important indicator for occupational biosafety concerns.”

According to the news reporters, the researchers concluded: “They also confirm that subjects with recent conversion should be retested before chest radiography and chemotherapy is offered.”

For more information on this research see: Outbreak of transient conversions of the QuantiFERON-TB Gold In-Tube test in laboratory health care worker screenings. *Clinical and Vaccine Immunology,*
Seoul National University: Adjuvant interferon-gamma treatment in two cases of refractory tuberculosis of the brain

By a News Reporter-Staff News Editor at Pain & Central Nervous System Week – Current study results on Clinical Neurology have been published. According to news reporting originating from Seoul, South Korea, by NewsRx correspondents, research stated, “Tuberculosis (TB) of the brain is often refractory and has the highest morbidity and mortality among the mycobacterial infections.”

Our news editors obtained a quote from the research from Seoul National University, “A recent report suggests that interferon-gamma may be of help since it can modulate the host inflammatory response against mycobacteria in the brain. Here, we report on a 44-year-old woman with multiple tuberculomas in the brainstem and a 40-year-old man with two large TB abscesses in the brain, both of whom had no response to anti-TB medications for 5 and 7 months, respectively, but with near-complete resolution with adjuvant interferon-gamma therapy (50 μg/m(2), subcutaneously, three times per week).”

According to the news editors, the researchers concluded: “Our cases show that refractory brain TB in immunocompetent patients can be successfully treated with adjuvant interferon-gamma therapy, without any significant side effects.”


The news editors report that additional information may be obtained by contacting J.Y. Lee, Seoul National University, Coll Med, Lung Inst, Seoul National University, Seoul, South Korea. (2012 Aug 06)
University of Colorado School of Medicine, Aurora:
Multidrug-resistant pulmonary tuberculosis: surgical challenges

By a News Reporter-Staff News Editor at Tuberculosis Week – Investigators publish new report on Mycobacterium Infections. According to news reporting from Aurora, Colorado, by NewsRx journalists, research stated, “Multidrug-resistant tuberculosis (MDR-TB) continues to be a significant public health problem worldwide. The treatment of MDR-TB consists mainly of chemotherapy.”

The news correspondents obtained a quote from the research from the University of Colorado School of Medicine, “However, surgery has been reported to be an effective adjunctive therapy in selected cases. This article discusses the scope of the problem of MDR-TB and the most accepted modern standard therapy.”

According to the news reporters, the researchers concluded: “The indications for surgical intervention as well as an analysis of the results of this therapy are also discussed.”


Our news journalists report that additional information may be obtained by contacting M.J. Weyant, Section of General Thoracic Surgery, Division of Cardiothoracic Surgery, Dept. of Surgery, University of Colorado School of Medicine, 12631 East 17th Avenue, MSC310, Aurora, CO 80045, United States. (2012 Aug 06)

Department of Pharmaceutical Sciences, Sagar:
Tuberculosis: from molecular pathogenesis to effective drug carrier design

By a News Reporter-Staff News Editor at Biotech Week – Research findings on Mycobacterium Infections are discussed in a new report. According to news reporting out of Sagar, India, by NewsRx editors, researchers stated “In the past two decades, tuberculosis has gone from being a forgotten disease to a modern and recrudescent pathology. Tuberculosis is a curable infection and most of the negative therapeutic outcomes are related to poor patient compliance, which could be solved by new drug delivery approaches.”

Our news journalists obtained a quote from the research from the Department of Pharmaceutical Sciences, “By using such approaches the technological drawbacks of the currently used therapeutic agents
could be addressed. In addition, optimum effectiveness of the drug by targeting the infection reservoirs could be achieved.”

According to the news editors, the researchers concluded: “In this article we compile the general physiological aspects of the infection along with new research updates especially on novel carriers used in the prevention of tuberculosis which might enhance therapeutic efficacy and patient compliance.”


Our news journalists report that additional information may be obtained by contacting D. Dube, Dept. of Pharmaceutical Sciences, Dr H S Gour University, Sagar 470 003, MP, India. (2012 Aug 01)

University Hospital, Stoke On Trent: A centralised electronic Multidrug-Resistant Tuberculosis Advisory Service: the first 2 years

By a News Reporter-Staff News Editor at Biotech Week – Current study results on Multidrug Resistant Tuberculosis have been published. According to news reporting originating in Stoke On Trent, United Kingdom, by NewsRx journalists, researchers stated “Multidrug-resistant tuberculosis (MDR-TB, defined as resistance to at least both rifampicin and isoniazid) has become a serious problem in the United Kingdom. As it is uncommon, no one clinician has sufficient experience of it to be confident in providing the best management for the patient.”

The news reporters obtained a quote from the research from University Hospital, “The model of a centralised system of management, such as is used in the Baltic countries, would seem a suitable method to adapt to the United Kingdom. With the agreement of the relevant professional organisations, a virtual electronic expert panel, the UK Multidrug-Resistant Tuberculosis Service, has been developed. This body gives advice via a secure website on MDR-TB patients referred by e-mail by clinicians across the country managing MDR-TB cases. In the first 2 years of operation, advice was sought on 60 patients with culture-proven MDR-TB (54% of the UK total). The number of clinicians accessing the advisory service increased from 27 in 2008 to 33 in 2009. Patients of non-UK origin accounted for 90% of all cases, including all four extensively drug-resistant tuberculosis cases. A central electronic virtual committee providing advice via a secure website has proved to be practical, economical and efficient.”
According to the news reporters, the researchers concluded: “It could provide a model for MDR-TB management in other countries and for the management of other uncommon diseases.”


Our news correspondents report that additional information may be obtained by contacting T.S. Jordan, Univ Hosp N Staffordshire, Dept. of Resp Med, Stoke On Trent, Staffs, United Kingdom. (2012 Aug 01)

**Seoul National University, Songnam: Vitamin D deficiency and changes in serum vitamin D levels with treatment among tuberculosis patients in South Korea**

By a News Reporter-Staff News Editor at Asia Business Newsweekly – Investigators publish new report on Mycobacterium Infections. According to news originating from Songnam, South Korea, by VerticalNews correspondents, researchers stated “Vitamin D deficiency has been reported to be associated with the development of active tuberculosis (TB), but many discrepancies exist among studies. The aims of this study were to compare the frequency of vitamin D deficiency in a Korean population of TB patients and control subjects, and to monitor the changes in vitamin D levels during TB treatment.”

Our news journalists obtained a quote from the research from Seoul National University, “Patients with newly diagnosed TB were prospectively enrolled. In addition, healthy volunteers or patients with diseases other than TB were enrolled as controls. Baseline serum 25-hydroxyvitamin D (25-OHD) levels were measured in both groups and compared. In the TB patients, measurements of serum 25-OHD were repeated 1 month after the initiation of treatment and again after completion of treatment. In total, 116 patients with TB and 86 control subjects were recruited. The median 25-OHD concentration was not different in TB patients at diagnosis (13.9 ng/mL; interquartile range (IQR) 8.80-21.8) compared with control subjects (13.2 ng/mL; IQR 9.61-19.3) (P = 0.97). The frequency of vitamin D deficiency (=10 ng/mL) was also not different in TB patients (36.2%) compared with controls (27.3%) (P = 0.21). In TB patients, the median 25-OHD concentration decreased significantly during treatment, to 12.5 ng/mL at 1 month and 11.0 ng/mL on completion of treatment (P = 0.01). Vitamin D levels do not appear to be associated with the development of TB in the Korean population.”

According to the news editors, the researchers concluded: “The median 25-OHD concentration decreased after treatment for TB.”

The news correspondents report that additional information may be obtained from H.K. Koo, Seoul National University, Bundang Hosp, Dept. of Internal Med, Div Pulm & Crit Care Med, Songnam, South Korea. (2012 Jul 31)

**Yale University, New Haven: Isoniazid preventive therapy in correctional facilities: a systematic review**

By a News Reporter-Staff News Editor at Ivy League Week – Data detailed on Mycobacterium Infections have been presented. According to news reporting out of New Haven, Connecticut, by NewsRx editors, researchers stated “Tuberculosis (TB) remains a major cause of morbidity and mortality worldwide and the main cause of death in correctional facilities in middle- and low-income countries. Due to the closed environment and the concentration of individuals with TB-related risk factors, effective measures are required to control TB in such settings.”

Our news journalists obtained a quote from the research from Yale University, “Isoniazid preventive therapy (IPT) represents an effective and cost-effective measure. Despite international recommendations that IPT be integral to TB control, it is seldom deployed. A systematic review of interventions used to assess IPT initiation and completion in correctional facilities was conducted using published studies from two biomedical databases and relevant keywords. Additional references were reviewed, resulting in 18 eligible studies. Most (72%) studies were conducted in the United States and in jail settings (60%), with the main objective of improving completion rates inside the facility or after release. Studies that provided data about initiation and completion rates showed poor success in correctional facilities. Adverse consequences and treatment interruption ranged from 1% to 55% (median 5%) in reported studies; hepatotoxicity was the most prevalent adverse reaction. Despite its accelerating effect on the development of active TB, information on human immunodeficiency virus (HIV) status was provided in only half of the studies. Among the four studies where IPT effectiveness was assessed, the results mirror those described in community settings.”

According to the news editors, the researchers concluded: “Future studies require thorough assessments of IPT initiation and completion

Our news journalists report that additional information may be obtained by contacting H.A.A. Al-Darraji, Yale University, Sch Med, Dept. of Internal Med, Infect Dis SectAIDS Program, New Haven, CT 06510, United States. *(2012 Jul 31)*

**University of KwaZulu-Natal, Durban: Trends in drug-resistant tuberculosis in a gold-mining workforce in South Africa, 2002-2008**

By a News Reporter-Staff News Editor at AIDS Weekly – New research on Mycobacterium Infections is the subject of a report. According to news reporting from Durban, South Africa, by NewsRx journalists, researchers stated “AND To describe trends in drug-resistant tuberculosis (TB) in two gold-mining work-forces, South Africa, 2002-2008. TB programme data analysis.”

The news correspondents obtained a quote from the research from the University of KwaZulu-Natal, “TB case notification rates decreased between 2002 and 2008 from 4006 to 3018 per 100000 and from 3192 to 2468/100 000 for Companies A and B, respectively. Human immunodeficiency virus (HIV) prevalence exceeded 80% in TB episodes with known status. The proportion of TB episodes with multidrug-resistant TB (MDR-TB) increased from 6/129 (4.7%) to 17/85 (20.0%) among previously treated cases, and from 4/38 (10.4%) to 7/28 (25.0%) in Companies A and B, respectively (tests for trend, Company A, P&lt; 0.001; Company B, P = 0.304). Case notifications of MDR-TB increased during 2002-2008 from 39.8 to 122.9/100 000/year in Company A and from 7.8 to 96.8/100 000/year in Company B. Coverage of second-line drug susceptibility testing (DST) among MDR-TB episodes was low. Previous treatment exposure was a strong risk factor for MDR-TB (prevalence ratio 8.78, 95%CI 5.94-12.97 in previously treated vs. untreated individuals). Despite decreasing TB notifications overall, MDR-TB notifications and proportions of episodes with MDR-TB increased in the larger company. Cure must be ensured in first episodes to prevent acquired resistance.”
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According to the news reporters, the researchers concluded: “Improved coverage of culture, DST and HIV testing is required to allow treatment to be optimised.”


Our news journalists report that additional information may be obtained by contacting C.L. van Halsema, University of KwaZulu Natal, Center AIDS Programme Res, Durban, South Africa. (2012 Jul 30)

University of Science Malaysia, Penang: Costs associated with tuberculosis diagnosis and treatment in Yemen for patients and public health services

By a News Reporter-Staff News Editor at Tuberculosis Week – A new study on Health and Medicine is now available. According to news originating from Penang, Malaysia, by NewsRx correspondents, researchers stated “This study determined the costs associated with tuberculosis (TB) diagnosis and treatment for the public health services and patients in Sana’a, Yemen. Data were collected prospectively from 320 pulmonary and extrapulmonary TB patients (160 each) who were followed until completion of treatment.”

Our news journalists obtained a quote from the research from the University of Science Malaysia, “Direct medical and nonmedical costs and indirect costs were calculated. The proportionate cost to the patients for pulmonary TB and extrapulmonary TB was 76.1% arid 89.4% respectively of the total for treatment. The mean cost to patients for pulmonary and extrapulmonary TB treatment was US$ 108.4 and US$ 328.0 respectively. The mean cost per patient to the health services for pulmonary and extrapulmonary TB treatment was US$ 34.0 and US$ 38.8 respectively. For pulmonary and extrapulmonary TB, drug treatment represented 59.3% and 77.9% respectively of the total cost to the health services.”

According to the news editors, the researchers concluded: “The greatest proportionate cost to patients for pulmonary TB treatment was time away from work (67.5% of the total cost), and for extrapulmonary TB was laboratory and X-ray costs (55.5%) followed by transportation (28%).”

For more information on this research see: Costs associated with tuberculosis diagnosis and treatment in Yemen for patients and public health services. Eastern Mediterranean Health Journal = La Revue De Sante De La Mediterranee Orientale, 2012;18(4):393-8.
The news correspondents report that additional information may be obtained from G.Q. Othman, Social & Administrative Pharmacy Discipline, School of Pharmaceutical Sciences, Universiti Sains Malaysia, Penang, Malaysia. (2012 Jul 30)

McGill University, Montreal: Representations of MDR and XDR-TB in South African newspapers

By a News Reporter-Staff News Editor at Biotech Week – Investigators publish new report on Mycobacterium Infections. According to news originating from Montreal, Canada, by NewsRx correspondents, researchers stated “The emergence of drug-resistant tuberculosis has brought with it diverse perspectives concerning the way in which the disease should be managed. The media is an important source of these perspectives, as they perform the dual role of reflecting and shaping public discourse.”

Our news journalists obtained a quote from the research by the authors from McGill University, “In this study, we are interested in how the media presents multi-drug resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) in South Africa, where both variants are a growing public health concern. We examined newspaper content from 310 South African newspaper articles from February 2004 to July 2009 that discussed MDR-TB and XDR-TB. Newspaper articles were collected from the Dow Jones Factiva database and imported into QDA Miner v3.2.1 for analysis. Using Attride-Stirling’s thematic network analysis method, articles were analyzed according to themes, sub-themes, and thematic networks. This analysis identified two main dimensions: causes of MDR/XDR-TB and treatment approaches/solutions. Causes of MDR/XDR-TB revolved around three main global themes: i) patient-centred causes (32.6%); ii) lack of infection control procedures (18.7%); and iii) health systems failures (19.4%). Treatment approaches or solutions to tackling MDR/XDR-TB focused on i) patient targeted solutions (38.4%); ii) improving infection control (12.3%); iii) systems restructuring (10.6%); and iv) new diagnostic and therapeutic options (10%). Our analysis identifies a trend in the South African media to identify a broad range of causes of MDR/XDR-TB, while emphasizing that treatment approaches should be directed primarily at the individual. Of particular importance is the fact that such a perspective runs contrary to the World Health Organization’s (WHO) recommendations for approaching the TB epidemic, in particular by insufficiently addressing systemic and social drivers of the epidemic.”

According to the news editors, the researchers concluded: “Due to the media’s potential influence on policy formation, how the media presents issues especially issues pertaining to emerging public health concerns should warrant more attention.”

The news correspondents report that additional information may be obtained from M. Daku, McGill University, Dept. of Epidemiol Biostat & Occupat Hlth, Montreal, PQ, Canada. (2012 Jul 25)

**Peking University, Beijing: Factors contributing to the high prevalence of multidrug-resistant tuberculosis: a study from China**

By a News Reporter-Staff News Editor at Asia Business Newsweekly – Investigators publish new report on Mycobacterium Infections. According to news reporting originating in Beijing, People’s Republic of China, by VerticalNews journalists, researchers stated “The rapid spread of multidrug-resistant tuberculosis (MDR-TB) has attracted global concerns. This study aimed to identify factors contributing to the high prevalence of MDR-TB in China’s Heilongjiang province.”

The news reporters obtained a quote from the research by the authors from Peking University, “A cross-sectional survey following the WHO/International Union Against Tuberculosis and Lung Disease guidelines was conducted with consecutive recruitment of patients with TB in 30 counties selected at random in Heilongjiang in 2004. A total of 1995 patients were tested for MDR-TB. Factors associated with MDR-TB were identified through multilevel models and traditional logistic regression analysis, along with in-depth interviews with nine patients, five healthcare managers and four doctors. Results 241 patients (12%) were identified with MDR-TB. The retreatment patients were 5.48 times (95% CI 4.04 to 7.44) more likely to have MDR-TB than newly diagnosed patients. The patients who were treated with isoniazid and rifampin for >180 days were 4.82 times (95% CI 2.97 to 7.81) more likely to develop MDR-TB than those treated <180 days. Age and delay in initiating TB treatment were associated with MDR-TB. Financial burden, poor knowledge and side effects of TB treatment were perceived by the interviewees as influencing factors. Lack of coordination of services, unsatisfactory supervision of treatment and infection control jeopardised the control of MDR-TB. Inappropriate treatment is the most important influencing factor of MDR-TB.”

According to the news reporters, the researchers concluded: “Increasing people’s awareness of TB, early detection and appropriate treatment of patients with TB should become a priority, which requires

Our news correspondents report that additional information may be obtained by contacting L.B. Liang, Peking University, Sch Public Hlth, Beijing 100871, People’s Republic of China. (2012 Jul 24)

**University of Amsterdam: Multidrug resistance after inappropriate tuberculosis treatment: a meta-analysis**

By a News Reporter-Staff News Editor at Tuberculosis Week – Research findings on Mycobacterium Infections are discussed in a new report. According to news reporting originating from Amsterdam, Netherlands, by NewsRx correspondents, researchers stated “We conducted a systematic review and meta-analysis to assess the evidence for the postulation that inappropriate tuberculosis (TB) regimens are a risk for development of multidrug-resistant (MDR)-TB. MEDLINE, EMBASE and other databases were searched for relevant articles in January 2011.”

Our news editors obtained a quote from the research by the authors from the University of Amsterdam, “Cohort studies including TB patients who received treatment were selected and data on treatment regimen, drug susceptibility testing results and genotyping results before treatment and at failure or relapse were abstracted from the articles. Four studies were included in the systematic review and two were included in the meta-analysis. In these two studies the risk of developing MDR-TB in patients who failed treatment and used an inappropriate treatment regimen was increased 27-fold (RR 26.7, 95% CI 5.0-141.7) when compared with individuals who received an appropriate treatment regimen. This review provides evidence that supports the general opinion that the development of MDR-TB can be caused by inadequate treatment, given the drug susceptibility pattern of the Mycobacterium tuberculosis bacilli. It should be noted that only two studies provided data for the meta-analysis.”

According to the news editors, the researchers concluded: “The information can be used to advocate for adequate treatment for patients based on drug resistance profiles.”

The news editors report that additional information may be obtained by contacting M.J. van der Werf, University of Amsterdam, Academy Med Center, Dutch Cochrane Center, NL-1105 AZ Amsterdam, Netherlands. (2012 Jul 23)

University of Cape Town: Population pharmacokinetics and pharmacodynamics of ofloxacin in South african patients with multidrug-resistant tuberculosis

By a News Reporter-Staff News Editor at Biotech Week – Fresh data on Mycobacterium Infections are presented in a new report. According to news reporting originating from Cape Town, South Africa, by NewsRx correspondents, researchers stated “Despite the important role of fluoroquinolones and the predominant use of ofloxacin for treating multidrug-resistant tuberculosis in South Africa, there are limited data on ofloxacin pharmacokinetics in patients with multidrug-resistant tuberculosis, no ofloxacin pharmacokinetic data from South African patients, and no direct assessment of the relationship between ofloxacin pharmacokinetics and the MIC of ofloxacin of patient isolates. Our objectives are to describe ofloxacin pharmacokinetics in South African patients being treated for multidrug-resistant tuberculosis and assess the adequacy of ofloxacin drug exposure with respect to the probability of pharmacodynamic target attainment (area under the time curve/MIC ratio of at least 100).”

Our news editors obtained a quote from the research by the authors from the University of Cape Town, “Sixty-five patients with multidrug-resistant tuberculosis were recruited from 2 hospitals in South Africa. We determined the ofloxacin MICs for the Mycobacterium tuberculosis isolates from baseline sputum specimens. Patients received daily doses of 800 mg ofloxacin, in addition to other antitubercular drugs. Patients underwent pharmacokinetic sampling at steady state. NONMEM was used for data analysis. The population pharmacokinetics of ofloxacin in this study has been adequately described. The probability of target attainment expectation in the study population was 0.45. Doubling the dose to 1,600 mg could increase this to only 0.77. The currently recommended ofloxacin dose appeared inadequate for the majority of this

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study population. Studies to assess the tolerability of higher doses are warranted.”

According to the news editors, the researchers concluded: “Alternatively, ofloxacin should be replaced with more potent fluoroquinolones.”


The news editors report that additional information may be obtained by contacting E. Chigutsa, Division of Clinical Pharmacology, Dept. of Medicine, University of Cape Town, Cape Town, South Africa. (2012 Jul 18)

**University of Lodz: Latent M. tuberculosis infection–pathogenesis, diagnosis, treatment and prevention strategies**

By a News Reporter-Staff News Editor at AIDS Weekly – Investigators discuss new findings in Mycobacterium Infections. According to news originating from Lodz, Poland, by NewsRx correspondents, researchers stated “One third of the earths population is infected with *Mycobacterium tuberculosis* (Mtb), but only 5-10% of the infected individuals develop active tuberculosis (TB) over their lifetime. The remaining 90-95% stay healthy and are called latently infected individuals.”

Our news journalists obtained a quote from the research by the authors from the University of Lodz, “They are the biggest reservoir of the tubercle bacilli and identifying the cases of latent TB is a part of the global plan of TB control. From the clinical point of view detection of latent TB infections (LTBI) in individuals with the highest active TB risk including cases of HIV infection, autoimmune inflammatory diseases or cancer, is a priority.”

According to the news editors, the researchers concluded: “This review summarizes the recent findings in the pathogenesis of latent TB, its diagnosis, treatment and prevention.”


The news correspondents report that additional information may be obtained from M. Druszczynska, Dept. of Immunology and Infectious Biology, Institute of Microbiology, Biotechnology and Immunology, University of Lodz, Lodz, Poland. (2012 Jul 16)
University of Cape Town, Rondebosch: Treatment outcomes for children with multidrug-resistant tuberculosis: a systematic review and meta-analysis

By a News Reporter-Staff News Editor at Biotech Week – Current study results on Mycobacterium Infections have been published. According to news reporting from Rondebosch, South Africa, by NewsRx journalists, researchers stated “Paediatric multidrug-resistant (MDR) tuberculosis is a public health challenge of growing concern, accounting for an estimated 15% of all global cases of MDR tuberculosis. Clinical management is especially challenging, and recommendations are based on restricted evidence.”

The news correspondents obtained a quote from the research by the authors from the University of Cape Town, “We aimed to assess existing evidence for the treatment of MDR tuberculosis in children. We did a systematic review and meta-analysis of published and unpublished studies reporting treatment outcomes for children with MDR tuberculosis. We searched PubMed, Ovid, Embase, Cochrane Library, PsychINFO, and BioMedCentral databases up to Oct 31, 2011. Eligible studies included five or more children (aged ≤ 16 years) with MDR tuberculosis within a defined treatment cohort. The primary outcome was treatment success, defined as a composite of cure and treatment completion. We identified eight studies, which reported treatment outcomes for a total of 315 patients. We recorded much variation in the characteristics of patients and programmes. Time to appropriate treatment varied from 2 days to 46 months. Average duration of treatment ranged from 6 months to 34 months, and duration of follow-up ranged from 12 months to 37 months. The pooled estimate for treatment success was 81.67% (95% CI 72.54-90.80). Across all studies, 5.9% (95% CI 1.3-10.5) died, 6-2% (2.3-10.2) defaulted, and 39-1% (28-7-49-4) had an adverse event. The most common drug-related adverse events were nausea and vomiting. Other serious adverse events were hearing loss, psychiatric effects, and hypothyroidism. The treatment of paediatric MDR tuberculosis has been neglected, but when children are treated outcomes can be achieved that are at least as good as those reported for adults.”

According to the news reporters, the researchers concluded: “Programmes should be encouraged to report outcomes in children to improve the knowledge base for care, especially as new drugs become available.”

For more information on this research see: Treatment outcomes for children with multidrug-resistant tuberculosis: a systematic review and meta-analysis. Lancet Infectious Diseases, 2012;12(6):449-456. Lancet Infectious Diseases can be contacted at: Elsevier Science Inc, 360 Park Ave South, New York, NY 10010-1710, USA. (El-
Medical Research Centre, Maharashtra: S1 tuberculosis treated with segmental lumbopelvic fixation: a case report

By a News Reporter-Staff News Editor at Tuberculosis Week – Investigators discuss new findings in Spinal Research. According to news reporting out of Maharashtra, India, by NewsRx editors, researchers stated “DESIGN.: A case report. To describe an effective surgical option for sacral tuberculosis (TB).”

Our news journalists obtained a quote from the research by the authors from Medical Research Centre, “OF DATA.: Sacral TB is a rare cause of low back pain. A differential diagnosis of TB should always be made, especially in India where TB cases are on a rampant rise with increasing drug resistance and immunosuppressed population. A retrospective review. We report on a 24-year-old woman with low back pain and radiculopathy. Magnetic Resonance Imaging (MRI) showed a destructive lesion in S1 body. Empirical antitubercular treatment was started elsewhere with no relief but worsening of the lesion. She underwent a Computed Tomography (CT)-guided biopsy and drug sensitivity test, which did not reveal anything. The patient was bedridden for almost a year. A lumbopelvic instrumented fixation and S1 body reconstruction with structural allograft was performed. Culture sensitivity revealed multidrug resistance. After surgery, the patient responded rapidly, and at 2-year follow-up, she is symptom-free. TB should always be considered as a differential diagnosis of sacral lesions, and identifying multidrug resistance is equally important in its treatment.”

According to the news editors, the researchers concluded: “Lumbopelvic fixation is a safe and reliable option as it unloads the S1 segment by achieving fixation in the lumbar sacral spine and iliac wings.”


Our news journalists report that additional information may be obtained by contacting S.P. Shah, From the Dept. of Orthopaedics, Bombay Hospital, New Wing, Medical Research Centre, Mumbai, Maharashtra, India. (2012 Jul 09)
Memorial Hospital, Maharashtra: Structural odontoid lesions in craniovertebral tuberculosis: a review of 15 cases

By a News Reporter-Staff News Editor at Tuberculosis Week – Current study results on Mycobacterium Infections have been published. According to news reporting from Maharashtra, India, by NewsRx journalists, researchers stated “DESIGN.: A retrospective chart review. To describe the presentation and the rationale for management of pathological odontoid fracture and complete odontoid destruction in craniovertebral junction tuberculosis (CVJ TB).”

The news correspondents obtained a quote from the research by the authors from Memorial Hospital, “OF DATA.: Presentation of CVJ TB ranges from minor osteomyelitic changes to severe structural damage leading to instability. Structural damage to the odontoid process is poorly characterized in the literature. Inadequate knowledge about the radiological presentations has led to controversy in the management of CVJ TB. The cohort consisted of 15 consecutive patients with CVJ TB, with structural damage to the odontoid process in the form of either odontoid fracture (n=7) or complete odontoid destruction (n=8). These patients presented with pain, neurological deficit, torticollis, dysphagia, or respiratory distress. The cause of neurological deficit was cranio cervical instability characterized as anterioposterior (n=15), rotatory (n=4), and vertical (n=6). Displacement reduced anatomically in 13 patients. Apart from antibiotics, all patients were treated surgically by either C1-C2 fusion (n=7) or occipitocervical fusion (n=8). Average duration of follow-up was 3.6 years (range, 1.5-8 yr). All patients achieved normal neurological status. No complications were noted, except for 1 case, who had a loss of reduction after the use of Hartshill rectangle for occipitocervical fusion. Postoperative computed tomographic scan showed nonunion of odontoid fracture in 2 of 4 patients. No patient of odontoid destruction, of the 5 investigated, revealed structural reformation of the dens. CVJ TB can severely damage the odontoid process, resulting in atlantoaxial dislocation. In these patients, surgery restores and maintains the cranio cervical alignment and has a predictable outcome compared with conservative therapy. Pathological odontoid fractures have the potential to go into nonunion.”

According to the news reporters, the researchers concluded: “Odontoid process once destroyed completely is rarely restored after antibiotic therapy.”

Our news journalists report that additional information may be obtained by contacting K. Chaudhary, From the King Edward VII Memorial Hospital, Mumbai, Maharashtra, India. (2012 Jul 09)

University of Cape Town: Audiological monitoring for ototoxic tuberculosis, human immunodeficiency virus and cancer therapies in a developing world setting

By a News Reporter-Staff News Editor at Biotech Week – A new study on Tuberculosis is now available. According to news reporting from Cape Town, South Africa, by NewsRx journalists, researchers stated “Ototoxic drugs are widely used in the developing world, without audiological monitoring. Epidemiological data on ototoxic deafness are lacking for developing countries.”

The news correspondents obtained a quote from the research by the authors from the University of Cape Town, “The public health aspect of ototoxicity is often overlooked, to the detriment of the individual patient. This paper reviews ototoxic hearing loss, particularly in sub-Saharan Africa, and also assesses the impact of treatments for tuberculosis, cancer and human immunodeficiency virus (the latter including highly active antiretroviral therapy) on ototoxic hearing loss.”

According to the news reporters, the researchers concluded: “The paper also discusses obstacles to audiological monitoring for ototoxicity in the developing world, and the potential of audiology screening using applications for mobile devices.”


Our news journalists report that additional information may be obtained by contacting T. Harris, University of Cape Town, Fac Hlth Sci, Div Otorhinolaryngol, ZA-7925 Cape Town, South Africa. (2012 Jul 04)
Department of Pediatrics, Maharashtra:
Multidrug-resistant tuberculosis in children from 2003 to 2005: A brief report

By a News Reporter-Staff News Editor at Journal of India – A new study on Tuberculosis is now available. According to news originating from Maharashtra, India, by VerticalNews editors, the researcher stated “Multidrug-resistant tuberculosis (MDR-TB) has rarely been reported from children in India. Their response to therapy is also not known.”

Our news journalists obtained a quote from the research by the author from the Department of Pediatrics, “We present four HIV-negative children with MDR-TB (3 children with extra-pulmonary TB and 1 child with pulmonary TB) who presented in 2003-2005. All the four children were already on antituberculous therapy (ATT) for 3-9 months prior to being detected as MDR-TB. These patients were started on second-line ATT for 18 months.”

According to the news editors, the researchers concluded: “In three patients, there was complete resolution, and one patient with severe bilateral pulmonary TB had the disease localized to one lung after 18 months of therapy.”


The news correspondents report that additional information may be obtained from I. Shah, Dept. of Pediatrics, BJ Wadia Hospital for Children, Mumbai, Maharashtra, India. *(2012 Jul 03)*

Infectious Disease Unit, London: Direct costs of pulmonary tuberculosis among patients receiving treatment in Bauchi State, Nigeria

By a News Reporter-Staff News Editor at Life Science Weekly – Current study results on Tuberculosis have been published. According to news reporting originating from London, United Kingdom, by NewsRx correspondents, researchers stated “To access tuberculosis (TB) services, patients have to bear the costs of out-of-pocket expenditures or direct costs for transport, drugs and other services that are not provided free-of-charge. These costs could represent a barrier to care, especially in a country such as Nigeria, where per capita gross national income is only US$1160 and 46% of the urban population live below the poverty line.”

Our news editors obtained a quote from the research by the authors from Infectious Disease Unit, “To describe the direct costs of TB diagnosis and treatment in Bauchi State, Nigeria, from the patient’s perspective. A cross-sectional study. A sample size of 255 patients
was randomly selected from 27 of 67 facilities in Bauchi State, Nigeria. The median out-of-pocket cost for hospitalised patients was estimated at US$166.11, while ambulatory patients paid an estimated median cost of US$94.16, equivalent to about 9-38% of their average annual income. Female patients spent a higher proportion of their income on diagnosis and treatment than males ($P <0.0001$). The median out-of-pocket costs borne by patients before, during and after diagnosis were estimated at respectively US$35.23, US$27.12 and US$23.43 for ambulatory patients, and additional average out-of-pocket spending of US$66.44 for patients hospitalised during their illness. Pre-diagnosis, diagnosis and post-diagnosis out-of-pocket spending did not vary significantly by human immunodeficiency virus status ($P >0.05$) and sex ($P >0.05$).

According to the news editors, the researchers concluded: “The costs of anti-tuberculosis treatment found in this study are expensive and potentially catastrophic for many patients and their families.”

For more information on this research see: Direct costs of pulmonary tuberculosis among patients receiving treatment in Bauchi State, Nigeria. *International Journal of Tuberculosis and Lung Disease*, 2012;16(6):835-840. *International Journal of Tuberculosis and Lung Disease* can be contacted at: Int Union Against Tuberculosis Lung Disease (I U A T L D), 68 Boulevard Saint-Michel, 75006 Paris, France.

The news editors report that additional information may be obtained by contacting N.A. Umar, Hlth Protect Agcy, Infect Dis Unit, London, United Kingdom. *(2012 Jul 03)*

**Tokyo Medical and Dental University: Non-hospital DOT and early diagnosis of tuberculosis reduce costs while achieving treatment success**

By a News Reporter-Staff News Editor at Asia Business Newsweekly – Investigators discuss new findings in Tuberculosis. According to news reporting from Tokyo, Japan, by VerticalNews journalists, researchers stated “1) To evaluate the tuberculosis (TB) related financial burden of patients and health care providers over the course of diagnosis and treatment by choice of directly observed treatment (DOT); and 2) to examine treatment outcomes for different DOT programmes in Cambodia. Subjects were patients diagnosed with smear-positive pulmonary TB between July 2008 and January 2009 at 17 health facilities providing multiple DOT programmes.”

The news correspondents obtained a quote from the research by the authors from Tokyo Medical and Dental University, “Treatment outcomes for the different DOT programmes as well as direct and indirect household costs and medical delivery costs for the treatment and care of 277 patients were examined. Per patient costs of anti-tuberculosis
treatment for patients with non-multidrug-resistant TB who did not have human immunodeficiency virus co-infection ranged from a high of \( US\$1900 \) for in-patient DOT to a low of \( US\$395 \) for DOT provided at home. All costs among patients treated with hospital DOT were consistently higher than for those treated with non-hospital DOT. The percentage of treatment success was not significantly different between hospital and non-hospital DOT programmes (all >89%)."

According to the news reporters, the researchers concluded: “Non-hospital DOT programmes ease the financial burden on both patients and health care providers, while resulting in treatment success rates similar to those of hospital DOT.”


Our news journalists report that additional information may be obtained by contacting K. Pichenda, Tokyo Medical & Dental University, Hlth Promot Sect, Div Public Hlth, Grad Sch, Tokyo 1138519, Japan. (2012 Jul 03)

**Aga Khan University, Karachi: Implementing a public-private mix model for tuberculosis treatment in urban Pakistan: lessons and experiences**

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – A new study on Tuberculosis is now available. According to news reporting from Karachi, Pakistan, by NewsRx journalists, researchers stated “Six towns of Karachi, Pakistan. 1) To strengthen the capacity of general practitioners (GPs) in providing tuberculosis (TB) treatment through DOTS; and 2) to enhance collaboration between the public and private sectors in TB management and case reporting.”

The news correspondents obtained a quote from the research by the authors from Aga Khan University, “A quasi-experimental study design was adopted to ensure enrolment of TB patients through trained GPs with the support of laboratory networks and to improve the case detection rate. The following challenges were faced during implementation of the model in urban settings: no systematic list of GPs was available; the majority of the GPs were untrained health practitioners working in squatter settlements, where formally trained GPs are most needed; the motivation of GPs with high patient loads is very low; and access to a laboratory is difficult. Of 35 patients enrolled in the first quarter (third quarter 2009), 87% completed their treatment successfully. Public-private mix (PPM) DOTS is feasible in the cities of Pakistan.”
According to the news reporters, the researchers concluded: “However, the cost, time and effort required to establish the programme is higher than in many other developing countries.”


Our news journalists report that additional information may be obtained by contacting S.A. Naqvi, Aga Khan University, Div Environm Hlth Sci, Dept. of Community Hlth Sci, Karachi 74800, Pakistan. (2012 Jul 02)

**National Institute for Medical Research, London:** Understanding latent tuberculosis: the key to improved diagnostic and novel treatment strategies

By a News Reporter-Staff News Editor at Biotech Week – Research findings on Latent Tuberculosis are discussed in a new report. According to news reporting from London, United Kingdom, by NewsRx journalists, researchers stated “Treatment of latent tuberculosis (LTBI) is a vital component of tuberculosis (TB) elimination but is not efficiently implemented with currently available diagnostics and therapeutics. The tuberculin skin test and interferon-gamma release assays can inform that infection has occurred, but do not prove that it persists.”

The news correspondents obtained a quote from the research by the authors from National Institute for Medical Research, “Treatment of LTBI with isoniazid targets actively replicating bacilli but not non-replicating populations, prolonging treatment duration. Developing more predictive diagnostic tests and treatments of shorter duration requires a greater understanding of the biology of LTBI, from both host and bacillary perspectives.”

According to the news reporters, the researchers concluded: “In this article, we discuss the basis of current diagnosis and treatment of LTBI and review recent developments in understanding the biology of latency that might enable future improved diagnostic and treatment strategies.”

Central South University, Changsha: Surgical management for multilevel noncontiguous thoracic spinal tuberculosis by single-stage posterior transforaminal thoracic debridement, limited decompression, interbody fusion, and posterior instrumentation (modified TTIF)

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators publish new report on Osteoarticular Tuberculosis. According to news reporting originating from Changsha, People’s Republic of China, by NewsRx correspondents, researchers stated “Multilevel noncontiguous thoracic spinal tuberculosis has rarely been reported in the literature. We present a retrospective clinical study of 14 patients with multilevel noncontiguous thoracic spinal tuberculosis treated by single-stage posterior transforaminal thoracic debridement, limited decompression, interbody fusion, and posterior instrumentation (modified TTIF) and determine the clinical effectiveness of such surgical treatment for MNTST.”

Our news editors obtained a quote from the research by the authors from Central South University, “Fourteen patients with multilevel noncontiguous thoracic spinal tuberculosis were treated with modified TTIF. The mean follow-up was 27.36 +/- A 10.46 months (range 13-42 months). The kyphotic angle ranged from -2A degrees to 47A degrees before operation, with an average of 19.21A degrees A A +/- A 12.63A degrees. The erythrocyte sedimentation rate (ESR) of patients upon admission ranged from 30 to 62 mm/h before operation, with an average of 46.43 +/- A 10.77 mm/h. The Frankel Grade was used to evaluate the neurological deficits. The average ESR got normal (8.14 +/- A 5.89 mm/h) within 3 months in all patients. The average kyphotic angle decreased to 8.07A degrees A A +/- A 6.91A degrees postoperatively. Mean deformity angle was measured as 8.79A degrees A A +/- A 7.29A degrees at the last visit. Solid fusion was achieved in all cases.”

According to the news editors, the researchers concluded: “Neurologic status of the 12 patients with preoperative neurologic deficit was 6 with grade D recovered to normal; 2 with grade B, both of them to grade D; 4 with grade C, 2 to grade D, 1 to grade E, and 1 still in grade C. Modified TTIF can be an effective treatment method of multilevel noncontiguous thoracic spinal tuberculosis.”
For more information on this research see: Surgical management for multilevel noncontiguous thoracic spinal tuberculosis by single-stage posterior transforaminal thoracic debridement, limited decompression, interbody fusion, and posterior instrumentation (modified TTIF). *Archives of Orthopaedic and Trauma Surgery*, 2012;132(6):751-757. *Archives of Orthopaedic and Trauma Surgery* can be contacted at: Springer, 233 Spring St, New York, NY 10013, USA. (Springer - www.springer.com; *Archives of Orthopaedic and Trauma Surgery* - http://www.springerlink.com/content/0936-8051/)

The news editors report that additional information may be obtained by contacting H.Q. Zhang, Central South University, Dept. of Spine Surg, Xiangya Hosp, Changsha 410008, Hunan, People’s Republic of China. (*2012 Jun 26*)

**Great Ormond Street Hospital for Children NHS Trust, London: Tuberculosis in childhood**

By a News Reporter-Staff News Editor at Tuberculosis Week – Researchers detail new data in Tuberculosis. According to news originating from London, United Kingdom, by NewsRx editors, the researcher stated “There has been a recent global resurgence of tuberculosis (TB) fuelled by HIV infection and migration. Childhood TB represents a sentinel event in the community, suggesting recent transmission from an infectious adult.”

Our news journalists obtained a quote from the research by the author from Great Ormond Street Hospital for Children NHS Trust, “The diagnosis of TB in children is based on chest X-ray, tuberculin skin testing and mycobacterial staining/culture, although the diagnostic yield from these investigations is often lower than in adults. Newer diagnostic tests are being developed and may improve the diagnostic yield in childhood TB. Treatment of TB in children is similar to adults in that short-course multidrug treatment has been adopted as standard therapy in many national TB programmes. Compliance is a major determinant of the success of drug treatment and directly observed therapy has been adopted as a key component of TB treatment programmes.”

According to the news editors, the researchers concluded: “Although uncommon in children, multidrug-resistant TB is also increasing and treatment often involves longer courses of therapy with second-line drugs.”

For more information on this research see: Tuberculosis in childhood. *Therapeutic Advances In Respiratory Disease*, 2012;6(3):161-71. *Therapeutic Advances In Respiratory Disease* can be contacted at: SAGE Publications, USA, 2455 Teller Road, Thousand Oaks, CA 91320, USA. (Sage Publications - http://www.sagepub.com/; *Therapeutic Advances In Respiratory Disease* - tar.sagepub.com)
The news correspondents report that additional information may be obtained from D. Shingadia, Dept. of Infectious Diseases, Great Ormond Street Hospital for Children, Great Ormond Street, London, UK.

The publisher’s contact information for the journal *Therapeutic Advances In Respiratory Disease* is: SAGE Publications, USA, 2455 Teller Road, Thousand Oaks, CA 91320, USA. (2012 Jun 25)

**University of Pretoria: Hearing profile of gold miners with and without tuberculosis**

By a News Reporter-Staff News Editor at Tuberculosis Week – Current study results on Tuberculosis have been published. According to news reporting originating from Pretoria, South Africa, by NewsRx correspondents, researchers stated “To compare the hearing of gold miners with and without tuberculosis (TB) to determine the effect of TB and its associated risk profile on hearing. Audiological and medical surveillance data of 2698 South African gold miners for 2001-2009 were analysed in a retrospective cohort design.”

Our news editors obtained a quote from the research by the authors from the University of Pretoria, “Hearing thresholds for the air conduction frequencies (0.5, 1, 2, 3, 4, 6, 8 kHz) in both ears were analysed together with biographical and occupational data. Subjects were divided into two experimental (single TB treatment, n=911 and multiple TB treatment, n=376) and one control group (n=1411). Comparisons between groups included (1) change from baseline to most recent audiogram, (2) most recent hearing thresholds and (3) most recent thresholds in a subset of noise exposed and unexposed groups. Hearing thresholds for the TB groups were significantly (p <0.01) elevated compared to the control group, after correcting for time between baseline and most recent audiogram, threshold at baseline and age at test. Pair-wise comparisons demonstrated the largest threshold differences between the control and multiple TB group. Changes in mean thresholds across TB treatment groups were independent of noise exposure. Hearing thresholds over time also deteriorated significantly more (p <0.01) in workers with TB (single and multiple treatment) than in workers without TB. Gold miners with TB, especially with more than one episode of TB, demonstrate significantly poorer hearing thresholds and more pronounced decline in hearing over time independent of noise exposure.”

According to the news editors, the researchers concluded: “The exact cause is likely a complex interaction between TB, including treatment, and its associated risk profile.”

Enhanced Cellular Uptake of a New, in Silico Identified Antitubercular Candidate by Peptide Conjugation

By a News Reporter-Staff News Editor at Biotech Week – Investigators publish new report on Proteomics. According to news reporting originating in Budapest, Hungary, by NewsRx journalists, researchers stated “Mycobacterium tuberculosis is a successful pathogen, and it can survive in infected macrophages in dormant phase for years and decades. The therapy of tuberculosis takes at least six months, and the slow-growing bacterium is resistant to many antibiotics.”

The news reporters obtained a quote from the research by the authors, “The development of novel antimicrobials to counter the emergence of bacteria resistant to current therapies is urgently needed. In silico docking methods and structure-based drug design are useful bioinformatics tools for identifying new agents. A docking experiment to M. tuberculosis dUTPase enzyme, which plays a key role in the bacterial metabolism, has resulted in 10 new antitubercular drug candidates. The uptake of antituberculars by infected macrophages is limited by extracellular diffusion. The optimization of the cellular uptake by drug delivery systems can decrease the used dosages and the length of the therapy, and it can also enhance the bioavailability of the drug molecule. In this study, improved in vitro efficacy was achieved by attaching the TB5 antitubercular drug candidate to peptide carriers. As drug delivery components, (i) an antimicrobial granulysin peptide and (ii) a receptor specific tuftsin peptide were used. An efficient synthetic approach was developed to conjugate the in silica identified TB5 coumarone derivative to the carrier peptides. The compounds were effective on M. tuberculosis H(37)Rv culture in vitro; the chemical linkage did not affect the antimycobacterial activity. Here, we show that the OT20 tuftsin and GranF2 granulysin peptide conjugates have dramatically enhanced uptake into human MonoMac6 cells.”

According to the news reporters, the researchers concluded: “The TB5-OT20 tuftsin conjugate exhibited significant antimycobacterial activity on M. tuberculosis H(37)Rv infected MonoMac6 cells and inhibited intracellular bacteria.”

For more information on this research see: Enhanced Cellular Uptake of a New, in Silico Identified Antitubercular Candidate by Peptide
Sungkyunkwan University, Seoul: Daily 300 mg dose of linezolid for multidrug-resistant and extensively drug-resistant tuberculosis: updated analysis of 51 patients

By a News Reporter-Staff News Editor at Biotech Week – Investigators discuss new findings in Tuberculosis. According to news reporting from Seoul, South Korea, by NewsRx journalists, researchers stated “Linezolid may be an effective treatment for multidrug-resistant (MDR) and extensively drug-resistant (XDR) tuberculosis (TB). The objective was to evaluate the efficacy, tolerability and adverse events of a 300 mg daily dose of linezolid in the treatment of MDR/XDR-TB.”

The news correspondents obtained a quote from the research by the authors from Sungkyunkwan University, “We retrospectively reviewed the medical records of 51 MDR-TB patients, including 26 patients (51) with XDR-TB, to evaluate the safety, tolerability and efficacy of therapy with 300 mg/day linezolid. All patients had failed previous treatments with second-line anti-TB drugs. Patients were treated with linezolid for a median of 413 days (IQR 237-622 days). Favourable treatment outcome (treatment success or still on treatment after culture conversion) was achieved in 40 patients (78) with culture conversion at a median of 55 days (IQR 419-61 days) from the start of linezolid therapy. Eleven patients (22) had unfavourable outcomes (treatment failure or death) and 14 (27) discontinued treatment due to neurotoxicity (peripheral or optic neuropathy) after a median of 278 days (IQR 174-412 days).”

According to the news reporters, the researchers concluded: “Our findings suggest that linezolid at a daily dose of 300 mg is effective against intractable MDR/XDR-TB, and may be associated with fewer neuropathic side effects than a daily dose of 600 or 1200 mg.”

Our news journalists report that additional information may be obtained by contacting W.J. Koh, Sungkyunkwan University Sch Med, Samsung Med Center, Dept. of Med Div Pulm & Crit Care Med, Seoul, South Korea. (2012 Jun 20)

**Peking Union Medical College Hospital, Beijing: Acute paradoxical reaction of cervical tuberculous lymphadenitis prompted by a misuse of etimicin sulphate**

By a News Reporter-Staff News Editor at Life Science Weekly – Fresh data on Tuberculosis are presented in a new report. According to news reporting originating in Beijing, People’s Republic of China, by NewsRx journalists, researchers stated “A 45-year-old HIV-negative man was treated with intravenous etimicin sulphate for an unintentionally found, non-tender neck mass at a local outpatient clinic. His symptoms seemed improved initially.”

The news reporters obtained a quote from the research by the authors from Peking Union Medical College Hospital, “However, the unilateral mass subsequently became enlarged quickly and painful. Spontaneous discharge occurred after admission to our department. The smear of the pus from surgical drainage was positive for acid-fast bacilli and the presence of *Mycobacterium tuberculosis* was confirmed by culture. He was diagnosed with an acute paradoxical reaction (PR) of cervical tuberculous lymphadenitis. Our case was unusual in that acute PR of tuberculosis was caused by receiving single aminoglycoside agent which has not been proven to have therapeutic effect on TB infection and it is also the first case of PR induced by etimicin.”

According to the news reporters, the researchers concluded: “The patient recovered well from a 6-month antituberculosis chemotherapy.”

For more information on this research see: Acute paradoxical reaction of cervical tuberculous lymphadenitis prompted by a misuse of etimicin sulphate. *Bmj Case Reports*, 2012;2012():. (BMJ Publishing Group - http://group.bmj.com/; Bmj Case Reports - http://casereports.bmj.com/)

Our news correspondents report that additional information may be obtained by contacting Y. Jiao, Dept. of General Internal Medicine, Peking Union Medical College Hospital & Chinese Academy of Medical Sciences, Beijing, People’s Taiwan. (2012 Jun 19)
CHAPTER 7  THERAPIES AND TREATMENTS

University of Oslo: Humiliation or care? A qualitative study of patients’ and health professionals’ experiences with tuberculosis treatment in Norway

By a News Reporter-Staff News Editor at Life Science Weekly – Researchers detail new data in Tuberculosis. According to news reporting out of Oslo, Norway, by NewsRx editors, researchers stated “Scand J Caring Sci; 2012; 26; 313323 Humiliation or care? A qualitative study of patients and health professionals experiences with tuberculosis treatment in Norway

Aim: Directly observed treatment (DOT) has been implemented globally as a strategy in treatment of tuberculosis. Studies from high-endemic settings show that DOT involves social and economical burdens for patients, but little is known about experiences with practicing DOT in low-endemic settings.”

Our news journalists obtained a quote from the research by the authors from the University of Oslo, “The present study explores patients and health professionals views and experiences with DOT in Norway. In-depth interviews were conducted with 22 patients originating from Somalia and Ethiopia and with 20 health professionals. Data from the interviews were analysed using systematic text condensation. We found that there was little room for patients to negotiate whether or not to consent to the organization of treatment (DOT). Patients told that it was difficult to question the way treatment was organized, as they got the impression that there was no other way of gaining access to medication. Both patients and health professionals reported that persuasion based on authority and subtle threats was used as means to facilitate patients acceptance of DOT. A majority of patients experienced DOT as humiliating and discriminating, while some had the experience of being cared for. Patients who attended school or had occupational obligations reported high social costs related to the treatment. Patients with positive experiences told that they had been given an opportunity to negotiate flexible treatment schedules and emphasized the importance of continuity among health professionals. Health professionals had divergent views and practices. Some argued that patients should be treated equally, while others argued for an individualized and flexible approach. The practice of DOT reflects societal power structures that influence the clinical interactions between health professionals and patients.”

According to the news editors, the researchers concluded: “To avoid experiences of disempowerment and humiliation among patients, treatment and care should be organized in a way that safeguards patients right to consent to treatment and that allows patients to negotiate an individualized treatment schedule.”

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Our news journalists report that additional information may be obtained by contacting M. Sagbakken, University of Oslo, Inst Hlth & Soc, Dept. of Hlth Management & Hlth Econ, Oslo, Norway. (2012 Jun 19)

**University of Science Malaysia, Kelantan: Ocular tuberculosis with multiple cerebral abscesses**

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators publish new report on Ocular Tuberculosis. According to news reporting from Kelantan, Malaysia, by NewsRx journalists, researchers stated “A 23-year-old Malay man presented with headache for one-month duration. It was associated with painless blurring of vision of the right eye.”

The news correspondents obtained a quote from the research by the authors from the University of Science Malaysia, “He had loss of appetite and reduced weight but no night sweats or hemoptysis. His visual acuity on the right eye was 6/45 and improved to 6/15 with pinhole. Right fundus examination revealed a choroidal tuberculoma located at one disc diameter away from optic disc superiorly with mild vitritis. Systemic examinations revealed no significant finding. Mantoux test reading was 22?mm with erythrocyte sedimentation rate that was 14?mm/h. Other blood investigations were negative with normal chest radiography. The computerized tomography scan of the brain revealed multiple cerebral abscesses. A clinical diagnosis of right ocular tuberculosis with multiple cerebral abscesses was made. He was treated with antituberculosis chemotherapy for one year which divided into intensive phase for three months and maintenance phase for nine months.”

According to the news reporters, the researchers concluded: “Cerebral abscesses resolved after three months of antituberculosis drugs and at one-year follow-up, and the choroidal tuberculoma resolved completely with scar formation and significant macular striae.”

For more information on this research see: Ocular tuberculosis with multiple cerebral abscesses. *Case Reports In Ophthalmological Medicine*, 2012;2012():606741. (Hindawi Publishing - www.hindawi.com; Case Reports In Ophthalmological Medicine - http://www.hindawi.com/crim/ophthalmological/)
Catholic University of the Sacred Heart, Rome: Chest wall TB and low 25-hidroxy-vitamin D levels in a 15-month-old girl

By a News Reporter-Staff News Editor at Pediatrics Week – Investigators discuss new findings in Tuberculosis. According to news originating from Rome, Italy, by VerticalNews correspondents, researchers stated “Parietal chest wall tuberculosis is an extremely rare manifestation of tuberculosis (TB) in children. We present the case of a 15 month-old girl presenting with a chest wall lesion initially thought to be of neoplastic origin and eventually diagnosed as chest wall TB, which was treated with surgical debridement and specific antitubercular therapy.”

Our news journalists obtained a quote from the research by the authors from the Catholic University of the Sacred Heart, “The girl had not-measurable 25-hidroxy-vitamin D levels, an increasingly recognized risk factor for the development of active TB. To our knowledge, in the English literature there are no similar described cases in such young infants. This case highlight the possibility of dealing with TB and its different manifestations also in low TB burden countries, due to continuously increasing migration flows. A detailed history is a key point to reach the diagnosis.”

According to the news editors, the researchers concluded: “Moreover, our case confirm the possible non casual relationship between TB and low 25-hidroxy-vitamin D levels, pointing out the importance of measuring its levels in all TB patients and considering its supplementation in addition to specific antitubercular therapy.”


The news correspondents report that additional information may be obtained from D. Buonsenso, Dept. of Pediatrics, Catholic University of the Sacred Heart - A, Gemelli Hospital, Lgo A, Gemelli 8, 00168 Rome, Italy. (2012 Jun 16)
Harvard University, Boston: The cost-effectiveness of routine tuberculosis screening with Xpert MTB/RIF prior to initiation of antiretroviral therapy: a model-based analysis

By a News Reporter-Staff News Editor at Biotech Week – A new study on Antiretrovirals is now available. According to news reporting out of Boston, Massachusetts, by NewsRx editors, researchers stated “In settings with high tuberculosis (TB) prevalence, 15-30% of HIV-infected individuals initiating antiretroviral therapy (ART) have undiagnosed TB. Such patients are usually screened by symptoms and sputum smear, which have poor sensitivity.”

Our news journalists obtained a quote from the research by the authors from Harvard University, “To project the clinical and economic outcomes of using Xpert MTB/RIF(Xpert), a rapid TB/rifampicin-resistance diagnostic, to screen individuals initiating ART. We used a microsimulation model to evaluate the clinical impact and cost-effectiveness of alternative TB screening modalities - in all patients or only symptomatic patients - for hypothetical cohorts of individuals initiating ART in South Africa (mean CD4 cell count = 171 cells/μl; TB prevalence 22%). We simulated no active screening and four diagnostic strategies, smear microscopy (sensitivity 23%); smear and culture (sensitivity, 100%); one Xpert sample (sensitivity in smear-negative TB: 43%); two Xpert samples (sensitivity in smear-negative TB: 62%). Outcomes included projected life expectancy, lifetime costs (2010 US$), and incremental cost-effectiveness ratios (ICERs). Strategies with ICERs less than $7100 (South African gross domestic product per capita) were considered very cost-effective. Compared with no screening, life expectancy in TB-infected patients increased by 1.6 months using smear in symptomatic patients and by 6.6 months with two Xpert samples in all patients. At 22% TB prevalence, the ICER of smear for all patients was $2800 per year of life saved (YLS), and of Xpert (two samples) for all patients was $5100/YLS. Strategies involving one Xpert sample or symptom screening were less efficient.”

According to the news editors, the researchers concluded: “Model-based analysis suggests that screening all individuals initiating ART in South Africa with two Xpert samples is very cost-effective.”

For more information on this research see: The cost-effectiveness of routine tuberculosis screening with Xpert MTB/RIF prior to initiation of antiretroviral therapy: a model-based analysis. *Aids*, 2012;26(8):987-995. *Aids* can be contacted at: Lippincott Williams & Wilkins, 530 Walnut St, Philadelphia, PA 19106-3621, USA. (Lippincott Williams and Wilkins - [www.lww.com](http://www.lww.com); *Aids* - [http://journals.lww.com/aidsonline/pages/default.aspx](http://journals.lww.com/aidsonline/pages/default.aspx))
Our news journalists report that additional information may be obtained by contacting J.R. Andrews, Harvard University, Sch Public Hlth, Dept. of Hlth Policy & Management, Boston, MA 02115, United States. (2012 Jun 13)

Department of Internal Medicine, Cordoba: Tuberculosis in solid organ transplant patients

By a News Reporter-Staff News Editor at Life Science Weekly – Fresh data on Tuberculosis are presented in a new report. According to news reporting originating from Cordoba, Spain, by NewsRx correspondents, researchers stated “Tuberculosis is an opportunistic infection with high morbidity and mortality in solid organ transplant patients. The reasons for this high morbidity and mortality lie mostly in diagnostic difficulties, which cause delays in starting treatment, and associated pharmaceutical toxicity.”

Our news editors obtained a quote from the research by the authors from the Department of Internal Medicine, “There are still major issues and difficulties in managing tuberculosis in solid organ transplant patients. These include problems due to interactions between antituberculosis and immunosuppressant drugs, the high risk of toxicity of antituberculosis drugs (particularly in liver transplant patients) and the absence of clear indications for the treatment of latent tuberculous infection.”

According to the news editors, the researchers concluded: “This article updates current understanding of tuberculosis in solid organ transplant patients.”

For more information on this research see: Tuberculosis in solid organ transplant patients. *Enfermedades Infecciosas Y Microbiologia Clínica*, 2012;30 Suppl 2():34-9.

The news editors report that additional information may be obtained by contacting A. Doblas, Dept. of Internal Medicine, Hospital de Alta Resolucion Valle del Guadiato, Penarroya-Pueblonuevo, Cordoba, Spain. (2012 Jun 12)
Case Western Reserve University, Cleveland: Hepatotoxicity during treatment for multidrug-resistant tuberculosis: occurrence, management and outcome

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – Data detailed on Multidrug Resistant Tuberculosis have been presented. According to news reporting from Cleveland, Ohio, by NewsRx journalists, researchers stated “Multidrug-resistant tuberculosis (MDR-TB) treatment program in Tomsk, Russia. To describe the incidence and management of hepatotoxicity during treatment of MDR-TB, and to assess risk factors associated with its development and impact on treatment outcomes.”

The news correspondents obtained a quote from the research by the authors from Case Western Reserve University, “A retrospective case series performed among 608 patients. Hepatotoxicity, using American Thoracic Society (2006) definitions, was observed in 91/568 patients (16.5%). The median time to the first hepatotoxic event was 196 days post treatment commencement. Baseline factors associated with hepatotoxicity included elevated alanine aminotransferase/aspartate aminotransferase/bilirubin (OR 53.9, 95%CI 6.30-438.7), and renal insufficiency (OR 19.6, 95%CI 2.71-141.6). High treatment adherence (OR 3.25, 95%CI 2.07-5.09) and starting treatment in prison (OR 1.77, 95%CI 1.04-3.01) were associated with treatment success. Smoking (OR 0.44, 95%CI 0.21-0.92) and bilateral cavitary disease (OR 0.51, 95%CI 0.34-0.77) were associated with worse outcomes. For alcohol users, developing hepatotoxicity was associated with better outcomes (OR 4.40, 95%CI 1.79-10.81) than not (OR 0.42, 95%CI 0.25-0.68). One or more medications were permanently stopped in 10/91 patients, but in no case was treatment entirely discontinued.”

According to the news reporters, the researchers concluded: “MDR-TB treatment in the face of hepatotoxicity during therapy did not result in a statistically significant increase in poor outcomes.”


Our news journalists report that additional information may be obtained by contacting S. Keshavjee, Case Western Reserve University, Cleveland, OH 44106, United States. (2012 Jun 11)
Indian Institute of Science Education and Research, Pune: Synthesis and antimycobacterial activity of prodrugs of sulfur dioxide (SO(2))

By a News Reporter-Staff News Editor at Tuberculosis Week – A new study on Tuberculosis is now available. According to news reporting originating in Pune, India, by NewsRx journalists, researchers stated “Here, we synthesized and studied a library of 2,4-dinitrophenylsulfonamides that closely resembled N-benzyl-2,4-dinitrophenylsulfonamide (1), a thiol-activated prodrug of sulfur dioxide (SO(2)) which has shown high potency as a Mycobacterium tuberculosis (Mtb) inhibitory agent. The ability of these compounds to generate SO(2) in the presence of a thiol was evaluated.”

The news reporters obtained a quote from the research by the authors from the Indian Institute of Science Education and Research, “A good correlation between pK(aH) of the corresponding amine and reactivity with thiols to generate SO(2) was found suggesting that the rate determining step of SO(2) generation involved protonation of the amine. Amongst analogues with measurable MICs, we also found a correlation between ability to generate SO(2) and Mtb growth inhibitory activity.”

According to the news reporters, the researchers concluded: “Together, we report several thiol-mediated prodrugs of SO(2) which strongly inhibited Mtb growth (MIC <1gmL(-1)) with potential for further development as tuberculosis drug candidates.”


Our news correspondents report that additional information may be obtained by contacting S.R. Malwal, Dept. of Chemistry, Indian Institute of Science Education and Research, Pune 411 008, India. (2012 Jun 11)

Public Health Service, San Diego: Treatment of multidrug-resistant tuberculosis in a high-prevalence region through a binational consortium

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – New research on Multidrug Resistant Tuberculosis is the subject of a report. According to news reporting from San Diego, California, by NewsRx journalists, researchers stated “We describe the outcome of treatment of multidrug-resistant tuberculosis (MDR-TB) in Baja California, Mexico, by a United States-Mexico consortium. From June 2006 to December 2010, 42 patients started treatment.”
The news correspondents obtained a quote from the research by the authors from Public Health Service, “Strains were resistant to 4.15 +/- 1.3 drugs; all patients achieved culture conversion on treatment after an average of 3.4 +/- 1.6 months. A total of 19 patients (47.5%) were discharged as cured, 3 died (7.5%) and 1 defaulted (2.5%).”

According to the news reporters, the researchers concluded: “MDR-TB cases can be cured under a well-organized out-patient program; in this consortium, the US partner introduced program elements that were gradually integrated into the Mexican state TB program.”

For more information on this research see: Treatment of multidrug-resistant tuberculosis in a high-prevalence region through a binational consortium. *International Journal of Tuberculosis and Lung Disease*, 2012;16(5):610-611. *International Journal of Tuberculosis and Lung Disease* can be contacted at: Int Union Against Tuberculosis Lung Disease (I U A T L D), 68 Boulevard Saint-Michel, 75006 Paris, France.

Our news journalists report that additional information may be obtained by contacting R. Laniado-Laborin, San Diego Cty Hlth & Human Serv Agcy, TB & Refugee Hlth Branch, Public Hlth Serv, San Diego, CA, United States. (2012 Jun 11)

Kuwait University: Role of Diabetes in the Prognosis and Therapeutic Outcome of Tuberculosis

By a News Reporter-Staff News Editor at Biotech Week – A new study on Diabetes is now available. According to news originating from Kuwait, Kuwait, by NewsRx correspondents, researchers stated “Increased susceptibility of diabetic mellitus (DM) patients to infection, including tuberculosis (TB), is well documented. The prevalence of DM in Malaysia is reaching epidemic proportions.”

Our news journalists obtained a quote from the research by the authors from Kuwait University, “In this study, we sought to assess risk factors for TB and the impact of DM on the outcome of TB treatment. TB patients, diabetic patients, and diabetic patients with TB were divided into three groups of 200 subjects each. Data were obtained from patients’ medical files at the beginning and end of the study period. Prevalence rates of DM and HIV among TB patients were assessed. Prognosis, TB-related complications, anatomical site of infection, and duration of infection and diabetes were also examined. The prevalence rates of HIV and DM amongst TB patients were 7.7 and 30%, respectively. The diabetic TB patient group contained more males (72%) and smokers (45.5%) compared to the nondiabetic group (58.3% and 33.5%, resp.). Approximately 74% of diabetic patients were Mycobacterium sputum positive compared to only 51% of nondiabetic patients. Diabetic patients were also more likely to develop pulmonary TB (87%) compared to nondiabetic TB patients (59%). Diabetic TB patients had a higher
mortality rate (7.5%) compared to the TB only and DM only groups (1 and 2%, resp.). The duration of TB symptoms was longer in nondiabetic TB patients compared to diabetic TB patients (4.5 versus 2.6 months, resp.). Diabetes antedated TB by a mean time of 4 years.”

According to the news editors, the researchers concluded: “We found a higher number of sputum-smear-positive cases and pulmonary TB cases as well as a greater number of males and higher mortality rate in diabetic patients compared to nondiabetic patients.”


The news correspondents report that additional information may be obtained from S.A.S. Suleiman, Kuwait University, Fac Med, Dept. of Community Med & Behav Sci, Kuwait, Kuwait. (2012 Jun 06)

Birla Institute of Technology and Science-Pilani, Andhra Pradesh: Novel antitubercular diallyl/dibenzylthiosemicarbazones endowed with high activity toward multi-drug-resistant tuberculosis

By a News Reporter-Staff News Editor at Life Science Weekly – Current study results on Tuberculosis have been published. According to news reporting from Andhra Pradesh, India, by NewsRx journalists, researchers stated “Novel diallyl and dibenzylthiosemicarbazones were prepared by three-step reactions.”

The news correspondents obtained a quote from the research by the authors from the Birla Institute of Technology and Science-Pilani, “The compounds were tested for their in vitro activity against Mycobacterium tuberculosis H37Rv (MTB) and multi-drug-resistant Mycobacterium tuberculosis (MDR-TB). Most of the compounds showed excellent activity toward MDR-TB.”

According to the news reporters, the researchers concluded: “Among the thirty compounds (4,5a-o) tested N,N-dibenzyl-2-((5-nitrofuran-2-yl)methylene)hydrazinecarbothioamide (5g) was found to be the most potent compound MICs of 0.55 and 0.12 μM against MTB and MDR-TB.”

For more information on this research see: Novel antitubercular diallyl/dibenzylthiosemicarbazones endowed with high activity toward multi-drug-resistant tuberculosis. Medicinal Chemistry Research, 2012;21(6):810-815. Medicinal Chemistry Research can be contacted at:
University of Liverpool: An Exploration of Patient Perceptions of Adherence to Tuberculosis Treatment in Tanzania

By a News Reporter-Staff News Editor at Life Science Weekly – A new study on Tuberculosis is now available. According to news reporting originating in Liverpool, United Kingdom, by NewsRx journalists, researchers stated “In this study, we aimed to explore patient perceptions of adherence to tuberculosis (TB) treatment and construct a theoretical model of treatment adherence behavior. We conducted semistructured interviews with 11 adherent patients from Tanzania whom we recruited by purposive sampling.”

The news reporters obtained a quote from the research by the authors from the University of Liverpool, “The interview data were analyzed by content analysis. We found that the patient’s intention to adhere is the most important determinant of adherence behavior. This intention is preceded by the decision to seek biomedical health care, and based on knowledge and beliefs about TB treatment and the motivation to be cured. The intention to adhere helps patients to cope with perceived barriers to adherence, such as socioeconomic difficulties, and to create an adherence-enabling environment in which the presence of social support plays an important role.”

According to the news reporters, the researchers concluded: “Our preliminary adherence behavior model should be validated in larger, nonadherent patient populations and evaluated for its applicability to the development of adherence-promoting strategies.”

For more information on this research see: An Exploration of Patient Perceptions of Adherence to Tuberculosis Treatment in Tanzania. *Qualitative Health Research*, 2012;22(6):835-845. *Qualitative Health Research* can be contacted at: Sage Publications Inc, 2455 Teller Rd, Thousand Oaks, CA 91320, USA. (Sage Publications - http://www.sagepub.com/; Qualitative Health Research - qhr.sagepub.com)

Our news correspondents report that additional information may be obtained by contacting J. van den Boogaard, University of Liverpool, Liverpool L69 3BX, Merseyside, United Kingdom. (*2012 Jun 05*)
Research Hospital, Istanbul: Non-tuberculous mycobacteria infection: 75 cases

By a News Reporter-Staff News Editor at Tuberculosis Week – New research on Tuberculosis is the subject of a report. According to news originating from Istanbul, Turkey, by NewsRx correspondents, researchers stated “Non-tuberculosis mycobacterium is especially seen in AIDS and non-immunosuppressant patients. This study was designed to evaluate data relating to non-tuberculosis mycobacterium content in patients’ sputum for the clinical importance.”

Our news journalists obtained a quote from the research by the authors from Research Hospital, “During 2009-2010 at Sureyyapasa Chest Diseases and Chest Surgery Training and Research Hospital clinics, 75 patients [30 women (40%) and 45 men (69%); mean age (SD): 48.7 (15.9) years] with non-tuberculosis mycobacterium were determined by the rapid test and NAP test in Mycobacteria Growth Indicator Tube (MGIT), which had atypical growth in 51.864 Lowenstein-Jensen. Identification was done with Hsp65PCRREA methods in 32 (43%) cases. Treatment management, radiology, bacteriology, co-morbidity, treatment outcomes were evaluated from medical records, calling patients and from tuberculosis dispensaries. In 9 (28%) patients Mycobacterium abscessus, in 8 (25%) patients Mycobacterium avium complex (MAC), in 5 (16%) patients Mycobacterium kansasii was found with identification Hsp65PCRREA methods. In 18 (24%) of 75 cases with American Thoracic Society definition and treatment criteria, treatment was administered using major and minor drugs. Standard tuberculosis treatment was administered in 25 (33%) of the 75 cases. In 8 of 25 (32%) cases identification of non-tuberculosis mycobacterium was evident. In 32 of 75 cases follow up was performed with no treatment. One positive atypical growth culture was identified in 23 (72%) of 32 patients. Treatment was administered in 43 cases while 25 (58%) of 43 were cured, 3 (7%) of 43 were default and 3 (7%) died. Drug resistance was the outcome in 36 cases. While 31 (86%) had any drug resistance, 27 (75%) had HR drug resistance. Past history of tuberculosis treatment was evident in 20 (40%) cases. Respiratory and non-respiratory diseases were identified equally in 18 (38%) cases. Radiological consolidation in 28 (65%), and cavity in 16 (37%) cases were determined.”

According to the news editors, the researchers concluded: “In order to carry out the right treatment and epidemiologic evaluation, it is important to identify non-tuberculosis mycobacterium by culture methods.”


The news correspondents report that additional information may be obtained from A. Babalik, Clinic of Chest Diseases, Sureyyapasa Chest
St. Jude Children’s Hospital and Research Center, Memphis: Screening a library of 1600 adamantyl ureas for anti-Mycobacterium tuberculosis activity in vitro and for better physical chemical properties for bioavailability

By a News Reporter-Staff News Editor at Tuberculosis Week – Investigators discuss new findings in Tuberculosis. According to news reporting originating from Memphis, Tennessee, by NewsRx correspondents, researchers stated “Adamantyl ureas were previously identified as a group of compounds active against Mycobacterium tuberculosis in culture with minimum inhibitor concentrations (MICs) below 0.1 µg/ml. These compounds have been shown to target MmpL3, a protein involved in secretion of trehalose mono-mycolate.”

Our news editors obtained a quote from the research by the authors from St. Jude Children’s Hospital and Research Center, “They also inhibit both human soluble epoxide hydrolase (hsEH) and M. tuberculosis epoxide hydrolases. However, active compounds to date have high cLogP’s and are poorly soluble, leading to low bioavailability and thus limiting any therapeutic application. In this study, a library of 1600 ureas (mostly adamantyl ureas), which were synthesized for the purpose of increasing the bioavailability of inhibitors of hsEH, was screened for activity against M. tuberculosis. 1-Adamantyl-3-phenyl ureas with a polar para substituent were found to retain moderate activity against M. tuberculosis and one of these compounds was shown to be present in serum after oral administration to mice. However, neither it, nor a closely related analog, reduced M. tuberculosis infection in mice. No correlation between in vitro potency against M. tuberculosis and the hsEH inhibition were found supporting the concept that activity against hsEH and M. tuberculosis can be separated. Also there was a lack of correlation with cLogP and inhibition of the growth of M. tuberculosis.”

According to the news editors, the researchers concluded: “Finally, members of two classes of adamantyl ureas that contained polar components to increase their bioavailability, but lacked efficacy against growing M. tuberculosis, were found to taken up by the bacterium as effectively as a highly active apolar urea suggesting that these modifications to increase bioavailability affected the interaction of the urea against its target rather than making them unable to enter the bacterium.”

University of Strathclyde, Glasgow: Strategies and challenges involved in the discovery of new chemical entities during early-stage tuberculosis drug discovery

By a News Reporter-Staff News Editor at Pediatrics Week – Investigators publish new report on Tuberculosis. According to news originating from Glasgow, United Kingdom, by VerticalNews correspondents, researchers stated “There is an increasing flow of new antituberculosis chemical entities entering the tuberculosis drug development pipeline. Although this is encouraging, the current number of compounds is too low to meet the demanding criteria required for registration, shorten treatment duration, treat drug-resistant infection, and address pediatric tuberculosis cases.”

Our news journalists obtained a quote from the research by the authors from the University of Strathclyde, “More new chemical entities are needed urgently to supplement the pipeline and ensure that more drugs and regimens enter clinical practice. Most drug discovery projects under way exploit enzyme systems deemed essential in a specific Mycobacterium tuberculosis biosynthetic pathway or develop chemical scaffolds identified by phenotypic screening of compound libraries, specific pharmacophores or chemical clusters, and natural products.”

According to the news editors, the researchers concluded: “Because the development of a compound for treating tuberculosis is even longer than for treating other infection indications, the identification of selective, potent, and safe chemical entities early in the drug development process is essential to ensure that the pipeline is filled with new candidates that have the best chance to reach the clinic.”

For more information on this research see: Strategies and challenges involved in the discovery of new chemical entities during early-stage tuberculosis drug discovery. The Journal of Infectious Diseases, 2012;205 Suppl():S258-64.

The news correspondents report that additional information may be obtained from G.D. Coxon, Strathclyde Institute for Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, UK. (2012 Jun 02)
Agency Reviews Patent Application Approval Request for “Quantitative Microfluidic Devices”

By a News Reporter-Staff News Editor at Gastroenterology Week – Diagnostics For All, Inc. has been issued patent application serial number 628336, according to news reporting originating out of Washington, D.C., by NewsRx editors.

The patent’s inventors are Rolland, Jason (Belmont, MA); Beattie, Patrick (Cambridge, MA); Kumar, Shailendra (Needham, MA).

This patent application was filed on September 27, 2012 and was made available online on April 11, 2013.

From the background information supplied by the inventors, news correspondents obtained the following quote: “Blood tests for monitoring analyte concentration in a sample from a patient are widely available. One example is devices for diagnosing the status of the liver, now a standard part of medical care in developed nations, particularly for individuals who have underlying liver disease or who are taking medications which can cause hepatotoxicity (drug-induced liver injury, or DILI). Medications which can lead to DILI, and the subsequent elevation of serum transaminase (aspartate aminotransferase (AST) and alanine aminotransferase (ALT) levels, include statins, acetaminophen, aspirin, ibuprofen, naproxen, phenylbutazone, anti-seizure medications, antibiotics, and antidepressants. Additionally, conditions such as acute viral hepatitis A or B, alcoholism, drug addiction, liver cancer, shock, liver steatosis or fatty liver, obesity, diabetes, hemochromatosis, Wilson’s disease, alpha-1-antitrypsin deficiency, environmental toxin exposure, and Crohn’s disease are correlated with increased transaminases and require frequent monitoring.

“A specific case of frequent DILI occurs in patients being treated for human immunodeficiency virus (HIV) or tuberculosis (TB). Accordingly, U.S. guidelines call for baseline and serial monitoring of serum transaminases in at-risk individuals while on standard TB and/or HIV therapy. The overall incidence of clinically significant hepatotoxicity on TB therapy (typically due to the medications isoniazid, rifampin, and/or pyrazinamide) ranges from 2-33%, and risk may be increased by multiple factors, such as abnormal baseline transaminases, increasing age, pre-existent liver disease (e.g. hepatitis B and/or C), alcohol use, pregnancy, and malnutrition.

“Monitoring for health-related parameters, e.g., for analytes indicative of liver health, via blood or urine tests in resource-limited settings—defined broadly as settings where access to modern equipment and instrumentation is limited—is often prohibited by relative expense and logistical and practical concerns. Testing is often done in centralized or regional laboratories in these settings, resulting often in significant delays in obtaining and acting on results. Because of these obstacles,
in many resource-limited settings, patients receive minimal or no monitoring. Low-cost, minimally invasive, point-of-care test devices for analytes of clinical significance would have a dramatic impact on patient care in both the developing and the developed world.”

Supplementing the background information on this patent application, NewsRx reporters also obtained the inventors’ summary information for this patent application: “A series of methods and structural improvements now have been developed which permit the efficient and extremely inexpensive manufacture of disposable, assay devices for detection and quantitation of analytes in liquid clinical samples, e.g., blood or urine. The test devices are versatile in that they can be adapted to detect a variety of analytes. In use, they are easy to use and are self-actuating: typically all that is needed to conduct the assay is to apply a drop of sample to the indicated location on the device. In addition, they are easy to interpret: typically being colorimetric and readable with the naked eye. Further, they are at least semi-quantitative. These methods and improvements, defined in greater detail below in the context of the design of a disposable, paper-based test for liver function, may be applied to develop a family of colorimetric clinical assay devices suitable for use in regions of the world where health care infrastructure is absent.

“In one broad aspect, the invention provides a test device for quantitative determination of an analyte in a liquid biological sample. The device comprises a porous, hydrophilic sheet, e.g. adsorptive paper or nitrocellulose, defining plural functional regions including a liquid sample input; a colorimetric test readout; a negative control that upon absorption of the sample maintains or displays a predetermined color; a positive control, and a liquid flow path which, responsive to application of a liquid sample to the input, transports liquid between the input and both the readout and controls. Disposed in the device, e.g., adjacent the input region or in the test region, or in a reagent reservoir in fluid communication with the liquid flow path, is at least one dried, color-producing reagent arranged to produce a shade or pattern of color in a readout as a function of the concentration of an analyte in the sample. Also disposed in the device is a dried, color-producing reagent which reacts at the positive control to produce color. In these embodiments of devices of the invention, a valid test is indicated by only if there is a color change in the positive control and maintenance or display of a predetermined color at the negative control.

“In another aspect, the invention provides a family of test devices for quantitative determination of an analyte in a liquid biological sample which have elements in common with the embodiment described in the previous paragraph, but the colorimetric test readout includes a region of a color backing the readout, e.g., a region of printed color, which optically interacts with color developed at the readout to improve
visual discrimination among different analyte concentrations in an applied sample. Thus, this type of device comprises a porous, hydrophilic sheet defining plural functional regions including a liquid sample input; a colorimetric test readout including the region of a color backing the readout which optically interacts with color developed at the readout to improve visual discrimination among different analyte concentrations in an applied sample; a colorimetric control; and a liquid flow path which transports liquid between the input and both the readout and the control. Again, disposed in the device is a dried, color-producing reagent which, responsive to application of a liquid sample to the input, is entrained and reacts with an analyte, if present in the applied sample, to produce a visually detectable change of color (as opposed to an intensity of a single color) in the readout as a function of the concentration of an analyte in the sample.

“In preferred embodiments, the device comprises a plurality of sheets disposed parallel to one another, e.g., stacked or laminated, at least two of which are separated by a liquid impermeable barrier layer defining an opening permitting liquid flow communication between the sheets. The color producing reagent may react with any analyte, and in one preferred embodiment, reacts with one or more liver enzymes to detect pathologic liver function such as elevated levels or concentrations of aspartate aminotransferase, alanine aminotransferase, or a mixture thereof. The negative control may comprise a colored area applied to a sheet which has an appearance when wetted different from when dry. The readout may comprise an area of a sheet comprising an immobilized binder which captures a colored species produced by the color-producing reagents. This permits display or a readout of the concentration of analyte in a sample as a portion of the area that develops color responsive to application of liquid to said input. The area may be continuous so that the concentration of analyte in a said sample is indicated, as in a mercury thermometer, by the linear extent of color development in the area. Alternatively, the area comprises a plurality of separate areas and the concentration of analyte in the sample is indicated by the number of areas that develop color.

“In still additional forms and embodiments of the invention the device further comprises a region defining a timer comprising a reservoir disposed in the device in liquid communication with the inlet which, after application of a sample, receives liquid from the sample over a predetermined time interval and comprises indicia that the reservoir is filled and the device is ready to be read. The timer may for example comprise a channel of predefined dimensions which determines the length of time that liquid takes to reach the reservoir and to activate the indicia, which may comprise a printed message visible when the device is ready to be read. The timer also may function as a positive colorimetric control. Often, the timer is disposed downstream from the
Many of the devices of the invention comprise a filter disposed upstream of the inlet, e.g., to exclude colored components such as red blood cells or hemoglobin from transport through the flow structure of the device and to permit unhindered colorimetric readout.

“In yet additional forms and embodiments of the invention the device further comprises downstream of the color-producing reagent and upstream of the colorimetric test readout, a dwell region which transports therethrough a mixture of analyte from a sample and the color-producing reagent, the dwell region comprising a multiplicity of micro flow paths including hydrophobic flow impeding surfaces, the numbers and dimensions of the micropaths serving to set the incubation time within a predetermined time interval as the mixture passes therethrough. The dwell region may be, for example, impregnated with a hydrophobic material (e.g., wax) which impedes the rate of liquid passage through the dwell region. In some cases, the dwell region is manufactured by printing a hydrophobic material onto a surface of a sheet and heating to absorb the hydrophobic material into the pores of the sheet.

“In some embodiments, the device may comprise an adsorptive reservoir downstream of the colorimetric test readout for drawing liquid along the flow path and through the dwell region and colorimetric test readout thereby to remove unbound colored species from the colorimetric test readout. A device may comprise in some instances an immobilized binder (e.g., an antibody) at the colorimetric test readout for capturing a complex formed during incubation in the dwell region. The device may include a sheet holding a dried, color-producing reagent in fluid communication with a parallel disposed sheet defining the dwell region. In certain embodiments, at least two of the following elements of the device are defined on a single said adsorptive sheet: a region holding a dried, color-producing reagent; a sample input; a colorimetric test readout; a dwell region; and an adsorptive reservoir.

“In three-dimensional embodiments of the invention, the devices may comprise a patterned layer of adhesive which constitutes the barrier layer between adjacent adsorptive or absorptive sheets and which defines an opening permitting liquid flow communication between the sheets. This provides flexibility and control, as well as multiplexing of test paths on a single device. For example, the inlet and readout may be disposed on different sheets, or the readout and a the color-producing reagent(s) may be disposed on different sheets.

“The devices of the invention may further comprising a color chart relating color at the readout to analyte concentration, and this may optionally be integrated with a sheet. Of course, plural readouts serviced by respective different dried, color-producing reagents are enabled by the disclosure herein. Flow paths in the devices typically comprise one or a pattern of hydrophilic channels which direct transport of liquid flow.
and are defined by liquid impermeable boundaries substantially permeating the thickness of the hydrophilic sheet. The devices optionally may include an electrode assembly comprising one or more electrodes in liquid flow communication with the input region, and/or a thermally or electrically conductive material in communication with a flow path which can serve to control flow as a valve, or to evaporate fluid, for example. See, for example, International Patent Application Publication No. WO/2009/121041 and U.S. Ser. No. 13/254,967, the disclosures of which are incorporated herein by reference.

“In still another aspect the invention provides methods of manufacturing test devices for determination of one or more analytes in liquid biological samples enabling mass production of reliable, extremely inexpensive test devices designed for quantitative or semi-quantitative clinical assays for any one or combination of analytes. The method comprises the steps of a) providing a first porous, hydrophilic sheet which supports absorptive or adsorptive flow transport; b) printing onto the sheet an array of test device elements respectively comprising a pattern of hydrophobic barriers permeating the thickness of the porous sheet to define respective elements, each of which comprise plural functional regions including a liquid flow path and a colorimetric test readout; c) adhering to the first sheet a second porous, hydrophilic sheet to form a laminate; and d) cutting the laminate to separate individual elements to form a multiplicity of functional test devices. In preferred embodiments, prior to step d) one or more reagents are applied on each of the test device elements, e.g., by robotically pipetting. The reagents may be deposited on the first or second porous, hydrophilic sheet, or onto a separate structure that serves as a reagent reservoir located to be contacted with liquid sample applied to the input. The first and second sheets are aligned prior to step c to register structural features so as to implement fluid flow communication between the sheets. Also, the method may include the additional steps of providing a third sheet or additional multiple sheets defining other structure, e.g. an array of filter elements, and laminating the third or additional sheets to the first and second sheets to position functional structure such as a filter element in fluid communication with respected liquid flow paths of respective test device elements. Step c often comprises the step of providing a liquid impermeable layer between the first and second sheets, which may itself act as an adhesive layer. This may be done by application of two-sided adhesive sheet material designed to isolate flow of liquid on respective sheets except for one or more defined holes positioned to permit liquid flow communication between the sheets. Preferably, the liquid impermeable layer is produced by applying an adhesive to a sheet in a pattern.

“In another embodiment of the invention a method of manufacturing further comprises applying by printing onto a region of the surface of a
sheet a predetermined density of ink, causing the ink to penetrate the sheet, and hardening the ink to form a dwell region comprising a multiplicity of micro flow paths including hydrophobic flow impeding surfaces defined by the ink, the numbers and dimensions of the micropaths serving to set a predetermined time interval for liquid sample to pass through the dwell region. The method may further comprise the additional step of applying by printing onto the surface of the sheet a higher density of the ink to define a border of a flow path, causing the ink to penetrate the sheet, and hardening the ink to produce a liquid impermeable barrier defining a liquid flow path in fluid communication with the dwell region. Also, the method may include the additional step of laminating the sheet to at least one additional porous, hydrophilic sheet which supports absorptive flow transport, at least a portion of which is in liquid communication with the sheet, and which additional sheet defines at least one element selected from the group consisting of a flow path; a colorimetric test readout; an immobilized binder at a test region for capturing a complex; a second dwell region; a liquid sample inlet; a control site; a dried, color-producing reagent reservoir, an adsorptive reservoir, and a sample split layer. A sample split layer allows a sample to be divided, for example, so that multiple assays can be run in parallel.

“The method may include yet another additional step of applying by printing onto the surface of the sheet a higher density of the ink to define a border of at least one element selected from the group consisting of a flow path; a colorimetric test readout; an immobilized binder at a test region for capturing a complex; a second dwell region; a liquid sample inlet; a control site; a dried, color-producing reagent reservoir; an adsorptive reservoir; and a sample split layer in liquid communication with the sheet, causing the ink to penetrate the sheet, and hardening the ink to produce a liquid impermeable barrier defining a border of the element. In some embodiments, method may comprise providing a filter or a color-producing reagent reservoir in fluid flow communication with the dwell region. The method may include applying by printing onto plural regions of the surface of the sheet in an array a predetermined density of ink to produce an array of the dwell regions, laminating the sheet to at least one additional porous, hydrophilic sheet which supports absorptive flow transport, at least a portion of which is in liquid communication with the sheet, and which additional sheet defines a corresponding array of at least one element selected from the group consisting of a flow path; a colorimetric test readout; an immobilized binder at a test region for capturing a complex; a second dwell region; a liquid sample inlet; a control site; a dried color-producing reagent reservoir; an adsorptive reservoir; and a sample split layer.

DESCRIPTION OF THE DRAWINGS
The invention is herein described, by way of example only, with reference to the accompanying drawings, wherein dimensions are not to scale, but rather are selected as a means of describing the structure and operation of the various devices discussed. Further, this patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

FIG. 1 shows an exploded perspective view of a device comprising a plurality of parallel-disposed sheets (panel a), schematic diagram illustrating a method for performing an assay using the device (panel b), and read guides for quantifying the results of the assay (panel c), according to an embodiment;

FIG. 2 shows a liver enzyme test device that includes two tests and three controls and exemplary result outputs, according to an embodiment;

FIG. 3 shows a control region of a device that undergoes a color change from white to yellow when wet, according to an embodiment;

FIG. 4 shows a comparison of color readout on a white background (top panel) and a yellow background (bottom panel) illustrating improved contrast with the yellow background;

FIG. 5 shows exemplary useful AST assay chemistry (FIG. 5A) and exemplary ALT assay chemistry (FIG. 5B);

FIG. 6 illustrates designs for multiplexed devices, according to various embodiments;

FIG. 7 is a diagram useful in illustrating a method of manufacturing a plurality of devices, according to an embodiment;

FIG. 8 illustrates a device incorporating a timing element, according to an embodiment;

FIG. 9 illustrates a plasma separation membrane filter attachment process in a device fabrication method, according to an embodiment;

FIG. 10 shows an exploded view of a device configured for quantitative colorimetric readout (left panel) and exemplary assay readouts (right panel), according to an embodiment;

FIG. 11 shows a device configured for quantitative colorimetric readout; more filled circles means higher concentration of analyte;

FIG. 12 is a plan and perspective view of a device for quantitative colorimetric readout that includes a color chart for automated calibration;

FIGS. 13A and 13B are bottom and top views of a liver enzyme test device embodying the invention;

FIG. 14 shows a device displaying a gradation of color from yellow to red for an ALT assay as a function of increasing ALT concentration and a gradation of color from dark blue to pink in an AST assay as a function of increasing AST concentration;
“FIG. 15 shows a calibration plot of the output signal of the liver function test (LFT) versus the concentration of AST (left panel) or ALT (right panel) (N=7 for each concentration), according to an embodiment; and

“FIG. 16 shows standard curves generated for the ALT test as a function of ALT concentration (left panel) and the AST test as a function of AST concentration (right panel), according to an embodiment.”


By a News Reporter-Staff News Editor at Life Science Weekly – The Regents Of The University Of Michigan has been issued patent application serial number 679224, according to news reporting originating out of Washington, D.C., by NewsRx editors.

The patent’s inventors are Miller, Josef (Ann Arbor, MI); LePrell, Colleen (Gainesville, FL); Schact, Jochen (Ann Arbor, MI); Prieskorn, Diane (Livonia, MI).

This patent application was filed on November 16, 2012 and was made available online on April 4, 2013.

From the background information supplied by the inventors, news correspondents obtained the following quote: “The present invention generally relates to a composition for treating hearing loss. More specifically, the composition includes components that provide an additive effect that is equal to or greater than the sum of the effects of the individual components.

“Extensive studies have been performed on compositions for treating side effects to antibiotic treatment, along with methods of treating the side effects using various compositions. Particularly problematic side effects from antibiotic treatment include kidney damage, loss of balance, and hearing loss attributable to antibiotic treatment such as aminoglycoside or glycopeptide antibiotic treatments. The damaging side effects of many aminoglycoside antibiotics were first reported in the 1940s, and the damaging side effects have long been an impediment to use of aminoglycoside antibiotics. Aminoglycoside antibiotics cause permanent deficits in the vestibular system (balance) and irreversible cell death in the cochlea, resulting in hearing impairment.
“While the damaging side effects of aminoglycoside antibiotics, in particular, have impeded their use, it has not eliminated their use. Aminoglycoside antibiotics are the only ‘standard of treatment’ in certain severe gram-negative bacterial infections, and the only inexpensive antibiotics that are available in developing countries. In the USA and European countries where the side effects are well recognized, and where 2.sup.nd and 3.sup.rd generation antibiotics are substituted wherever possible, side effects such as inner ear damage and hearing loss in patients can be minimized through careful monitoring of aminoglycoside antibiotic treatment. However, in countries in which there are fewer alternative drugs and monitoring is less rigorous or non-existent, side effects associated with aminoglycoside antibiotic treatment is more prevalent.

“Notably, HIV death is often driven by tuberculosis as a secondary infection to HIV. In developing countries, aminoglycoside antibiotic treatment is widely used against tuberculosis. Given the generally lax monitoring and the high incidence of side effects associated with aminoglycoside antibiotic treatment in developing countries, poor patient compliance in completing proscribed aminoglycoside antibiotic treatment is common, contributing to the development of drug-resistant strains of tuberculosis.

“Historically, from the first identification of side effects such as hearing loss attributable to aminoglycoside antibiotic treatment in the 1940s, research focused on identification of the aminoglycoside-induced pathophysiology and otohistopathology, the pharmacokinetics of the aminoglycoside antibiotics, and methods of monitoring early damage and thereby avoiding serious side effects attributable to aminoglycoside antibiotic treatment in humans. Mechanistic studies of aminoglycoside ototoxicity began in the 1980s. Findings that free-radical formation played a role in aminoglycoside ototoxicity were first indicated by reports of efficacy of some free radical scavengers in reducing ototoxicity. More direct evidence was uncovered in the mid to late 1990s of free radical formation by gentamicin (which is one type of aminoglycoside antibiotic), while ototoxicity attributable to aminoglycoside treatment was found to be inversely related to glutathione levels (endogenous antioxidant) in inner ear tissues. It has since been shown that ototoxicity of aminoglycoside antibiotics could be reduced by treatment with some radical scavengers.

“Free radical formation has been shown to play a role in many instances of stress-induced cell pathology. High intensity noise has been shown to induce free radical formation. For the inner ear, the mechanism by which high intensity noise induces cell death in the cochlea and hearing impairment has been shown to be dependent on free radical formation. Noise-induced trauma to the inner ear has been shown
to be inversely related to endogenous levels of glutathione in cochlear tissues.

“The parallels between the mechanisms of noise- and antibiotic-induced cell death in the inner ear suggest that they share a common cell death pathway such that it is natural to speculate that agents found effective to attenuate noise-induced hearing loss may be effective to attenuate antibiotic-induced hearing loss. However, it is clear from the literature that great variability is found in the efficacy of some of the agents to reduce the damaging side effects of aminoglycoside antibiotics. To some extent, the variable efficacy may reflect differential mechanisms of action of the scavengers or unique molecular structures of the free radicals formed. Some agents have been tested for efficacy against noise-induced hearing loss (NIHL) and their relative efficacy has been found to differ from their relative efficacy for drug-induced hearing loss. For example, allopurinol is ineffective in reducing gentamicin-induced ototoxicity, but is effective in reducing noise-induced hearing loss. Given such observations (and other similar ones in literature), there is no substantial basis for believing that a formulation for treating noise-induced hearing loss will be effective to treat antibiotic-induced hearing loss and other side effects of antibiotic treatment.

“In view of the foregoing, there remains further opportunities to develop effective methods of treating side effects of antibiotic treatment, including antibiotic-induced hearing loss, kidney damage, and loss of balance, the methods including the step of administering a composition that includes a specific combination of components, in biologically effective amounts, in conjunction with administration of antibiotics that are capable of causing side effects such as hearing loss in mammals.

“There is also an opportunity to provide a composition and a method of treating hearing loss including the step of administering the composition that includes a specific combination of components having an additive effect that is equal to or greater than the sum of the effect of the individual components in treating hearing loss when used in biologically effective amounts.”

Supplementing the background information on this patent application, NewsRx reporters also obtained the inventors’ summary information for this patent application: “The subject invention provides a composition to be administered to a mammal for treating hearing loss. The composition consists essentially of biologically effect amounts of vitamin A, vitamin E, vitamin C, a vosidilator comprising magnesium, and, optionally, a withanoloid and/or resveratrol, to provide an additive effect that is equal to or greater than a sum of the effects of the individual components.

BRIEF DESCRIPTION OF THE DRAWINGS
“Other advantages of the present invention will be readily appreciated, as the same becomes better understood by reference to the following detailed description when considered in connection with the accompanying drawings wherein:

“FIG. 1 is a graph showing the effect of a Comparative Example of a composition used to treat hearing loss including Trolox® (vitamin E) and betahistine on reduction of a threshold shift in guinea pigs from baseline threshold sensitivity at 4, 8, and 16 kHz after exposure to 120 decibel SPL Octave Band Noise centered at 4 kHz for five hours;

“FIG. 2 is a graph showing the effect of treatment in accordance with the instant invention using a composition including vitamins A, C, and E and magnesium, and comparative examples of treatments using compositions that include only some of those components, on average reduction of a threshold shift in guinea pigs from baseline threshold sensitivity at 4, 8, and 16 kHz after exposure to 120 decibel SPL Octave Band Noise centered at 4 kHz for five hours;

“FIG. 3 is a graph showing the effect of treatment in accordance with the instant invention using the composition of the subject invention and treatments using Comparative Examples of compositions of FIG. 2 on an amount of missing hair cells in the region of the cochlea that is most damaged after the noise exposure specified above for FIG. 2;

“FIG. 4 is a graph showing the effect of treatment in accordance with the instant invention using the composition including vitamins A, C, and E and magnesium and treatments using Comparative Examples of compositions of FIG. 2 on an amount of missing hair cells in the whole cochlea after the noise exposure specified above for FIG. 2;

“FIG. 5 is a graph showing the effect of treatment of side effects of antibiotic treatment, as a measurement of percentage of outer hair cells and inner hair cells lost in guinea pigs, when the composition including vitamins A, C, and E and magnesium is administered in conjunction with administration of aminoglycoside antibiotics in accordance with the method of the subject invention versus a control in which aminoglycoside antibiotic is administered alone;

“FIG. 6 is a graph showing a mean threshold shift of hearing loss in guinea pigs treated with an inventive composition consisting essentially of vitamin A, vitamin C, vitamin E, and magnesium, and treated with comparative compositions including i) saline, ii) magnesium, iii) vitamins A, C, and E, iv) creatine, v) vitamin A, vitamin C, vitamin E, magnesium, and creatine, and vi) vitamin A, vitamin C, vitamin E, magnesium, creatine, and salicylate, where the mean threshold shift is measured at baseline threshold sensitivities of 4, 8, and 16 kHz after exposure to 120 decibel SPL Octave Band Noise centered at 4 kHz for five hours; and
“FIG. 7 is a graph showing side effects of treatment of the guinea pigs by an inventive composition consisting essentially of vitamin A, vitamin C, vitamin E, and magnesium, and by comparative compositions including i) saline, ii) magnesium, iii) vitamins A, C, and E, iv) creatine, v) vitamin A, vitamin C, vitamin E, magnesium, and creatine, and vi) vitamin A, vitamin C, vitamin E, magnesium, creatine, and salicylate, the side effects of the treatment being a measurement of percentage of outer hair cells lost in the guinea pig in the whole cochlea and in the trauma region after the noise exposure.”


**Patent Issued for Use of Polymorphic Forms of Rifaximin for Medical Preparations**

By a News Reporter-Staff News Editor at Physician Law Weekly – According to news reporting originating from Alexandria, Virginia, by NewsRx journalists, a patent by the inventors Viscomi, Giuseppe Claudio (Bologna, IT); Campana, Manuela (Bologna, IT); Confortini, Donatella (Bologna, IT); Barbanti, Miriam (Bologna, IT); Calanni, Fiorella (Bologna, IT), filed on March 4, 2011, was published online on March 26, 2013.

The assignee for this patent, patent number 8404704, is Alfa Wassermann S.p.A. (Alanno (PE), IT).

Reporters obtained the following quote from the background information supplied by the inventors: “Rifaximin (INN; see The Merck Index, XIII Ed., 8304) is an antibiotic belonging to the rifamycin class of antibiotics, e.g., a pyrido-imidazo rifamycin. Rifaximin exerts its broad antibacterial activity, for example, in the gastrointestinal tract against localized gastrointestinal bacteria that cause infectious diarrhea, irritable bowel syndrome, small intestinal bacterial overgrowth, Crohn’s disease, and/or pancreatic insufficiency. It has been reported that rifaximin is characterized by a negligible systemic absorption, due to its chemical and physical characteristics (Descombe J. J. et al. Pharmacokinetic study of rifaximin after oral administration in healthy volunteers. Int J Clin Pharmacol Res, 14 (2), 51-56, (1994)).

“Rifaximin is described in Italian Patent IT 1154655 and EP 0161534, both of which are incorporated herein by reference in their
entirety for all purposes. The EP patent discloses a process for rifaximin production using rifamycin O as the starting material (The Merck Index, XIII Ed., 8301). These patents generically describe purification strategies of rifaximin by crystallization in suitable solvents or solvent systems and summarily show in some examples that the resulting product can be crystallized from the 7:3 mixture of ethyl alcohol/water and dried both under atmospheric pressure and under vacuum. Neither patent discloses any experimental conditions, or further guidance for crystallization and drying or any indication that rifaximin exists in polymorphic forms. U.S. Pat. No. 7,045,620 B1 discloses the identification, characterization and process for obtaining polymorphic forms of rifaximin.

“The identification and characterization of polymorphic forms, as well as the experimental conditions for obtaining polymorphs, is important for therapeutic compounds. Polymorphs of a compound can influence the pharmaco-toxicologic properties of the drug, such as bioavailability, solubility, stability, colour, compressibility, flowability and workability with consequent modification of the profiles of toxicological safety, clinical effectiveness and productive efficiency.

“Rifaximin is approved for the treatment of pathologies caused by non-invasive strains as Escherichia coli, micro-organism which are not able to penetrate into GI mucosa and they remain in contact with the GI fluids.

“Since 1980, when discovered, rifaximin appeared to be a non-adsorbed antibiotic and the published data on the bioavailability of rifaximin indicate that the maximum plasma level of rifaximin after oral administration appeared to be almost negligible, being in the range from 2 and 5 ng/ml (Descombe J. J. et al. Pharmacokinetic study of rifaximin after oral administration in healthy volunteers. Int J Clin Pharmacol Res, 14 (2), 51-56, (1994)).

“This was considered an intrinsic property of the compound and the pharmaceutical develop was designed on this property.

“As far as the drug safety profile is concerned, it should be reminded that in the therapeutic practice, antibiotics may cause bacterial resistance to the same or other similar antibiotics. This is particularly relevant to rifaximin because it belongs to the rifamycin family along with rifampicin, which is the standard of care for the treatment of tuberculosis. The current short course treatment for tuberculosis is a combination therapy involving four active pharmaceutical ingredients: rifampicin, isoniazid, ethambutol and pyrazinamide, with rifampicin playing a pivotal role. Therefore, any drug which jeopardizes the efficacy of the therapy by selecting for resistance to rifampicin would be harmful. (Kremer L. et al. ‘Re-emergence of tuberculosis: strategies and treatment’, Expert Opin. Investig. Drugs, 11 (2), 153-157, (2002)). Thus, it is possible that the use of rifaximin might induce the selection
resistant strains of M. tuberculosis and cross-resistance to rifampicin. Polymorphic forms may provide a mechanism to avoid this negative event because the quantity of systemically absorbed rifaximin may be controllable through the use of polymorphic forms.”

In addition to obtaining background information on this patent, NewsRx editors also obtained the inventors’ summary information for this patent: “It has now been unexpectedly found that polymorphic forms of rifaximin described in U.S. Pat. No. 7,045,620 B1, have different in vivo bioavailability properties and, therefore, are useful in the preparation of pharmaceuticals with different characteristics for the treatment of infections. Thus allowing one to generate rifaximin preparations that show significantly different levels of adsorption with C.sub.max values from about 0.0 ng/ml to 5.0 μg/ml. This also allows one to obtain rifaximin preparations ranging from being negligibly to significantly adsorbed forms. It was unexpectedly found that rifaximin polymorphic form is endowed with distinct pharmaceutical properties compared with what was known for rifaximin.

“By the present invention it is possible to modulate the therapeutic action by selecting the proper polymorphic form.

“In case of invasive bacteria, it may be useful to use the most bioavailable polymorphic form, whereas in case of non-invasive pathogens it may be more appropriate to use the less adsorbed forms, since they are safer.

“Some features of polymorph .alpha.include, for example: a water content (w/w) from about 0 to about 3.0%. a C.sub.max of polymorph a from about 0.0 ng/ml to about 5.5 ng/ml. a t.sub.max from about 1.0 h to about 6 h. a AUC.sub.0-24h from about 0 to about 100 ngh/ml. a AUC.sub.0-inf from about 0 to 110 ngh/ml.

“Some features of polymorph .beta. include, for example: a water content from about 4.5 to about 100%. a C.sub.max from about 0.0 to about 40 ng/ml. a t.sub.max between about 1 and about 6 h a AUC.sub.0-24h from about 0 to about 40 ngh/ml. a AUC.sub.0-inf from about 0 to about 45 ngh/ml. an intrinsic dissolution rate between about 0.001 and about 0.016 mg/min/cm.sup.2.

“Some features of polymorph .gamma. include, for example: a water content from about 0% to about 2%. a C.sub.max from about 0.0 to about 5000 ng/ml. a t.sub.max from about 1.0 h to about 6.0 h. a AUC.sub.0-24h from about 0.0 to about 22000 ngh/ml. a AUC.sub.0-inf from about 0.0 to about 22000 ngh/ml. an intrinsic dissolution rate from about 0.1 to about 0.16 mg/min/cm.sup.2.

“In one aspect, a pharmaceutical composition is presented, which comprises one or more of a Form .alpha., Form .beta., or Form .gamma. polymorph of rifaximin and a pharmaceutically acceptable carrier.

“In one embodiment, the pharmaceutical composition further comprises excipients.
“According to another embodiment, the excipients are one or more of a diluting agent, binding agent, lubricating agent, disintegrating agent, colouring agent, flavouring agent or sweetening agent.

“In another embodiment, the composition is formulated for selected coated and uncoated tablets, hard and soft gelatine capsules, sugar-coated pills, lozenges, wafer sheets, pellets and powders in sealed packet.

“In one embodiment, the composition is formulated for topical use.

“Presented herein, according to one aspect, are methods of treating, preventing, or alleviating a bowel related disorder comprising administering to a subject in need thereof a cell infected with a virus with an effective amount of one or more of a Form .alpha., Form .beta., or Form .gamma. polymorph of rifaximin.

“According to another embodiment, wherein the bowel related disorder is one or more of irritable bowel syndrome, travelers’ diarrhea, small intestinal bacterial overgrowth, Crohn’s disease, chronic pancreatitis, pancreatic insufficiency, or colitis.

“Presented herein, according to one aspect, are methods of assessing the efficacy of a bowel related disorder treatment in a subject, monitoring the progress of a subject being treated for a bowel related disorder, or a method of selecting a subject for treatment of a bowel disorder, comprising:

“determining a pre-treatment level of bacterial overgrowth;

“administering a therapeutically effective amount of one or more of a Form .alpha., Form .beta., or Form .gamma. polymorph of rifaximin to the subject; and

“determining a post-treatment level of bacterial overgrowth after an initial period of treatment with the one or more of Form .alpha., Form .beta., or Form .gamma. polymorph of rifaximin.

“In one embodiment, the modulation of the level of bacterial overgrowth indicates efficacy of the treatment.

“In another embodiment, a decrease in bacterial overgrowth indicates that the treatment is efficacious.

“In another embodiment, the modulation of the bacterial overgrowth is an indication that the subject is likely to have a favourable clinical response to the treatment.

“Presented herein, according to one aspect, are kits for treating a bowel disorder in a subject, comprising one or more actions for use.

“Also presented herein, according to one aspect are packaged compositions comprising a therapeutically effective amount of one or more of a Form .alpha., Form .beta., or Form .gamma. polymorph of rifaximin and a pharmaceutically acceptable carrier or diluents, wherein the composition is formulated for treating a subject suffering from or susceptible to a bowel disorder, and packaged with instructions to treat a subject suffering from or susceptible to a bowel disorder.
“Presented herein, according to another aspect, are processes for the production of one or more of a Form .alpha., Form .beta., or Form .gamma. polymorph of rifaximin, comprising:

“reacting a molar equivalent of rifamycin O with an excess of 2-amino-4-methylpyridine in a solvent mixture comprising water and ethyl alcohol in volumetric ratios between 1:1 and 2:1 for a time between 2 and 8 hours;

“treating the reaction mixture at room temperature with a solution of ascorbic acid in a mixture of water, ethyl alcohol and concentrated aqueous hydrochloric acid;

“adjusting the pH of the solution to 2.0 with hydrochloric acid concentrated aqueous solution,

“filtering and washing the resulting solid with the same water/ethyl alcohol solvent mixture;

“purifying the raw rifaximin by dissolution in ethyl alcohol;

“precipitating rifaximin by addition of water, with between about 15% to about 70% to the weight amount of ethyl alcohol used for the dissolution at a temperature of from between about 50.degree. C. to about 0.degree. C. under stirring for between about 4 to about 36 hours;

“filtering and washing a resulting solid with water; and

“drying the rifaximin at a temperature of from between about room temperature to about 105.degree. C.

“According to one embodiment, the drying is for Form .alpha., Form .beta., or Form .gamma. between about 2 hours and about 72 hours.

“According to another embodiment, the reacting a molar equivalent of rifamycin O with an excess of 2-amino-4-methylpyridine is at a temperature of from between about 40.degree. C. to about 60.degree. C.

“In another embodiment, the purifying the raw rifaximin by dissolution in ethyl alcohol is at a temperature of from between about 45.degree. C. to about 65.degree. C.

“According to one embodiment, the reacting a molar equivalent of rifamycin O with an excess of 2-amino-4-methylpyridine is from between about 2.0 to about 3.5 molar equivalents.

“According to another embodiment, after precipitating rifaximin by addition of water, the method further comprises lowering the temperature to between about 28.degree. C. to about 32.degree. C. to start crystallization.

“In one embodiment, the resulting suspension is kept at a temperature of from between about 40.degree. C. to about 50.degree. C. under stirring for a time from between about 6 to about 24 hours.

“In one embodiment, the process further comprises cooling the suspension to about 0.degree. C. for from between about 15 minutes and one hour; filtering the resulting solid; and drying the solid to a water content of lower than 4.5%, preferably from between 0% and about 3% water to form Form .alpha..
“According to another embodiment, after precipitating rifaximin by addition of water, the method further comprises:

“cooling the solution to a temperature of from between about 28 degree. C. to about 32 degree. C.;
“maintaining the solution at from between about 40 degree. C. and 50 degree. C. under stirring for between about 6 to about 24 hours;
“cooling the solution to about 0 degree. C. for between about 15 minutes to about one hour;
“filtering a resulting solid;
“drying the solid from between about 4.5 to about 40% water content to form Form \( \beta \).

In one embodiment, after precipitating rifaximin by addition of water, the method further comprises:

“cooling the solution to a temperature of from between about 28 degree. C. to about 32 degree. C.;
“cooling the solution to about 0 degree. C., under stirring, for between about 6 to about 24 hours;
“filtering a resulting solid; and
“drying the solid to a water content of between 0% and about 2.0% to form Form \( \gamma \).

Presented herein, according to one aspect, are methods for the production of rifaximin O, comprising:

“reacting a molar equivalent of rifamycin O with an excess of 2-amino-4-methylpyridine in a solvent mixture comprising water and ethyl alcohol to form a reaction mixture;
“treating the reaction mixture with a solution of a weak acid, water, and alcohol to lower the pH of the solution to form a suspension;
“filtering the suspension and washing the resulting solid with a water, alcohol, and solvent mixture to form raw rifaximin;
“purifying the raw rifaximin by dissolution in an alcohol at a temperature between 45 degree. C. and 65 degree. C.;
“precipitating the raw rifaximin by the addition of water;
“lowering of the temperature of the suspension to between about 50 degree. C. to about 0 degree. C. under stirring to form a second suspension;
“filtering the second suspension; and
“washing a resulting solid with water and drying.

“In one embodiment, the reacting a molar equivalent of rifamycin O with an excess of 2-amino-4-methylpyridine is from between about 2.0 to about 3.5 molar equivalents.

“In another embodiment, the reacting a solvent mixture comprising water and ethyl alcohol is in volumetric ratios from between about 1:1 to about 2:1.

“According to one embodiment, the alcohol is one or more of ethyl alcohol, menthol, propanol, or 2-butanol.
“According to another embodiment, the reacting a solvent mixture comprising water and ethyl alcohol is for a time from between about 2 to about 8 hours.

“In one embodiment, the reacting a solvent mixture comprising water and alcohol is at a temperature from between about 40.degree. C. to about 60.degree. C.

“In one embodiment, the treating the reaction mixture is at about room temperature.

“In one embodiment, the solution to treat the reaction mixture comprises a weak reducing agent in a mixture of water, alcohol and a strong acid.

“In one embodiment, the weak reducing agent is one or more of ascorbic acid, sodium dithionate, or sodium thiosulphate.

“In another embodiment, the strong acid is one or more of hydrochloric acid, sulphuric acid, or phosphoric acid.

“According to one embodiment, when treating the reaction mixture the pH is lowered to about 2.0.

“In one embodiment, the drying is by one or more of under vacuum, under conditions of normal pressure, or in the presence of a drying agent.

“In another embodiment, the drying is at a temperature between about room temperature to about 105.degree. C.

“According to one embodiment, the drying is for a time from between about 2 to about 72 hours.

“According to another embodiment, the precipitating the rifaximin is by the addition of water in weight amounts of from between about 15% to about 70% of the weight amount of ethyl alcohol used for the reacting.

“According to one embodiment, the under stirring for a time from between about 4 to about 36 hours.

“According to another embodiment, after the precipitation of raw rifaximin the method further comprises:

“lowering the temperature to between about 28.degree. C. to about 32.degree. C.;

“maintaining the temperature at between about 40.degree. C. to about 50.degree. C. under stirring for between about 6 to about 24 hours;

“cooling to about 0.degree. C. for between about 15 minutes to about one hour;

“filtering a resulting solid; and

“drying the resulting solid to a water content from between about 3.0% to 0%, wherein the method forms Form .alpha. of rifaximin.

“In one embodiment, after the precipitation of raw rifaximin the method further comprises:
“lowering the temperature to between about 28.degree. C. to about 32.degree. C.;
“maintaining the temperature at between about 40.degree. C. to about 50.degree. C. under stirring for between about 6 to about 24 hours;
“cooling to about 0.degree. C. for between about 15 minutes and about one hour;
“filtering a resulting solid; and
drying the solid to a water content greater than about 4.5% to form Form .beta. of rifaximin.
“According to one embodiment, after the precipitation of raw rifaximin the method further comprises:
“lowering the temperature to between about 28.degree. C. to about 32.degree. C.;
“cooling the temperature to about 0.degree. C. under stirring for between about 6 to about 24 hours;
“filtering a resulting solid; and
“drying the solid to a water content of between about 1.0% to about 2.0%, wherein the method produces Form .gamma. of rifaximin.”

For more information, see this patent: Viscomi, Giuseppe Claudio; Campana, Manuela; Confortini, Donatella; Barbanti, Miriam; Calanni, Fiorella. Use of Polymorphic Forms of Rifaximin for Medical Preparations. U.S. Patent Number 8404704, filed March 4, 2011, and published online on March 26, 2013. Patent URL: http://patft.uspto.gov/netacgi/nph-Parser?Sect1=PTO2&Sect2=HITOFF&p=71&u=%2Fnetahtml%2FPTO%2Fsearch-bool.html&r=3516&f=G&l=50&co1=AND&d=PTXT&s1=20130326.PD.&OS=ISD/20130326&RS=ISD/20130326 (2013 Apr 10)

By a News Reporter-Staff News Editor at Life Science Weekly – A patent application by the inventors Kolattukudy, Pappachan E. (Orlando, FL); Sirakova, Tatiana (Orlando, FL); Daniel, Jaiyanth (Orlando, FL); Deb, Chirajoti (Orlando, FL), filed on August 13, 2012, was cleared for further review on February 21, 2013, according to news reporting originating from Washington, D.C., by NewsRx correspondents.

Patent serial number 572888 is assigned to University of Central Florida Research Foundation, Inc.

The following quote was obtained by the news editors from the background information supplied by the inventors: “Tuberculosis (TB) remains the leading cause of preventable deaths in the world with 100 million new infections and two million deaths each year. TB is caused by Mycobacterium tuberculosis (hereinafter also referred to by the abbreviation ‘Mtb’), an acid-fast bacillus that is transmitted primarily via the respiratory route. The aerosol containing the pathogen is released from people with active TB when they cough or sneeze. When a person breathes in the pathogen it enters the alveolar macrophages via a variety of receptors. Mtb multiplies within the vacuoles in the macrophage, avoids fusion with the acidic lysosomes and eludes the host defenses. As the host defense system senses the multiplying pathogen and mounts its immune defense, the pathogen goes into a non-replicating, drug-resistant, latent state. The protective response by the immune system at the site of infection results in the formation of a granuloma that contains the infection and prevents its spread. Live bacilli have reportedly been isolated from granulomas or tubercles in the lungs of persons with clinically inactive tuberculosis, regarded as the latent form of TB, indicating that the organism can persist in granulomatous lesions for decades. It is estimated that one-third of the world population has latent TB. These individuals are asymptomatic latent carriers who exhibit no signs of disease. Their risk for reactivation is estimated to be 2-23% over their life time. One study concluded that a 25 year old with latent TB has a 7.3% life time risk of reactivation. The risk increases dramatically for persons coinfected with HIV, more like 10% per year. Thus, the advent of AIDS greatly amplified the TB threat to human health. The deadly partnership between TB and AIDS, especially with multi- and extremely drug-resistant TB, is contributing to a dramatic rise in TB cases worldwide leading to a grave situation. The emergence and spread of multi-drug resistant and extremely drug-resistant TB is widely recognized as a major threat to public health.

“The ability of the pathogen to go into the drug-resistant latent state is a major road block to the eradication of TB. It is known that latent Mtb persists in a non-replicating state. Antibiotics used to treat
bacterial infection are usually active against growing bacteria but not against the dormant pathogen. Correlation between antibiotic activity and bacterial growth state in streptomycin-dependent Mtb was shown almost 30 years ago. The antibiotic-resistance of non-growing bacteria is due to changes in bacterial metabolism or physiological state and is described as phenotypic resistance. The phenotypic resistance has been classified into three types based on the physiological state of bacteria as stationary phenotypic resistance, persister phenotypic resistance and phenotypic resistance in dormant bacteria. Mtb displays dormancy-related phenotypic resistance which is demonstrated by the Cornell mouse model. Traditionally, the phenotypic resistance is exemplified by resistance to the antibiotic Rifampicin (Rif) and is regarded as one of the hallmarks of latent TB. The mechanism of phenotypic resistance in dormant Mtb is not clearly understood.

"Development of drugs that can effectively kill dormant Mtb is of vital importance for the eradication of TB. If such drugs would prevent the pathogen from surviving in a drug-resistant state, a combination of such drugs with currently used antibiotics could drastically shorten the period of treatment for complete cure and lead to global eradication of TB. For this purpose, we need to identify processes that are necessary for the pathogen to go into dormancy, survive under the nonreplicating drug-resistant state, and get reactivated when the immune system of the host is weakened. Such steps, essential for the latent pathogen, could offer ideal targets for novel antilatency drugs that can eliminate the dormant pathogen. To achieve these objectives we explored the biochemical processes that the pathogen uses to survive for such long periods under a latent state. It has been known for many decades that Mtb in the host uses fatty acids as the major source of energy. It is well known that glyoxylate cycle is used by organisms that live on fatty acids. In recent years the important role of isocitrate lyase, a key enzyme uniquely used in the glyoxylate cycle, was shown to be required for the persistence of Mtb in the host demonstrating the central role played by fatty acid catabolism in persistence. However, the source of fatty acids used by the pathogen remains unclear. We postulated that the pathogen probably stores energy as triacylglycerol (TG) as it goes into dormancy and uses this stored energy to survive the long dormant period at very low metabolic rates as many living organisms such as hibernating animals, seeds and spores do for similar purposes. We began to identify the likely gene products that the pathogen uses to store TG and to release the fatty acids for catabolism. We also initiated the development of an in vitro dormancy model to test the hypothesis that lipid storage and mobilization are of importance for latency, a model that can be adapted for screening antilatency drug candidates.

"TG is an important storage form of lipid that accumulates in species belonging to the actinomycetes family, particularly Mtb. Intracellular
TG inclusion bodies were detected in mycobacteria isolated from organ lesions and Mycobacterium Bovis BCG was reported to preferentially use TG within macrophages indicating that TG is probably used as an energy source by Mtb during the course of the disease. We have shown that TG accumulates when Mtb is subjected to hypoxia or nitric oxide treatment that led to a dormancy-like state in culture. We identified fifteen members of a novel class of diacylglycerol acyltransferase genes which we designated as tgs (triacylglycerol synthase). Several of the tgs genes were significantly upregulated under hypoxic conditions and under nitric oxide treatment, particularly those that show the highest TG synthase activity when expressed in E. coli. We identified Rv3130c as the prime gene in the biosynthesis of TG in the bacterium under in vitro dormancy-like conditions. Our hypothesis was strongly supported by a recent important report on the W/Beijing lineage of Mtb strains which has been associated with the increasing incidence of multi-drug resistant (MDR) TB epidemic in Asia. The W/Beijing strains were shown to overproduce TG and the Rv3130c gene was constitutively upregulated along with the dormancy regulator protein DosR. The authors suggested that constitutive accumulation of TG by this strain may confer an adaptive advantage for growth in microaerophilic or anaerobic environments and thus be related to the epidemiological spread of this strain. Our hypothesis concerning the importance of Rv3130c is strongly supported by the remarkable finding by our collaborators. A recently developed two step multiplex and real time PCR method was adapted for reliable quantitative gene profiling of the small amount of latent Mtb expected to be found in infected animal and human host lung tissues. Remarkably, tgs1 (Rv3130c) was by far the most upregulated gene in the pathogen within the host, while dosR and aceAa that are well-known to be involved in dormancy, were much less induced. Many organisms use waxy esters (WE) as the major form of energy storage. Mtb also stores WE but the genes involved in the synthesis of WE and the growth conditions that cause its accumulation have not been identified. The basic mechanisms used for biosynthesis of WE were first elucidated in our laboratory several decades ago and the enzymatic strategy described more recently. We have recently shown that Rv3391 and Rv1543 encode acyl-CoA reductases involved in WE synthesis in Mtb. Rv3391 has been reported to be upregulated under nutrient stress conditions. We found that WE accumulates under stress conditions that lead to a dormancy-like state and the accumulated WE is utilized upon starvation. This utilization was reduced in lipY mutant, indicating the involvement of lipY in WE hydrolysis. Thus, Mtb can produce and use both major energy storage forms. TG and WE, and both forms are likely to be used for successfully going through dormancy. WE may also be a component of the cell wall lipids that control permeability.”
In addition to the background information obtained for this patent application, NewsRx journalists also obtained the inventors’ summary information for this patent: “With the foregoing in mind, the present invention advantageously provides a method of inducing latency in Mycobacterium, the method comprising growing a pure culture of Mycobacterium exposed to multiple stress conditions, the stress conditions including at least a low nutrient culture medium without glycerol, a low pH, a relatively high level of carbon dioxide and a relatively low gas phase oxygen level.

“A latent culture of Mycobacterium growing in vitro is particularly useful in evaluating the effectiveness of antimicrobial compounds against this form of the organism, which is prevalent throughout the world in infected but asymptomatic persons. Before the present invention, it was difficult to test drug effectiveness against latent Mtb due to the lack of an easily reproducible model system. Accordingly, the present invention discloses an in vitro model of latent mycobacterial infection which is useful in testing antimicrobials for activity against the infection in its latent stage.

“The method of the invention includes growing the Mtb in a low nutrient medium comprising approximately 10% Dubos medium, preferably at a pH of approximately 5 and in an atmosphere relatively high in level of carbon dioxide, at approximately 10%. Additionally, the atmosphere includes a relatively low oxygen level of approximately 5%. Preferably, in the method, the Mycobacterium is a strain of Mycobacterium tuberculosis.

“Another embodiment of the present invention includes a method of inducing a pure culture of Mycobacterium to become rifampicin resistant and to store an increased lipid content, two hallmarks of latency, the method comprising growing the culture simultaneously exposed to multiple stress conditions, the stress conditions including at least a low nutrient culture medium without glycerol, a low pH, a relatively high level of carbon dioxide and a relatively low gas phase oxygen level.

“The present invention also includes a pure culture, and even a single isolated cell of resistant Mycobacterium generated according to the method disclosed.

“The invention includes an in vitro model of latent tuberculosis, the model comprising an isolated culture of THP1 derived macrophages containing ingested Mycobacterium tuberculosis bacteria and incubated under hypoxic conditions for a time sufficient for the bacteria to accumulate increased lipids therein. More broadly, the invention also provides an in vitro model of latent mycobacterial infection, the model comprising an isolated culture of THP1 derived macrophages containing ingested Mycobacterium spp. cells and incubated under hypoxic conditions for a time sufficient for the bacteria to accumulate increased lipids therein. More broadly still, the invention teaches an in vitro
model of mycobacterial infection, the model comprising an isolated culture of THP1 derived macrophages containing ingested Mycobacterium spp. cells.

"With regard to the various models disclosed in the invention, the teachings also comprise a method of making a model of latent tuberculosis, the method including inducing cultured THP1 cells to differentiate into macrophages; infecting the macrophages with Mycobacterium tuberculosis bacteria; and incubating the infected macrophages under hypoxia, particularly wherein incubating is for a time sufficient for the bacteria to accumulate increased lipids therein, a hallmark of latency. This method is, in general, should also be applicable to other Mycobacterium species as well.

"The various in vitro models of latent tuberculosis and mycobacterial infection herein disclosed are useful in evaluating compounds for effectiveness against these bacterial pathogens.

BRIEF DESCRIPTION OF THE DRAWINGS

"Some of the features, advantages, and benefits of the present invention having been stated, others will become apparent as the description proceeds when taken in conjunction with the accompanying drawings, presented for solely for exemplary purposes and not with intent to limit the invention thereto, and in which:

"FIG. 1 is a demonstration of the accumulation of storage lipids in Mtb cells treated for the indicated periods under the multiple stress conditions, according to an embodiment of the present invention; TLC was performed as described; the plates were charred and quantitation was done by densitometry;

"FIG. 2 shows increasing lipid storage bodies in Mtb cells with increasing periods of multiple stress; non-acid fast staining cells (green) and lipid storage body staining (red) increased with time under multiple stresses; cells were stained with Auramine-O and Nile Red and examined by confocal laser scanning microscopy (Leica TCS SP5) with Z-stacking to get the depth of the scan field; scanned samples were analyzed by LAS AF software for image projection;

"FIG. 3 shows an increase in the percentage of lipid-stained cells and decrease in percentage of acidfast stained cells in Mtb culture when subjected to multiple stresses in vitro;

"FIG. 4 depicts TG accumulation by tgs1 (Rv3130c) and restoration of TG accumulation by complementation under 18 days of multiple stress; equal amounts of lipid were subjected to TLC as in FIG. 1; C-.DELTA.tgs1, is a complemented mutant;

"FIG. 5 shows real-time PCR measurements of transcript levels of tgs and stress responsive genes in Mtb H37Rv under in vitro multiple stress for 9 days; comparative C .sub.T method (.DELTA..DELTA.C .sub.T) was used to quantify and values obtained with starting aerated cells were used to calculate the fold induction;
“FIG. 6 shows expression profiles of genes encoding proteins involved in the glyoxylate cycle during the multiple stress treatment;

“FIG. 7 depicts a decrease in buoyant density of Mtb cells subjected to multiple stresses; Mtb cells subjected to the multiple stresses were placed on the preformed gradient and centrifuged at 400 g for 20 min; the center tube is a 3 day cell sample mixed with density marker beads; Percoll.RTM. gradients were self-formed by centrifugation from a starting solution with a density of 1.0925 gm/ml; the densities of selected bead layers (.rho., in gm/ml) are given on the right and the positions of one ml fractions collected for analyses are at the left; numbers below the tubes indicate the number of days under multiple stress:

“FIG. 8 is a bar graph showing that Alamar Blue assay reveals development of Rif resistance by multiple-stressed Mtb cultures; Mtb cultures subjected to multiple stresses were assayed by the specially adapted Alamar Blue method described in text for resistance to Rif and INH; fluorescence readings above 0 h controls are depicted;

“FIG. 9 shows real time PCR measurement of transcripts levels of a subset of selected dormancy metabolism and stress responsive genes in Mtb H37Rv under in vitro multiple stresses for 9 and 18 days; a relative quantitation method (ddCt) was used with the 7500 Fast real time system; samples of starter cultures were used as calibrator to calculate the fold induction:

“FIG. 10 are photomicrographs where Oil Red-O staining reveals lipid droplet accumulation in TDM incubated for 3-days in 1% O.sub.2, 5% CO.sub.2(a) compared to 0-day control (b);

“FIG. 11 indicates the increase in lipid bodies in TDM infected with Mtb and subjected to hypoxia for 0 and 3-days;

“FIG. 12 shows Mtb within TDM stained with Auramine-O and Nile Red showing spherical fluorescent lipid bodies and lack of acid fast staining;

“FIG. 13 shows that TG accumulated by TDM under hypoxia is utilized by Mtb; in A, lipids from uninfected (U) and infected (I) TDM, incubated in 20% O.sub.2 or 1% O.sub.2 for 7 days after infection, were resolved on TLC and visualized under UV light after spraying with 2’,7’-dichlorofluorescein; in B, lipids of Mtb recovered from TDM incubated in 20% O.sub.2 (i) or 1% O.sub.2 (ii); solvent was hexane-ether-formic acid (90:10:1, v/v/v) TG, triacylglycerol, FA, fatty acids;

“FIG. 14 depicts the fatty acid composition of TG from Mtb recovered after TDM infection; after infection with Mtb, TDM were incubated under 1% O.sub.2 for 7 days; TG from Mtb isolated from TDM was purified by preparative TLC. Fatty acid methyl esters were prepared from Mtb TG and analyzed using a Varian CP-TAP CB column attached to a Varian CP-3900 gas chromatograph under a temperature control program;

“FIG. 15 depicts transcriptional profiling of genes in Mtb H37Rv from infected TDM under hypoxia;
“FIG. 16 shows that Mtb inside [\(14^C\)acetate-labeled lipid-loaded macrophages mobilizes host lipids and accumulates TG enriched in saturated fatty acids; in A, AgNO.sub.3-impregnated silica-TLC purified from [\(14^C\)acetate-labeled lipids of infected macrophages (lane 1) and from Mtb recovered from such macrophages (lane 2); solvent system is 1% methanol in chloroform; in B, is shown reversed-phase TLC analysis of fatty acids methyl esters of TG from infected macrophages (lane 1) and from Mtb recovered from infected macrophages (lane 2); the solvent system is acetonitrile:methanol:water:acetic acid (30:70:5:1, by volume); in C, AgNO.sub.3-impregnated silica-TLC of fatty acids methyl esters of TG from infected macrophages (lane 1) and from Mtb recovered from infected macrophages (lane 2); the solvent system is hexane:diethyl ether:acetic acid, 94:4:2, v/v/v, (developed twice);

“FIG. 17 shows TDM infected with Mtb and incubated under hypoxia appear to fuse together; TDM infected with Mtb at an MOI of 0.1 and incubated for 7 days under 1% O.sub.2 were stained with carbol-fuscin followed by hematoxylin and eosin (A) or carbolfuschin followed by methylene blue (B); arrows show Mtb; and

“FIG. 18 shows Mtb inside TDM that accumulate neutral lipids lose acid-fastness; intact TDM harboring Mtb were fixed with 4% paraformaldehyde overnight and stained with the fluorescent mycolic acid staining dye Auramine-O (A) followed by the neutral lipid stain Nile Red (B); arrows indicate Mtb that stained strongly for Nile Red but weakly for Auramine-O.”


By a News Reporter-Staff News Editor at Politics & Government Week – A patent application by the inventors Hassan, Tarek Aboul-Fadl Mohamed (Riyadh, SA); Bin Jubair, Fayzah bint Ahmad S. (Riyadh, SA), filed on April 7, 2011, was cleared for further review on October 18, 2012, according to news reporting originating from Washington, D.C., by VerticalNews correspondents.
Patent application serial number 081521 has not been assigned to a company or institution.

The following quote was obtained by the news editors from the background information supplied by the inventors: “Tuberculosis remains amongst the world’s great public health challenges. Although drugs for treatment of tuberculosis (TB) have been available for nearly 50 years, TB remains a global health crisis, killing 2-3 million people annually and for a global economic toll of $12 billion each year. The recent emergence of multi drug-resistant (MDR) and extensively drug-resistant (XDR) tuberculosis resulted in a major setback in the global fight against TB. The prevailing situation is made worse by the continuous increase in the number of immune-compromised patients living with HIV who are more prone to TB and other bacterial infections. No new drugs have been developed specifically against mycobacteria since the 1960s and only within the last few years have some promising drug candidates emerged. Thus, more than ever, there is an urgent need to develop new anti-TB drugs to combat the spread of TB, particularly in its hard-to-kill multidrug-resistant, persistent and latent forms.

“There are two basic approaches to develop a new drug for TB:

“i) Synthesis of new analogues, modifications or derivatives of existing compounds for shortening and improving TB treatment.

“ii) Searching for novel structures, that the TB organism has never been presented with before, for the treatment of MDR-TB.

“Indoline-2,3-dione (isatin) derivatives have been reported to show antitubercular activities, see M.A. Hussein, T. Aboul-Fadl, A. Hussein, Bull. Pharm. Sci. Assiut Univ. 28 (2005) 131-136; L. Ballell, R. A. Field, K. Duncan, R. J. Young, Antimicrob. Agens Chemother. 49 (2005) 2153-2163. Isatin is considered as a versatile lead molecule for designing of potential anti tubercular agents.”

In addition to the background information obtained for this patent application, VerticalNews journalists also obtained the inventors’ summary information for this patent: “It is thus an object of the present invention to provide an anti-TB agent with improved properties such as enhanced activity against MDR strains, reduced toxicity, shortened duration of therapy, rapid mycobactericidal mechanism of action and the ability to penetrate host cells and exert antimycobacterial effects in the intracellular environment. Further, cross-resistance with current drugs should be avoided.”

CHAPTER 7 THERAPIES AND TREATMENTS

(2012 Nov 01)
Chapter 8

Vaccines

University of Southampton: Tuberculosis: Time for a new perspective?

By a News Reporter-Staff News Editor at Biotech Week – New research on Mycobacterium Infections is the subject of a report. According to news reporting from Southampton, United Kingdom, by NewsRx editors, the research stated, “Transmission of Mycobacterium tuberculosis (Mt) continues uninterrupted.”

The news correspondents obtained a quote from the research from the University of Southampton, “Pre-exposure vaccination remains a central focus of tuberculosis research but 25 years of follow up is needed to determine whether a novel childhood vaccination regime protects from adult disease, or like BCG assists Mt dissemination by preventing childhood illness but not infective adult pulmonary tuberculosis. Therefore, different strategies to interrupt the life cycle of Mt need to be explored.”

According to the news reporters, the research concluded: “This personal perspective discusses alternative approaches that may be delivered in a shorter time frame.”


Our news journalists report that additional information may be obtained by contacting P.T. Elkington, University of Southampton, Southampton General Hospital, Southampton SO16 1YD, Hants, United Kingdom. (2013 Apr 24)
Cost effectiveness of the interferon-gamma release assay for tuberculosis screening of hemodialysis patients

By a News Reporter-Staff News Editor at Life Science Weekly – Data detailed on Nephrology have been presented. According to news reporting from Tokyo, Japan, by NewsRx editors, the research stated, “The incidence of tuberculosis and latent tuberculosis infection in hemodialysis patients is higher than that in the general population. Our aim was to assess the cost effectiveness of QuantiFERON-TB Gold In-Tube (QFT) compared with the tuberculin skin test (TST) and the chest x-ray examination (CXR) for tuberculosis screening of hemodialysis patients.”

The news correspondents obtained a quote from the research, “Markov models were constructed using a societal perspective on the lifetime horizon. The target population was a hypothetical cohort of 40-year-old hemodialysis patients. All costs and clinical benefits were discounted at a fixed annual rate of 3. Three strategies QFT, TST and CXR were modeled. In the base-case analysis, QFT yielded the greatest benefits at the lowest cost [US$7694.43; 4.19 258 quality-adjusted life-years (QALYs)] compared with the TST (US$9337.81; 4.18 543 QALYs) and CXR (US$12 951.36; 4.14 821 QALYs) (year 2012 values). The cost effectiveness was sensitive to the the Bacillus Calmette Guerin (BCG) vaccination rate. The TST strategy was more cost effective than the QFT strategy at the willingness-to-pay level of US$50 000/QALY gained when the rate of BCG vaccination was 0.18 or lower. The cost-effectiveness acceptability curve of 40-year-old patients by Monte Carlo simulations for 10 000 trials demonstrated that the QFT was the most cost effective with a value of 100 at all willingness-to-pay levels compared with TST and CXR. The QFT is the most cost-effective method for the tuberculosis screening of hemodialysis patients.”

According to the news reporters, the research concluded: “Interferon- release assays should be recommended in clinical practice on the basis of their cost effectiveness, as well as their higher specificity, compared with TST and CXR.”


Our news journalists report that additional information may be obtained by contacting A. Kowada, Ota City Public Hlth Off, Kojiya Haneda Healthcare Serv, Tokyo, Japan. (2013 Apr 23)
University of Toulouse: Lipoarabinomannan mannose caps do not affect mycobacterial virulence or the induction of protective immunity in experimental animal models of infection and have minimal impact on in vitro inflammatory responses

By a News Reporter-Staff News Editor at Life Science Weekly – Current study results on Mycobacterium Infections have been published. According to news reporting originating in Toulouse, France, by NewsRx journalists, research stated, “Mannose-capped lipoarabinomannan (ManLAM) is considered an important virulence factor of Mycobacterium tuberculosis. However, while mannose caps have been reported to be responsible for various immunosuppressive activities of ManLAM observed in vitro, there is conflicting evidence about their contribution to mycobacterial virulence in vivo.”

The news reporters obtained a quote from the research from the University of Toulouse, “Therefore, we used Mycobacterium bovisBCG and M. tuberculosis mutants that lack the mannose cap of LAM to assess the role of ManLAM in the interaction of mycobacteria with the host cells, to evaluate vaccine-induced protection and to determine its importance in M. tuberculosis virulence. Deletion of the mannose cap did not affect BCG survival and replication in macrophages, although the capless mutant induced a somewhat higher production of TNF. In dendritic cells, the capless mutant was able to induce the upregulation of co-stimulatory molecules and the only difference we detected was the secretion of slightly higher amounts of IL-10 as compared to the wild type strain. In mice, capless BCG survived equally well and induced an immune response similar to the parental strain. Furthermore, the efficacy of vaccination against a M. tuberculosis challenge in low-dose aerosol infection models in mice and guinea pigs was not affected by the absence of the mannose caps in the BCG. Finally, the lack of the mannose cap in M. tuberculosis did not affect its virulence in mice nor its interaction with macrophages in vitro.”

According to the news reporters, the research concluded: “Thus, these results do not support a major role for the mannose caps of LAM in determining mycobacterial virulence and immunogenicity in vivo in experimental animal models of infection, possibly because of redundancy of function.”

For more information on this research see: Lipoarabinomannan mannose caps do not affect mycobacterial virulence or the induction of protective immunity in experimental animal models of infection and have minimal impact on in vitro inflammatory responses. Cellular Microbiology, 2013;15(4):660-674. Cellular Microbiology can be contacted at: Wiley-Blackwell, 111 River St, Hoboken 07030-5774, NJ,
Our news correspondents report that additional information may be obtained by contacting A. Afonso-Barroso, Univ Toulouse, UPS, IPBS, Toulouse, France. (2013 Apr 23)

**McGill University, Montreal: Genetic Determinants of Susceptibility to Mycobacterial Infections: IRF8, A New Kid on the Block**

By a News Reporter-Staff News Editor at Vaccine Weekly – A new study on Mycobacterium Infections is now available. According to news reporting from Montreal, Canada, by NewsRx journalists, research stated, “Genetic and population studies suggest that onset, progression and ultimate outcome of infection with Mycobacteria, including the agent of tuberculosis *Mycobacterium tuberculosis*, are strongly influenced by genetic factors. Family-based and case-control linkage and association studies have suggested a complex genetic component for susceptibility to tuberculosis.”

The news correspondents obtained a quote from the research from McGill University, “On the other hand, patients with inborn errors in the IL12/IFN? circuit may develop disseminated mycobacterial infections following perinatal BCG vaccination. The study of such MSMD (Mendelian Susceptibility to Mycobacterial Diseases) patients has provided much insight into innate and acquired immune defenses against mycobacteria. Parallel genetic analyses in mouse models of mycobacterial infections have also indicated complex genetic control, and have provided candidate genes for parallel testing in humans. Recently, mutations in human IRF8 were discovered and shown to cause two distinct forms of a novel primary immunodeficiency and associated susceptibility to mycobacteria. Autosomal recessive IRF8 deficiency is caused by mutation K108E and associated with severe disease with complete depletion of monocytes and dendritic cells. Mutation T80A causes autosomal dominant IRF8 deficiency and a milder form of the disease with selective loss of a subset of dendritic cells. These findings have established that IRF8 is required for ontogeny of the myeloid lineage and for host response to mycobacteria.”

According to the news reporters, the research concluded: “The ongoing study of the IRF8 transcriptome has shown promise for the identification of IRF8 dependent pathways that play a critical role in host defense against mycobacteria in particular, and against intracellular pathogens in general.”

For more information on this research see: Genetic Determinants of Susceptibility to Mycobacterial Infections: IRF8, A New Kid on the
McMaster University, Hamilton: Immunization strategies against pulmonary tuberculosis: considerations of T cell geography

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators publish new report on Experimental Biology and Medicine. According to news originating from Hamilton, Canada, by NewsRx correspondents, research stated, “Pulmonary tuberculosis (TB) remains a global health concern with an astounding 9 million new cases and 2 million deaths per year. This leading infectious cause of death remains highly prevalent with one third of the world’s population latently infected with Mycobacterium tuberculosis (M.tb) despite routine vaccination against TB in endemic areas.”

Our news journalists obtained a quote from the research from McMaster University, “The only approved TB vaccine is the Bacille Calmette-Guerin (BCG), which provides protection against childhood miliary tuberculosis and has been administered intradermally in humans for almost a century. While effective in preventing disseminated forms of TB, the BCG has variable efficacy in providing protection against pulmonary TB. Therefore, the BCG has been unable to control the instance of adult pulmonary TB which constitutes the global disease burden. Despite the fact that mechanisms underlying the lack of pulmonary protection provided by the BCG remain poorly understood, it remains the ‘Gold Standard’ for vaccine-mediated protection against M.tb and will continue to be used for the foreseeable future. Therefore, continued effort has been placed on understanding the mechanisms behind the failure of BCG to provide sufficient protection against M.tb in the lung and to design new vaccines to be used in conjunction with the BCG as boost strategies to install protective immunity at the site of infection. Growing evidence supports that the route of immunization dictates the geographical location of TB-reactive T cells, and it is this distribution which predicts the protective outcome of such vaccine-elicited immunity. Such vaccines that are able to localize TB-reactive T cells to the lung and airway mucosa are thought to fill the ‘immunological gap’ in the lung that is required for enhanced protection against M.tb infection.”
According to the news editors, the research concluded: “This chapter focuses on the critical importance of T cell geography when designing new immunization strategies against pulmonary TB.”

For more information on this research see: Immunization strategies against pulmonary tuberculosis: considerations of T cell geography. *Advances In Experimental Medicine and Biology*, 2013;783():267-78.

The news correspondents report that additional information may be obtained from C.N. Horvath, MDCL-Rm4012, Dept. of Pathology and Molecular Medicine, McMaster Immunology Research Centre, McMaster University, 1280 Main Street West, Hamilton, ON, L8S 4K1, Canada. (2013 Apr 02)

**Center for Disease Control and Prevention, Atlanta:**

**Infectious Disease Burden and Vaccination Needs Among Asylees Versus Refugees, District of Columbia**

By a News Reporter-Staff News Editor at AIDS Weekly – New research on Immune System Diseases and Conditions is the subject of a report. According to news reporting out of Atlanta, Georgia, by NewsRx editors, research stated, “Unlike US-bound refugees, asylum seekers (asylees) apply for asylum while residing in the United States and are not provided a medical screening. Infectious disease burden and vaccination needs have not been described among US asylees.”

Our news journalists obtained a quote from the research from Center for Disease Control and Prevention, “We conducted a retrospective cohort study of 630 asylees and 151 refugees referred to the District of Columbia (DC) Department of Health screening program for an initial US medical screening during September 2003 August 2007. We assessed the prevalence of latent tuberculosis infection (tuberculin skin test reactivity &gt;= 10 mm), human immunodeficiency virus (HIV) and hepatitis B seropositivity, intestinal parasite test positivity, need for vaccinations, and time from date of US arrival to receipt of screening. Asylees in DC had a similar prevalence as refugees of latent tuberculosis infection (39% vs 38%, respectively, P = .83), pathogenic intestinal parasites (4% vs 2%, P = .36), and need for adult vaccinations (80% vs 80%, P = .95). Asylees were screened significantly later after US arrival compared with refugees (55 weeks vs 1 week, P&lt; .001). Asylees had higher prevalence of latent tuberculosis infection, hepatitis B and HIV seropositivity, and child and adult vaccination needs than the US population (P &lt; .001). This study of the infectious disease concerns of a US asylee population suggests that in DC, asylees have similar infectious disease burden and prevention needs as refugees and should be screened with the same urgency.”
According to the news editors, the research concluded: “Because applicants for US asylum are not linked to prompt medical screenings, DC asylees are typically screened much later, placing them and US communities at risk.”


Our news journalists report that additional information may be obtained by contacting S.J. Chai, Center Dis Control & Prevent, Int Emergency & Refugee Hlth Branch, Atlanta, GA 30333, United States. (2013 Apr 01)

Norwegian Institute of Public Health, Oslo: An Unbiased Genome-Wide Mycobacterium tuberculosis Gene Expression Approach To Discover Antigens Targeted by Human T Cells Expressed during Pulmonary Infection

By a News Reporter-Staff News Editor at Vaccine Weekly – Investigators publish new report on Mycobacterium Infections. According to news reporting from Oslo, Norway, by NewsRx journalists, research stated, “Mycobacterium tuberculosis is responsible for almost 2 million deaths annually. Mycobacterium bovis bacillus Calmette-Guerin, the only vaccine available against tuberculosis (TB), induces highly variable protection against TB, and better TB vaccines are urgently needed.”

The news correspondents obtained a quote from the research from the Norwegian Institute of Public Health, “A prerequisite for candidate vaccine Ags is that they are immunogenic and expressed by M. tuberculosis during infection of the primary target organ, that is, the lungs of susceptible individuals. In search of new TB vaccine candidate Ags, we have used a genome-wide, unbiased Ag discovery approach to investigate the in vivo expression of 2170 M. tuberculosis genes during M. tuberculosis infection in the lungs of mice. Four genetically related but distinct mouse strains were studied, representing a spectrum of TB susceptibility controlled by the supersusceptibility to TB 1 locus. We used stringent selection approaches to select in vivo-expressed M. tuberculosis (IVE-TB) genes and analyzed their expression patterns in distinct disease phenotypes such as necrosis and granuloma formation. To study the vaccine potential of these proteins, we analyzed their immunogenicity. Several M. tuberculosis proteins were recognized by immune cells from tuberculin skin test-positive,
ESAT6/CFP10-responsive individuals, indicating that these Ags are presented during natural M. tuberculosis infection. Furthermore, TB patients also showed responses toward IVE-TB Ags, albeit lower than tuberculin skin test-positive, ESAT6/CFP10-responsive individuals. Finally, IVE-TB Ags induced strong IFN-gamma(+)/TNF-alpha(+) CD8(+) and TNF-alpha(+)/IL-2(+) CD154(+)/CD4(+) T cell responses in PBMC from long-term latently M. tuberculosis-infected individuals."

According to the news reporters, the research concluded: “These IVE-TB Ags are expressed during pulmonary infection in vivo, are immunogenic, induce strong T cell responses in long-term latently M. tuberculosis-infected individuals, and may therefore represent attractive Ags for new TB vaccines. The Journal of Immunology, 2013, 190:1659-1671.”

For more information on this research see: An Unbiased Genome-Wide Mycobacterium tuberculosis Gene Expression Approach To Discover Antigens Targeted by Human T Cells Expressed during Pulmonary Infection. Journal of Immunology, 2013;190(4):1659-1671. Journal of Immunology can be contacted at: Amer Assoc Immunologists, 9650 Rockville Pike, Bethesda, MD 20814, USA. (The American Association of Immunologists - www.aai.org; Journal of Immunology - www.jimmunol.org)

Our news journalists report that additional information may be obtained by contacting S. Commandeur, Norwegian Inst Public Hlth, Dept. of Bacteriol & Immunol, Div Infect Dis Control, NO-0403 Oslo, Norway. (2013 Mar 27)

Ohio State University, Wooster: Mycobacterium tuberculosis Whole Cell Lysate Enhances Proliferation of CD8 Positive Lymphocytes and Nitric Oxide Secretion in the Lungs of Live Porcine Respiratory and Reproductive Syndrome Virus Vaccinated Pigs

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators discuss new findings in Mycobacterium Infections. According to news originating from Wooster, Ohio, by NewsRx correspondents, research stated, “Porcine respiratory and reproductive syndrome (PRRS) is an economically important disease of pigs worldwide. Currently used PRRSV vaccines provide incomplete protection.”

Our news journalists obtained a quote from the research from Ohio State University, “Recently, we identified Mycobacterium tuberculosis whole cell lysate (Mtb WCL) as a potent mucosal adjuvant to modified live PRRSV vaccine (PRRS-MLV). In this study, pigs were unvaccinated or vaccinated with PRRS-MLV plus Mtb WCL, intranasally, and challenged with either homologous (strain VR2332) or virulent heterologous
(strain MN184) PRRSV; subsequently, euthanized at three time points post-challenge to evaluate lung immune responses. Microscopic examination of lung sections revealed reduced disruption of the lung architecture and less of interstitial pneumonia in vaccinated, compared to un-vaccinated MN184 challenged pigs. The restimulated lung and peripheral blood mononuclear cells revealed increased proliferation of CD8(+) lymphocytes, and in the lung homogenate increased secretion of nitric oxide was detected in vaccinated MN184 challenged pigs.”

According to the news editors, the research concluded: “In summary, the adjuvant effects of Mtb WCL to PRRS-MLV resulted in favorable anti-PRRSV immune microenvironment in the lungs to help better viral clearance.”

For more information on this research see: Mycobacterium tuberculosis Whole Cell Lysate Enhances Proliferation of CD8 Positive Lymphocytes and Nitric Oxide Secretion in the Lungs of Live Porcine Respiratory and Reproductive Syndrome Virus Vaccinated Pigs. Viral Immunology, 2013;26(1):102-108. Viral Immunology can be contacted at: Mary Ann Liebert Inc, 140 Huguenot Street, 3RD Fl, New Rochelle, NY 10801, USA. (Mary Ann Liebert, Inc. - www.liebertpub.com; Viral Immunology - http://www.liebertpub.com/overview/viral-immunology/57/)

The news correspondents report that additional information may be obtained from C. Manickam, Ohio State University, Dept. of Vet Prevent Med, Wooster, OH 44691, United States. (2013 Mar 26)

CXCR5(+) T helper cells mediate protective immunity against tuberculosis

By a News Reporter-Staff News Editor at Life Science Weekly – New research on Clinical Investigation is the subject of a report. According to news reporting from Mexico City, Mexico, by NewsRx journalists, research stated, “One third of the world’s population is infected with Mycobacterium tuberculosis (Mt disposing). Although most infected people remain asymptomatic, they have a 10% lifetime risk of developing active tuberculosis (TB).”

The news correspondents obtained a quote from the research, “Thus, the current challenge is to identify immune parameters that distinguish individuals with latent TB from those with active TB. Using human and experimental models of Mt disposing infection, we demonstrated that organized ectopic lymphoid structures containing CXCR5(+) T cells were present in Mt disposing-infected lungs. In addition, we found that in experimental Mt disposing infection models, the presence of CXCR5(+) T cells within ectopic lymphoid structures was associated with immune control. Furthermore, in a mouse model of Mt disposing infection, we showed that activated CD4(+)CXCR5(+) T cells accumulated in Mt disposing-infected lungs and
produced proinflammatory cytokines. Mice deficient in Cxcr5 had increased susceptibility to TB due to defective T cell localization within the lung parenchyma. We demonstrated that CXCR5 expression in T cells mediated correct T cell localization within TB granulomas, promoted efficient macrophage activation, protected against Mtb infection, and facilitated lymphoid follicle formation.

According to the news reporters, the research concluded: “These data demonstrate that CD4(+)CXCR5(+) T cells play a protective role in the immune response against TB and highlight their potential use for future TB vaccine design and therapy.”

For more information on this research see: CXCR5(+) T helper cells mediate protective immunity against tuberculosis. *Journal of Clinical Investigation*, 2013;123(2):712-726. *Journal of Clinical Investigation* can be contacted at: Amer Soc Clinical Investigation Inc, 35 Research Dr, Ste 300, Ann Arbor, MI 48103, USA.

Our news journalists report that additional information may be obtained by contacting S.R. Slight, Amer British Cowdray Med Center, Lab Surg Pathol, Mexico City, DF, Mexico. (2013 Mar 19)

**Chulalongkorn University, Bangkok: Enhancement of immune response to a DNA vaccine against Mycobacterium tuberculosis Ag85B by incorporation of an autophagy inducing system**

By a News Reporter-Staff News Editor at TB & Outbreaks Week – Data detailed on Vaccines have been presented. According to news reporting out of Bangkok, Thailand, by NewsRx editors, research stated, “DNA vaccines are a promising new generation of vaccines that can elicit an immune response using DNA encoding the antigen of interest. The efficacy of these vaccines, however, still needs to be improved.”

Our news journalists obtained a quote from the research from Chulalongkorn University, “In this study, we investigated the effect of autophagy on increasing the efficacy of a candidate DNA vaccine against Mycobacterium tuberculosis (MTB), a causative agent of tuberculosis. Low molecular weight chitosan was used to encapsulate plasmid DNA containing a gene encoding MTB Antigen 85B (Ag85B), a secreted fibronectin-binding protein. To induce autophagy upon DNA vaccination, the kinase defective mTOR (mTOR-KD) was transfected into cells, and autophagy was detected based on the presence of LC3II. To investigate whether autophagy enhances an immune response upon DNA vaccination, we coencapsulated the Ag85B-containing plasmid with a plasmid encoding mTOR-KD. Plasmids encapsulated by chitosan particles were used for primary subcutaneous immunization and for intranasal boost in mice. After the boost vaccination, sera from the mice...
were measured for humoral immune response. The DNA vaccine with the autophagy-inducing construct elicited significantly higher Ag85B-specific antibody levels than the control group treated with the Ag85B plasmid alone or with the Ag85B plasmid plus the wild type mTOR construct. Upon in vitro stimulation of splenocytes from mice immunized with recombinant Ag85B, the highest levels of secreted IFN-gamma and IL-2 were detected in mice immunized with the autophagy-inducing plasmid, while no differences in IL-4 levels were detected between the groups, suggesting that the DNA vaccine regimen with autophagy induction induced primarily a Th1 immune response. Furthermore, the enhanced proliferation of CD4+ T cells from mice receiving the autophagy-inducing vaccine was observed in vitro.

According to the news editors, the research concluded: “Based on the evidence presented, we conclude that incorporating an autophagy-inducing element into a DNA vaccine may help to improve immune response.”


Our news journalists report that additional information may be obtained by contacting J. Meerak, Chulalongkorn University, Fac Sci, Dept. of Chem, Bangkok 10330, Thailand. (2013 Mar 19)

University of Oxford: Environmental effects on protection against Mycobacterium tuberculosis after immunization with Ad85A

By a News Reporter-Staff News Editor at Life Science Weekly – Researchers detail new data in Vaccines. According to news reporting from Oxford, United Kingdom, by NewsRx journalists, research stated, “Previously we have shown that intradermal (i.d.) immunization with a recombinant adenovirus expressing antigen 85A (Ad85A) induced a strong splenic CD8 T cell response in BALB/c mice but a weak lung immune response and did not protect mice against challenge with Mycobacterium tuberculosis (Mtb). After moving to a new animal house, the same i.d. immunization induced a strong lung immune response and the mice were protected against Mtb challenge.”

The news correspondents obtained a quote from the research from the University of Oxford, “Increased numbers of antigen 85A-specific CD8 cells were present in lung tissue but were not recoverable by bronchoalveolar lavage (BAL). Mycobacterial growth was inhibited 21 days
after Mtb challenge. In contrast, the effects of intranasal (i.n.) immunization did not change between the animal houses; 85A-specific T cells were recovered by BAL and were able to inhibit Mtb growth early after challenge. The effect of alterations to the environment was investigated by administering BCG or Mycobacterium abscessus in the drinking water, which induced protection against Mtb challenge, while Mycobacterium smegmatis did not. However, when Ad85A was given i.d. at the same time as BCG or M. abscessus, but not M. smegmatis, the protection induced by Ad85A was abolished. Treatment of mice with a CD25 antibody during the challenge period, abolished the suppressive effect of oral mycobacterial administration, suggesting that regulatory T cells (T regs) were involved.”

According to the news reporters, the research concluded: “These results showed that exposure to environmental microorganisms can alter the protective immune response to a parenterally administered subunit vaccine, a result with important implications for the use of such vaccines in humans.”


Our news journalists report that additional information may be obtained by contacting P. Beverley, University of Oxford, John Radcliffe Hosp, Translat Gastroenterol Unit, Oxford OX3 9DU, United Kingdom. (2013 Mar 19)

University of Medicine and Pharmacy, Bucharest: Use of recombinant purified protein derivative (PPD) antigens as specific skin test for tuberculosis

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators publish new report on Mycobacterium Infections. According to news reporting originating in Bucharest, Romania, by NewsRx journalists, research stated, “Purified protein derivative (PPD) is currently the only available skin test reagent used worldwide for the diagnosis of tuberculosis (TB). The aim of this study was to develop a Mycobacterium tuberculosis specific skin test reagent, without false positive results due to Bacillus Calmette-Guerin (BCG) vaccination using recombinant antigens.”
The news reporters obtained a quote from the research from the University of Medicine and Pharmacy, “Proteins in PPD IC-65 were analyzed by tandem mass spectrometry and compared to proteins in M. tuberculosis culture filtrate; 54 proteins were found in common. Top candidates MPT64, ESAT 6, and CFP 10 were overexpressed in Escherichia coli expression strains and purified as recombinant proteins. To formulate optimal immunodiagnostic PPD cocktails, the antigens were evaluated by skin testing guinea pigs sensitized with M. tuberculosis H37Rv and BCG. For single antigens and a cocktail mixture of these antigens, best results were obtained using 3 μg/0.1 ml, equivalent to 105 TU (tuberculin units). Each animal was simultaneously tested with PPD IC-65, 2 TU/0.1 ml, as reference. Reactivity of the multi-antigen cocktail was greater than that of any single antigen. The skin test results were between 34.3 and 76.6 per cent the level of reactivity compared to that of the reference when single antigens were tested and 124 per cent the level of reactivity compared to the reference for the multi-antigen cocktail.”

According to the news reporters, the research concluded: “Our results showed that this specific cocktail could represent a potential candidate for a new skin diagnostic test for TB.”

For more information on this research see: Use of recombinant purified protein derivative (PPD) antigens as specific skin test for tuberculosis. Indian Journal of Medical Research, 2012;135(5):799-807. Indian Journal of Medical Research can be contacted at: Indian Council Medical Res, PO Box 4911 Ansari Nagar, New Delhi 110029, India.

Our news correspondents report that additional information may be obtained by contacting H. Stavri, Univ Med & Pharm Carol Davila, Bucharest, Romania. (2013 Mar 12)

Institute of General Pathology, Rome: M tuberculosis in the Adjuvant Modulates Time of Appearance of CNS-Specific Effector T Cells in the Spleen through a Polymorphic Site of TLR2

By a News Reporter-Staff News Editor at Vaccine Weekly – Investigators publish new report on Life Science Research. According to news reporting from Rome, Italy, by NewsRx journalists, research stated, “DC deliver information regulating trafficking of effector T cells along T-cell priming. However, the role of pathogen-derived motives in the regulation of movement of T cells has not been studied.”

The news correspondents obtained a quote from the research from the Institute of General Pathology, “We hereinafter report that amount of M tuberculosis in the adjuvant modulates relocation of PLP139-151 specific T cells. In the presence of a low dose of M tuberculosis in the
adjuvant, T cells (detected by CDR3 BV-BJ spectratyping, the so-called ‘immunoscope’) mostly reach the spleen by day 28 after immunization (‘late relocation’) in the SJL strain, whereas T cells reach the spleen by d 14 with a high dose of M tuberculosis (‘early relocation’). The C57Bl/6 background confers a dominant ‘early relocation’ phenotype to F1 (SJL x C57Bl/6) mice, allowing early relocation of T cells in the presence of low dose M tuberculosis. A single non-synonymous polymorphism of TLR2 is responsible for ‘early/late’ relocation phenotype. Egress of T lymphocytes is regulated by TLR2 expressed on T cells.”

According to the news reporters, the research concluded: “Thus, pathogens engaging TLR2 on T cells regulate directly T-cell trafficking, and polymorphisms of TLR2 condition T-cell trafficking upon a limiting concentration of ligand.”

For more information on this research see: M tuberculosis in the Adjuvant Modulates Time of Appearance of CNS-Specific Effector T Cells in the Spleen through a Polymorphic Site of TLR2. Plos One, 2013;8(2):e55819. (Public Library of Science - www.plos.org; Plos One - www.plosone.org)

Our news journalists report that additional information may be obtained by contacting C. Nicolo, Institute of General Pathology, Universita Cattolica del S Cuore, Rome, Italy. (2013 Mar 06)

University of Valladolid: Immunomodulatory nanoparticles from elastin-like recombinamers: single-molecules for tuberculosis vaccine development

By a News Reporter-Staff News Editor at Biotech Week – Researchers detail new data in Molecular Pharmaceutics. According to news reporting out of Valladolid, Spain, by NewsRx editors, research stated, “This study investigates both the physicochemical properties and immunogenicity of a genetically engineered elastin-like block corecombinamer (ELbcR) containing a major membrane protein sequence from Mycobacterium tuberculosis. The recombinant production of this ELbcR allows the production of large quantities of safe, antigenic particle-based constructs that directly and reversibly self-assemble into highly biocompatible, multivalent, monodisperse, and stable nanovesicles with a diameter of 55 nm from the same gene product using a highly efficient and cost-effective inverse transition cycling (ITC) procedure.”

Our news journalists obtained a quote from the research from the University of Valladolid, “The compositional complexity of these vesicles is retained after secondary processes such as endotoxin removal, sterilization, and lyophilization. An initial pro-chemotactic cytokine response (IL-1β) followed by a pro-Th2/IL-5 response was observed in mice plasma following subcutaneous administration of the antigen-loaded nanovesicles in mice.”
According to the news editors, the research concluded: “This biphasic model of cytokine production was coupled with humoral isotype switching from IgM-to IgG-specific antibodies against the antigen, which was only observed in the presence of both the antigen and the polymer in the same construct and in the absence of additional adjuvants.”


Our news journalists report that additional information may be obtained by contacting C. Garcia-Arevalo, Bioforge Group, University of Valladolid, CIBER-BBN, Paseo de Belen 11, 47011 Valladolid, Spain. (2013 Feb 27)

University of Central Florida, Orlando: Low cost tuberculosis vaccine antigens in capsules: expression in chloroplasts, bio-encapsulation, stability and functional evaluation in vitro

By a News Reporter-Staff News Editor at Vaccine Weekly – A new study on Life Science Research is now available. According to news reporting originating from Orlando, Florida, by NewsRx correspondents, research stated, “Tuberculosis (TB) caused by Mycobacterium tuberculosis is one of the leading fatal infectious diseases. The development of TB vaccines has been recognized as a major public health priority by the World Health Organization.”

Our news editors obtained a quote from the research from the University of Central Florida, “In this study, three candidate antigens, ESAT-6 (6kDa early secretory antigenic target) and Mtb72F (a fusion polypeptide from two TB antigens, Mtb32 and Mtb39) fused with cholera toxin B-subunit (CTB) and LipY (a cell wall protein) were expressed in tobacco and/or lettuce chloroplasts to facilitate bioencapsulation/oral delivery. Site-specific transgene integration into the chloroplast genome was confirmed by Southern blot analysis. In transplastomic leaves, CTB fusion proteins existed in soluble monomeric or multimeric forms of expected sizes and their expression levels varied depending upon the developmental stage and time of leaf harvest, with the highest-level of accumulation in mature leaves harvested at 6PM. The CTB-ESAT6 and CTB-Mtb72F expression levels reached up to 7.5% and 1.2% of total soluble protein respectively in mature tobacco leaves. Transplastomic CTB-ESAT6 lettuce plants accumulated up to 0.75% of total leaf protein. Western blot analysis of lyophilized lettuce leaves
stored at room temperature for up to six months showed that the CTB-ESAT6 fusion protein was stable and preserved proper folding, disulfide bonds and assembly into pentamers for prolonged periods. Also, antigen concentration per gram of leaf tissue was increased 22 fold after lyophilization. Hemolysis assay with purified CTB-ESAT6 protein showed partial hemolysis of red blood cells and confirmed functionality of the ESAT-6 antigen. GM1-binding assay demonstrated that the CTB-ESAT6 fusion protein formed pentamers to bind with the GM1-ganglioside receptor. The expression of functional *Mycobacterium tuberculosis* antigens in transplastomic plants should facilitate development of a cost-effective and orally deliverable TB booster vaccine with potential for long-term storage at room temperature.”

According to the news editors, the research concluded: “To our knowledge, this is the first report of expression of TB vaccine antigens in chloroplasts.”


The news editors report that additional information may be obtained by contacting P.S. Lakshmi, Burnett School of Biomedical Sciences, College of Medicine, University of Central Florida, Orlando, Florida, United States. (2013 Feb 20)

**Leiden University: A multistage-polyepitope vaccine protects against Mycobacterium tuberculosis infection in HLA-DR3 transgenic mice**

By a News Reporter-Staff News Editor at Life Science Weekly – Current study results on Immunization have been published. According to news reporting from Leiden, Netherlands, by NewsRx journalists, research stated, “Mycobacterium tuberculosis (Mtb) is responsible for almost 2 million deaths annually. BCG, currently the only TB vaccine, induces variable protection and does not protect against reactivation of latent TB.”

The news correspondents obtained a quote from the research from Leiden University, “Thus, efficient vaccines to supplement BCG are required urgently. Since Mtb’s proteome differs qualitatively and quantitatively during bacterial replication stages from that expressed during dormancy, improved TB vaccines should drive immune responses to Mtb antigens expressed during multiple stages of infection. Consequently, such ‘multistage’ vaccines should be composed of (immunodominant) antigens expressed during different phases of Mtb infection. As a concept multistage vaccine, we constructed a polyepitope by fusing five
HLA-DR3-restricted T-cell epitopes derived from different Mtb proteins either expressed highly by replicating bacteria (Ag85B, hsp65, 19 kDa lipoprotein), or abundantly expressed by dormant bacilli and recognized preferentially by TST+ individuals (hsp16, Rv1733c). PBMC of HLA-DR3(+) but not HLA-DR3(-) cured TB patients and TST+ individuals responded well to the multistage-polyepitope in vitro. The in vivo immunogenicity and protective efficacy of the multistage-polyepitope were analyzed using HLA-DR3 transgenic mice lacking endogenous murine class II as a model. Immunization with the multistage-polyepitope adjuvanted with CpG generated high IgG levels as well as polyfunctional CD4(+) T-cells producing IFN-gamma, TNF and IL-2, specific for these HLA-DR3-restricted epitopes. Importantly, multistage-polyepitope immunization reduced the number of bacilli in the lungs after Mtb challenge when administered as prophylactic vaccine.

According to the news reporters, the research concluded: “Given the extensive repertoire of potential Mtb antigens available for immune recognition, the data of our model demonstrate the potential of multistage-polyepitope vaccines to protect against TB.”


Our news journalists report that additional information may be obtained by contacting A. Geluk, Leiden University, Medical Center, Dept. of Infect Dis, NL-2300 RA Leiden, Netherlands. (2013 Feb 19)

Max-Planck-Institute for Infection Biology, Berlin: The recombinant tuberculosis vaccine rBCG Delta ureC::hly(+) induces apoptotic vesicles for improved priming of CD4(+) and CD8(+) T cells

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators publish new report on Vaccines. According to news reporting from Berlin, Germany, by NewsRx journalists, research stated, “The recombinant BCG Delta ureC::hly(+) (rBCG) vaccine candidate is more efficient than parental BCG (pBCG) against tuberculosis (TB) in preclinical models. Evidence exists for superior CD4 and CD8 T cell stimulation.”

The news correspondents obtained a quote from the research from Max-Planck-Institute for Infection Biology, “Although the responsible immune mechanisms are incompletely understood, crosspriming of CD8 T cells has been proposed as a major mechanism underlying better
protection of rBCG over pBCG. The present study investigates the role of apoptotic vesicles from pBCG- and rBCG-infected macrophages in crosspriming. Apoptotic vesicles were isolated from pBCG- and rBCG-infected mouse macrophages. The priming potential of the isolated vesicles was evaluated in terms of dendritic cell activation and specific T cell stimulation. Apoptotic vesicles from both pBCG- and rBCG-infected macrophages activated dendritic cells but to a different degree. Overall, rBCG-infected apoptotic vesicles induced more profound CD4 and CD8 T cell responses as compared to pBCG.”

According to the news reporters, the research concluded: “These data support the notion that the improved vaccine efficacy of rBCG rests on enhanced crosspriming as a consequence of stronger apoptosis.”

For more information on this research see: The recombinant tuberculosis vaccine rBCG Delta ureC::hly(+) induces apoptotic vesicles for improved priming of CD4(+) and CD8(+) T cells. Vaccine, 2012;30(52):7608-7614. Vaccine can be contacted at: Elsevier Sci Ltd, The Boulevard, Langford Lane, Kidlington, Oxford OX5 1GB, Oxon, England. (Elsevier - www.elsevier.com; Vaccine - http://www.journals.elsevier.com/vaccine)

Our news journalists report that additional information may be obtained by contacting M. Farinacci, Max Planck Inst Infect Biol, Dept. of Immunol, D-10117 Berlin, Germany. (2013 Feb 19)

University of Washington, Seattle: Risk-based immunization policies and tuberculosis screening practices for animal care and research workers in the United States: survey results and recommendations

By a News Reporter-Staff News Editor at Life Science Weekly – Data detailed on Mycobacterium Infections have been presented. According to news reporting originating from Seattle, Washington, by NewsRx correspondents, research stated, “A national survey was conducted to assess immunization practices and tuberculosis screening methods for animal care and research workers in biomedical settings throughout the United States. Veterinarians (n=953) were surveyed via a web-based mechanism; completed surveys (n=308) were analyzed.”

Our news editors obtained a quote from the research from the University of Washington, “Results showed that occupational health and safety programs were well-developed, enrolling veterinary, husbandry, and research staff at rates exceeding 90% and involving multiple modalities of health assessments and risk communication for vaccine-preventable diseases. Most (72.7%) institutions did not store serum samples from animal research personnel. More than half of the institutions housed nonhuman primates and maintained tuberculosis
screening programs, although screening methods varied. Immunization protocols included various recommended or required vaccines that differed depending on job duties, type of institution, and nature of scientific programs. A single case of an identified vaccine-preventable illness in a laboratory worker was noted. Tetanus toxoid was the predominant vaccine administered (91.7%) to animal care and research workers, followed by hepatitis B (54.8%), influenza (39.9%), and rabies (38.3%). For some immunization protocols, an inconsistent rationale for administration was evident. Indications that animal care and research workers are unprotected from work-related etiologic agents did not emerge from this survey; rather, existing guidelines from the Advisory Committee on Immunization Practices and available biologics seem sufficient to address most needs of the laboratory animal research community.”

According to the news editors, the research concluded: “Institutions should commit to performance-based standards in parallel with context-specific risk assessment methods to maintain occupational health and safety programs and practices appropriate to their needs.”


The news editors report that additional information may be obtained by contacting B.J. Weigler, Washington National Primate Research Center, Dept. of Comparative Medicine and Dept. of Epidemiology, University of Washington, Seattle, Washington, United States. (2013 Feb 05)

National JALMA Institute for Leprosy and Other Mycobacterial Diseases, Agra: Expression of CXCL10 (IP-10) and CXCL11 (I-TAC) chemokines during Mycobacterium tuberculosis infection and immunoprophylaxis with Mycobacterium indicus pranii (Mw) in guinea pig

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators discuss new findings in Molecular Epidemiology and Evolutionary Genetics. According to news originating from Agra, India, by NewsRx correspondents, research stated, “Mycobacterium indicus pranii (earlier known as Mycobacterium w) has been used as an immunomodulatory agent in leprosy and tuberculosis by mediating the release of various cytokines and chemokines. CXCL10 (IP-10) and CXCL11 (I-TAC) chemokines are involved in T-cell migration and stimulation of natural killer cells in Mycobacterium tuberculosis infection.”
Our news journalists obtained a quote from the research from National JALMA Institute for Leprosy and Other Mycobacterial Diseases, “In this study, the effect of heat killed M. indicus pranii (alone and in conjunction with chemotherapy) on disease progression was determined by colony forming units (CFUs) in guinea pig lung following their aerosol infection and the expression levels of CXCL10 and CXCL11 were studied by quantitative Reverse Transcriptase Polymerase Chain Reaction (qRT-PCR) and in situ RT-PCR. Four groups of animals included; infection only (Rv), immunoprophylaxis (RvMw), chemotherapy (RvCh) and combination of immunoprophylaxis with chemotherapy (RvChMw). In the group where immunoprophylaxis was given in combination with chemotherapy, the CFU counts reduced significantly at 4th week post-infection as compared to animals that received immunoprophylaxis or chemotherapy alone. At the same time, all groups of animals had elevated expression of CXCL 10 which was significantly high only in animals that received Mw with or without chemotherapy. Unlike to CXCL 10, study demonstrated suppressed expression CXCL 11 in both immunoprophylaxis as well as chemotherapy groups that became up-regulated in synergistic response of immunoprophylaxis and chemotherapy. Taken together, data indicates that the expression of CXCL10 and CXCL11 positively correlates with anti-tubercular treatment (at least with combination of immunoprophylaxis and chemotherapy).”

According to the news editors, the research concluded: “Therefore, prior immunization with Mw appears to be a good immunomodulator for release of chemokines and augments the effect of chemotherapy.”

For more information on this research see: Expression of CXCL10 (IP-10) and CXCL11 (I-TAC) chemokines during Mycobacterium tuberculosis infection and immunoprophylaxis with Mycobacterium indicus pranii (Mw) in guinea pig. Infection, Genetics and Evolution, 2013;13():11-7. (Elsevier - www.elsevier.com; Infection, Genetics and Evolution - http://www.elsevier.com/wps/product/cws_home/621317)

The news correspondents report that additional information may be obtained from K.D. Rawat, National JALMA Institute for Leprosy and Other Mycobacterial Diseases Tajganj, Agra 282 001, India. (2013 Jan 29)

Chongqing Medical University: Immunotherapy for Tuberculosis: what’s the better choice?

By a News Reporter-Staff News Editor at Tuberculosis Week – A new study on Biology is now available. According to news reporting originating in Chongqing, People’s Republic of China, by NewsRx journalists, research stated, “A Th1/Th2 imbalance in tuberculosis (TB) patients
caused by a decreased Th1 response and an increased Th2 response is a significant factor in the pathogenesis and development of TB. Protective immune responses to TB include bacteriostatic and bactericidal responses.”

The news reporters obtained a quote from the research from Chongqing Medical University, “Unfortunately, however, immunoprotection and immune pathology co-exist in TB patients. Immunotherapy for TB principally aims to restore the Th1/Th2 balance by enhancing the Th1 response and suppressing the excessive Th2 response. Immunotherapy for TB can be classified into three categories: immune-enhancing therapy using cytokines, immunosuppressive therapy, and immunomodulatory therapy. Immunomodulatory therapy targets the Th1/Th2 imbalance and includes cytokine regulation therapy, antibody regulation therapy, a multi-dose heat-inactivated Mycobacterium vaccae vaccine, thymosin hormones and a DNA vaccine. A new approach in supplementary TB immunotherapy is to simultaneously up-regulate the Th1 response and down-regulate the Th2 response. While immunotherapy can contribute to TB treatment, it may also cause immunopathological injury.”

According to the news reporters, the research concluded: “Therefore, immunotherapy needs to be improved and further studied to maximize its potential.”

For more information on this research see: Immunotherapy for Tuberculosis: what’s the better choice? Frontiers in Bioscience-Landmark, 2012;17():2684-2690. Frontiers in Bioscience-Landmark can be contacted at: Frontiers In Bioscience Inc, 16471 Scientific Way, Irvine, CA 92618, USA.

Our news correspondents report that additional information may be obtained by contacting S.L. Guo, Chongqing Med Univ, Affiliated Hosp 1, Dept. of Resp & Crit Care Med, Chongqing 400016, People’s Republic of China. (2013 Jan 28)

Colorado State University, Fort Collins: Assessment of vaccine testing at three laboratories using the guinea pig model of tuberculosis

By a News Reporter-Staff News Editor at Life Science Weekly – Data detailed on Vaccine Research have been presented. According to news reporting originating from Fort Collins, Colorado, by NewsRx correspondents, research stated, “The guinea pig model of tuberculosis is used extensively in different locations to assess the efficacy of novel tuberculosis vaccines during pre-clinical development. Two key assays are used to measure protection against virulent challenge: a 30 day post-infection assessment of mycobacterial burden and long-term post-infection survival and pathology analysis.”
Our news editors obtained a quote from the research from Colorado State University, “To determine the consistency and robustness of the guinea pig model for testing vaccines, a comparative assessment between three sites that are currently involved in testing tuberculosis vaccines from external providers was performed. Each site was asked to test two ‘subunit’ type vaccines in their routine animal model as if testing vaccines from a provider. All sites performed a 30 day study, and one site also performed a long-term survival/pathology study. Despite some differences in experimental approach between the sites, such as the origin of the *Mycobacterium tuberculosis* strain and the type of aerosol exposure device used to infect the animals and the source of the guinea pigs, the data obtained between sites were consistent in regard to the ability of each ‘vaccine’ tested to reduce the mycobacterial burden. The observations also showed that there was good concurrence between the results of short-term and long-term studies.”

According to the news editors, the research concluded: “This validation exercise means that efficacy data can be compared between sites.”


The news editors report that additional information may be obtained by contacting A. Grover, Colorado State University, Dept. of Microbiology, Immunology & Pathology, 1682 Campus Delivery, Fort Collins, CO 80523, United States. (2013 Jan 22)

**Wuhan University, Hubei: Immunogenicity and protective efficacy of heterologous prime-boost regimens with mycobacterial vaccines and recombinant adenovirus- and poxvirus-vectored vaccines against murine tuberculosis**

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators publish new report on Immunization and Public Health. According to news originating from Hubei, People’s Republic of China, by NewsRx correspondents, research stated, “To evaluate regimens using bacillus Calmette-Guerin (BCG) or recombinant BCG (rBCG) overexpressing Ag85B for priming, followed by boosting with a modified vaccinia virus Ankara strain (MVA) and/or adenovirus vector (AD) expressing an Ag85B-ESAT6 fusion protein. Cellular and humoral immune responses were determined after subcutaneous vaccination, which was employed to trigger systemic immunity against intravenous infection in a mouse model of tuberculosis (TB).”
Our news journalists obtained a quote from the research from Wuhan University, "Bacterial loads and lung histology were evaluated. The relative IgG2a and IgG1 antibody levels indicated that the viral-vectored vaccines generated a T-helper type 1 (Th1)-biased response after two doses of viral boost vaccinations. Boosting BCG-primed mice with viral vaccines induced a Th1 immune response that included both CD4 and CD8 T-cells generating antigen-specific interferon-gamma (IFN-gamma) and CD8 T cytotoxic activity. Only mice vaccinated with two different viral boosters after BCG priming exhibited a significant reduction in bacterial burden in the lung after challenge. Histology examinations confirmed the attenuation of lung damage and more compact granulomas. After mycobacteria priming, boosting with AD85B-E6 followed by MVA85B-E6 afforded better protection than the reverse order of administration of the viral vectors."

According to the news editors, the research concluded: "This study demonstrates the potential of multiple heterologous viral booster vaccines, although the exact correlates of protection and optimal regimens should be further investigated for the rational design of future vaccine strategies."


The news correspondents report that additional information may be obtained from Q.R. You, Wuhan University, ABSL Lab 3, Wuhan 430071, Hubei, People’s Republic of China. (2013 Jan 08)

**Yangzhou University: Attenuated Listeria monocytogenes, a Mycobacterium tuberculosis ESAT-6 antigen expression and delivery vector for inducing an immune response**

By a News Reporter-Staff News Editor at Life Science Weekly – Data detailed on Microbiology have been presented. According to news reporting originating from Yangzhou, People’s Republic of China, by NewsRx correspondents, research stated, “We selectively expressed protective Mycobacterium tuberculosis antigen ESAT-6 in recombinant strains Lm(esat-6) and Lm Delta actA/plcB(esat-6) to evaluate the capacity of Listeria monocytogenes to deliver antigens from M. tuberculosis, and
we studied the pathogenicity and immunogenicity of these strains compared with virulent parental strain yzuLm4 and attenuated strain Lm Delta actA/plcB.”

Our news editors obtained a quote from the research from Yangzhou University, “The two recombinant strains retained listeriolyisin O hemolytic activity, escaped into the cytosol niche and established replication in the macrophage-like RAW264.7 cell line; however, these strains showed decreased virulence in C57BL/6 mice. Histopathology revealed no obvious pathological changes following administration of the recombinant strains to mice, indicating that they were significantly safer than parental strains.”

According to the news editors, the research concluded: “Moreover, intravenous vaccination of mice with the recombinant strains elicited specific Th1-type cellular immunity, splenocyte proliferation and effective CTL activity in vivo. Thus, attenuated L. monocytogenes strains can be used as effective vectors for delivering M. tuberculosis ESAT-6 and inducing a cellular immune response, suggesting that such vectors may be effective as novel vaccines for preventing tuberculosis.”

For more information on this research see: Attenuated Listeria monocytogenes, a Mycobacterium tuberculosis ESAT-6 antigen expression and delivery vector for inducing an immune response. Research in Microbiology, 2012;163(8):540-549. Research in Microbiology can be contacted at: Elsevier Science Bv, PO Box 211, 1000 Ae Amsterdam, Netherlands. (Elsevier - www.elsevier.com; Research in Microbiology - http://www.elsevier.com/wps/product/cws_home/522493)

The news editors report that additional information may be obtained by contacting Y.L. Yin, Yangzhou University, Jiangsu Key Lab Zoonosis, Yangzhou 225009, Jiangsu, People’s Republic of China. (2013 Jan 01)

Louisiana State University, New Orleans: Prime-boost approaches to tuberculosis vaccine development

By a News Reporter-Staff News Editor at Life Science Weekly – Research findings on Vaccines are discussed in a new report. According to news reporting originating in New Orleans, Louisiana, by NewsRx journalists, research stated, “Four individuals die from active TB disease each minute, while at least 2 billion are latently infected and at risk for disease reactivation. BCG, the only licensed TB vaccine, is effective in preventing childhood forms of TB; however its poor efficacy in adults, emerging drug-resistant TB strains and tedious chemotherapy regimes, warrant the development of novel prophylactic measures.”

The news reporters obtained a quote from the research from Louisiana State University, “Designing safe and effective vaccines against TB will require novel approaches on several levels, including
the administration of rationally selected mycobacterial antigens in efficient delivery vehicles via optimal immunization routes. Given the primary site of disease manifestation in the lungs, development of mucosal immunization strategies to generate protective immune responses both locally, and in the circulation, may be important for effective TB prophylaxis.”

According to the news reporters, the research concluded: “This review focuses on prime-boost immunization strategies currently under investigation and highlights the potential of mucosal delivery and rational vaccine design based on systems biology.”

For more information on this research see: Prime-boost approaches to tuberculosis vaccine development. Expert Review of Vaccines, 2012;11(10):1221-33.

Our news correspondents report that additional information may be obtained by contacting N. Dalmia, Dept. of Microbiology, Immunology and Parasitology, Louisiana State University Health Sciences Center, 1901 Perdido Street, New Orleans, LA 70112, United States. (2012 Dec 25)

Department of Immunology, Chennai: Mycobacterium tuberculosis H37Rv is more effective compared to vaccine strains in modulating neutrophil functions: an in vitro study

By a News Reporter-Staff News Editor at Life Science Weekly – Research findings on Immunology and Medical Microbiology are discussed in a new report. According to news originating from Chennai, India, by NewsRx correspondents, research stated, “Neutrophils are the primary cells contributing to initial defense against mycobacteria. Yet, little is known about the potential of various mycobacterial strains to stimulate neutrophils.”

Our news journalists obtained a quote from the research from the Department of Immunology, “This study was focused to compare the differential capacity of vaccine strains, Mycobacterium bovis bacillus Calmette-Guerin (BCG) and Mycobacterium indicus pranii (Mw), and laboratory strain H37Rv to activate and enhance neutrophil functions. The expression of phenotypic markers like Fc? receptor, toll-like receptor (TLR), and chemokine receptor; secretion of pro-inflammatory cytokines; and the rate of apoptosis were studied in infected neutrophils. Increased expression of CD32, CD64, TLR4, and CXCR3; increased TNF-a secretion; and downregulation of early apoptosis were observed in H37Rv-infected neutrophils. Among the vaccine strains, BCG increased the expression of only CD32 on neutrophils, while Mw was comparatively ineffective. To understand the paracrine role of neutrophils, the supernatants from infected neutrophils were used to stimulate monocytes and T helper cells. The secretory molecules from all
infected neutrophils increased the expression of CCR5 on monocytes, whereas only H37Rv-infected supernatant increased the expression of CCR7 on monocytes and CD69 on T cells. Thus, H37Rv was more effective in activating neutrophils and in turn stimulating monocytes and T cells.”

According to the news editors, the research concluded: “By comparison, vaccine strains were less effective in modulating neutrophil functions.”


The news correspondents report that additional information may be obtained from J. Nancy Hilda, Dept. of Immunology, National Institute for Research in Tuberculosis, Chetput, Chennai, India. (2012 Dec 18)

ICMR, Tamil Nadu: Trend in tuberculosis infection prevalence in a rural area in South India after implementation of the DOTS strategy

By a News Reporter-Staff News Editor at Biotech Week – Investigators publish new report on Mycobacterium Infections. According to news reporting out of Tamil Nadu, India, by NewsRx editors, research stated, “Three tuberculin surveys were conducted at intervals of 5 years following the implementation of a DOTS-based programme in 1999 in Tiruvallur District, South India. To estimate the trend in the prevalence of tuberculosis (TB) infection among children and to evaluate the impact of the DOTS strategy.”

Our news journalists obtained a quote from the research from ICMR, “Children aged 1-9 years in the sample for each survey were registered and administered 1 tuberculin unit of purified protein derivative RT 23 with Tween 80 by intradermal injection on the volar aspect of the left forearm. The induration diameter of the reaction was measured in mm after 72 h (3 days) and the prevalence of TB infection estimated. The induration data of bacille Calmette-Guerin (BCG) vaccinated and non-vaccinated children were analysed using the mixture model. The estimated prevalence of TB infection among non-BCG-vaccinated children in the three tuberculin surveys were respectively 19.4%, 13.8% and 11.4%, with an average annual decline of 5.2% (95%CI 3.6-6.8). The prevalence of TB infection among BCG-vaccinated children decreased, with an average annual decline of 5.4% (95%CI 10.0-18.6).”
According to the news editors, the research concluded: “A significant declining trend in the prevalence of TB infection among children was observed following the implementation of the DOTS strategy in the area.”

For more information on this research see: Trend in tuberculosis infection prevalence in a rural area in South India after implementation of the DOTS strategy. *International Journal of Tuberculosis and Lung Disease*, 2012;16(10):1315-1319. *International Journal of Tuberculosis and Lung Disease* can be contacted at: Int Union Against Tuberculosis Lung Disease (I U A T L D), 68 Boulevard Saint-Michel, 75006 Paris, France.

Our news journalists report that additional information may be obtained by contacting C. Kolappan, ICMR, Natl Inst Res TB, Madras 600031, Tamil Nadu, India. *(2012 Dec 12)*

**University of Washington, Seattle: Cryopreservation of Mycobacterium tuberculosis Complex Cells**

By a News Reporter-Staff News Editor at Life Science Weekly – Data detailed on Clinical Microbiology have been presented. According to news reporting originating in Seattle, Washington, by NewsRx journalists, research stated, “Successful long-term preservation of *Mycobacterium tuberculosis* cells is important for sample transport, research, biobanking, and the development of new drugs, vaccines, biomarkers, and diagnostics. In this report, *Mycobacterium bovis* bacillus Calmette-Guerin and *M. tuberculosis* H37Ra were used as models of *M. tuberculosis* complex strains to study cryopreservation of *M. tuberculosis* complex cells in diverse sample matrices at different cooling rates.”

The news reporters obtained a quote from the research from the University of Washington, “Cells were cryopreserved in diverse sample matrices, namely, phosphate-buffered saline (PBS), Middlebrook 7H9 medium with or without added glycerol, and human sputum. The efficacy of cryopreservation was quantified by microbiological culture and microscopy with BacLight LIVE/DEAD staining. In all sample matrices examined, the microbiological culture results showed that the cooling rate was the most critical factor influencing cell viability. Slow cooling (a few degrees Celsius per minute) resulted in much higher *M. tuberculosis* complex recovery rates than rapid cooling (direct immersion in liquid nitrogen) (p <0.05). Among the three defined cryopreservation media (PBS, 7H9, and 7H9 plus glycerol), there was no significant differential effect on viability (p=0.06 to 0.87). Preincubation of thawed *M. tuberculosis* complex cells in 7H9 broth for 20 h before culture on solid Middlebrook 7H10 plates did not help the recovery of the cells from cryoinjury (p=0.14 to 0.71). The BacLight LIVE/DEAD staining kit, based on Syto 9 and propidium iodide (PI), was also applied to assess
cell envelope integrity after cryopreservation. Using the kit, similar percentages of ‘live’ cells with intact envelopes were observed for samples cryopreserved under different conditions, which was inconsistent with the microbiological culture results.”

According to the news reporters, the research concluded: “This implies that suboptimal cryopreservation might not cause severe damage to the cell wall and/or membrane but instead cause intracellular injury, which leads to the loss of cell viability.”


Our news correspondents report that additional information may be obtained by contacting Z. Shu, Dept. of Mechanical Engineering, University of Washington, Seattle, Washington, United States. (2012 Nov 06)

**University of Washington, Seattle: Early Secreted Antigenic Target of 6-kDa Protein of Mycobacterium tuberculosis Primes Dendritic Cells To Stimulate Th17 and Inhibit Th1 Immune Responses**

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators publish new report on Immunology. According to news reporting from Seattle, Washington, by NewsRx journalists, research stated, “Early secreted antigenic target of 6 kDa (ESAT-6) of Mycobacterium tuberculosis is a T cell Ag that is a potential vaccine candidate, but it is also a virulence factor that mediates pathogenicity. To better understand the effects of ESAT-6 on the immune response, we studied the effect of ESAT-6 on human dendritic cells (DCs).”

The news correspondents obtained a quote from the research from the University of Washington, “Peripheral blood monocytes were treated with GM-CSF and IL-4 to yield immature DCs, which were matured by addition of LPS and CD40 ligand (CD40L), with or without ESAT-6. ESAT-6 inhibited LPS/CD40L-induced DC expression of costimulatory molecules, reduced DC-stimulated allogeneic T cell proliferation and IL-2 and IFN-gamma production, and enhanced IL-17 production. ESAT-6-treated DCs also increased IL-17 and reduced IFN-gamma production by M. tuberculosis-specific autologous T cells. ESAT-6 inhibited LPS/CD40L-induced DC production of IL-12 and enhanced that of IL-23 and IL-1 beta, without affecting secretion of TNF-alpha, IL-6, or IL-8 through specific interaction with immature DCs. The effects of ESAT-6 were not mediated through cAMP or p38 MAPK. Medium from ESAT-6-conditioned DCs increased IL-17 and reduced
IFN-gamma production by T cells stimulated with anti-CD3 plus anti-CD28, and ESAT-6-induced IL-17 production was blocked by neutralizing both IL-23 and IL-1 beta. ESAT-6 reduced LPS/CD40L-stimulated transcription of IL-12p35 and enhanced that of IL-23p19 through inhibition of IFN regulatory factor-1 and upregulation of activating transcription factor-2 and c-Jun, transcriptional regulators of IL-12p35 and IL-23p19, respectively.

According to the news reporters, the research concluded: “ESAT-6 increases DC production of IL-23 and IL-1 beta while inhibiting that of IL-12, thus enhancing Th17 at the expense of protective Th1 responses. The Journal of Immunology, 2012, 189:3092-3103.”

For more information on this research see: Early Secreted Antigenic Target of 6-kDa Protein of Mycobacterium tuberculosis Primes Dendritic Cells To Stimulate Th17 and Inhibit Th1 Immune Responses. Journal of Immunology, 2012;189(6):3092-3103. Journal of Immunology can be contacted at: Amer Assoc Immunologists, 9650 Rockville Pike, Bethesda, MD 20814, USA. (The American Association of Immunologists - www.aai.org; Journal of Immunology - www.jimmunol.org)

Our news journalists report that additional information may be obtained by contacting X.S. Wang, University of Washington, Mol & Cellular Biol Program, Seattle, WA 98109, United States. (2012 Nov 06)

University of Oxford: Effect of vaccine dose on the safety and immunogenicity of a candidate TB vaccine, MVA85A, in BCG vaccinated UK adults

By a News Reporter-Staff News Editor at Vaccine Weekly – Fresh data on Vaccines are presented in a new report. According to news reporting from Oxford, United Kingdom, by NewsRx journalists, research stated, “A non-randomised, open-label, Phase I safety and immunogenicity dose-finding study to assess the safety and immunogenicity of the candidate TB vaccine Modified Vaccinia virus Ankara expressing Antigen 85A (MVA85A) from Mycobacterium tuberculosis (MTB) in healthy adult volunteers previously vaccinated with BCG. Healthy BCG-vaccinated volunteers were vaccinated with either 1 x 10(7) or 1 x 10(8) PFU of MVA85A.”

The news correspondents obtained a quote from the research from the University of Oxford, “All adverse events were documented and antigen specific T cell responses were measured using an ex vivo IFN-gamma ELISPOT assay. Safety and immunogenicity were compared between the 2 dose groups and with a previous trial in which a dose of 5 x 10(7) PFU MVA85A had been administered. There were no serious adverse events recorded following administration of either 1 x 10(7) or 1 x 10(8) PFU of MVA85A. Systemic adverse events were more frequently reported following administration of 1 x 10(8) PFU of MVA85A
when compared to either 5 x 10(7) or 1 x 10(7) PFU of MVA85A but were mild or moderate in severity and resolved completely within 7 days of immunisation. Antigen specific T cell responses as measured by the IFN-gamma ELISPOT were significantly higher following immunisation in adults receiving 1 x 10(8) PFU compared to the 5 x 10(7) and 1 x 10(7) doses. Additionally, a broader range of Ag85A epitopes are detected following 1 x 10(8) PFU of MVA85A.”

According to the news reporters, the researchers concluded: “A higher dose of 1 x 10(8) PFU of MVA85A is well-tolerated, increases the frequency of IFN-gamma secreting T cells detected following immunisation and broadens the range of Ag85A epitopes detected.”


Our news journalists report that additional information may be obtained by contacting A.A. Pathan, University of Oxford, Jenner Inst, Oxford OX3 7LE, United Kingdom. (2012 Oct 17)

**ICMR, Tamil Nadu: Immunology of tuberculosis**

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators publish new report on Mycobacterium Infections. According to news originating from Tamil Nadu, India, by NewsRx editors, the research stated, “Tuberculosis is a major health problem throughout the world causing large number of deaths, more than that from any other single infectious disease. The review attempts to summarize the information available on host immune response to Mycobacterium tuberculosis.”

Our news journalists obtained a quote from the research from ICMR, “Since the main route of entry of the causative agent is the respiratory route, alveolar macrophages are the important cell types, which combat the pathogen. Various aspects of macrophage-mycobacterium interactions and the role of macrophage in host response such as binding of M. tuberculosis to macrophages via surface receptors, phagosome-lysosome fusion, mycobacterial growth inhibition/killing through free radical based mechanisms such as reactive oxygen and nitrogen intermediates; cytokine-mediated mechanisms; recruitment of accessory immune cells for local inflammatory response and presentation of antigens to T cells for development of acquired immunity have been described. The role of macrophage apoptosis in containing the growth of...
the bacilli is also discussed. The role of other components of innate immune response such as natural resistance associated macrophage protein (Nramp), neutrophils, and natural killer cells has been discussed. The specific acquired immune response through CD4 T cells, mainly responsible for protective Th1 cytokines and through CD8 cells bringing about cytotoxicity, also has been described. The role of CD-I restricted CD8(+) T cells and non-MHC restricted gamma/delta T cells has been described although it is incompletely understood at the present time. Humoral immune response is seen though not implicated in protection. The value of cytokine therapy has also been reviewed. Influence of the host human leucocyte antigens (HLA) on the susceptibility to disease is discussed. Mycobacteria are endowed with mechanisms through which they can evade the onslaught of host defense response. These mechanisms are discussed including diminishing the ability of antigen presenting cells to present antigens to CD4(+) T cells; production of suppressive cytokines; escape from fused phagosomes and inducing T cell apoptosis.

According to the news editors, the researchers concluded: “The review brings out the complexity of the host-pathogen interaction and underlines the importance of identifying the mechanisms involved in protection, in order to design vaccine strategies and find out surrogate markers to be measured as in vitro correlate of protective immunity.”

For more information on this research see: Immunology of tuberculosis. Indian Journal of Medical Research, 2012;136(1):213-232. Indian Journal of Medical Research can be contacted at: Indian Council Medical Res, PO Box 4911 Ansari Nagar, New Delhi 110029, India.

The news correspondents report that additional information may be obtained from A. Raja, TB Res Center ICMR, Dept. of Immunol, Chennai 600031, Tamil Nadu, India. (2012 Oct 09)

Department of Immunology, Chennai: Polymorphism in the RD1 locus and its effect on downstream genes among South Indian clinical isolates of Mycobacterium tuberculosis

By a News Reporter-Staff News Editor at Vaccine Weekly – Investigators discuss new findings in Medical Microbiology. According to news reporting out of Chennai, India, by NewsRx editors, research stated, “RD1, the region of difference between the virulent strains of Mycobacterium tuberculosis and Mycobacterium bovis BCG, is the most explored region in terms of mycobacterial virulence and vaccine design. This study found a polymorphic intergenic region between two genes, Rv3870 and Rv3871, in the RD1 region.”
Our news journalists obtained a quote from the research from the Department of Immunology, “Sequence analysis revealed a 53 bp repeat element that created a polymorphism among the clinical isolates, reported previously as the mycobacterial interspersed repetitive unit (MIRU) 39 locus. The discriminatory power of this locus was found to be high for EAI strains, as indicated by a Hunter-Gaston diversity index value of 0.58, and low for Beijing (0.26) and CAS (0.29) strains. The presence and variability of MIRU 39 in the intergenic region led us to investigate the functional role of the repeat element by measuring the transcription levels of the downstream genes Rv3871 and Rv3874 by quantitative RT-PCR among the different clades of clinical strains. Higher transcription levels of Rv3871 were observed in strains with four copies of the repeat element in the upstream region, whereas the transcription level of Rv3874 was higher in strains with six copies of the repeat element.”

According to the news editors, the researchers concluded: “These data suggest that changes in transcription levels resulting from insertion of different copy numbers of the repeat element may affect regulation of gene expression in M.”

For more information on this research see: Polymorphism in the RD1 locus and its effect on downstream genes among South Indian clinical isolates of Mycobacterium tuberculosis. Journal of Medical Microbiology, 2012;61(Pt 10):1352-9.

Our news journalists report that additional information may be obtained by contacting A.K. Refaya, Dept. of Immunology, National Institute for Research in Tuberculosis, Chetput, Chennai 600 031, India. (2012 Oct 03)

National Institute of Medical Sciences, Mexico City: Expression of Beta Defensin 2 in Experimental Pulmonary Tuberculosis: Tentative Approach for Vaccine Development

By a News Reporter-Staff News Editor at Biotech Week – Investigators discuss new findings in Medical Research. According to news reporting originating from Mexico City, Mexico, by NewsRx correspondents, research stated, “Defensins are low molecular weight antimicrobial and immuno-modulatory peptides. Their participation against Mycobacterium tuberculosis (MTb) infection has been scarcely studied.”

Our news editors obtained a quote from the research from the National Institute of Medical Sciences, “We describe the kinetics of murine beta-defensin 2 (mBD-2) expression by quantitative real-time PCR and
cellular location by immunohistochemistry in murine models of progressive pulmonary tuberculosis and latent infection. During progressive disease, mBD2 gene expression raised its peak at 14 days postinfection, whereas in latent infection it was at 90 days. In both models, mBD-2 immunostaining was essentially located in cells with dendritic morphology located near mediastinal lymph nodes, which correlated with the previous reported highest expression of cell-mediated protected immunity in both models. These results suggest that mBD-2 may play a role in the control of bacilli growth by contributing to establish a Th1 response, being a link between innate and adaptative immunity.”

According to the news editors, the researchers concluded: “These data may be used for the development of new vaccine approaches.”


The news editors report that additional information may be obtained by contacting B. Rivas-Santiago, Natl Inst Med Sci & Nutr Salvador Zubiran, Dept. of Expt Pathol, Mexico City, DF, Mexico. (2012 Oct 03)

National Institute of Immunology, New Delhi: Protective efficacy of Mycobacterium indicus pranii against tuberculosis and underlying local lung immune responses in guinea pig model

By a News Reporter-Staff News Editor at Life Science Weekly – Data detailed on Vaccines have been presented. According to news reporting from New Delhi, India, by NewsRx journalists, research stated, “Tuberculosis kills two million people each year. As the current vaccine BCG fails to prevent adult cases of TB, an improved vaccine and/or vaccination strategy is urgently needed to combat TB.”

The news correspondents obtained a quote from the research from the National Institute of Immunology, “Previously we reported the higher protective efficacy of Mycobacterium indicus pranii (MIP), formerly known as Mycobacterium w (M.w) as compared to BCG in murine model of TB. In this study we further evaluated the protective efficacy of MIP in guinea pig model of TB. Modulation of post infection immune response was analyzed in the lungs of MIP immunized and control groups. We found reduced bacterial loads, improved pathology and organized granulomatous response at different post infection
time points in the MIP-immunized group as compared to the BCG-immunized group. Combined results suggest that MIP-immunization results in heightened protective Th1 response as compared to BCG group, early after infection with M.tb and a balanced Th1 versus immunosuppressive response at late chronic stage of infection. The study demonstrates the higher antigen presenting cells function both inside the granuloma as well as in the single cell suspension of the lung in the MIP-immunized group. We further demonstrate that live MIP is safe to use in vivo as we observed quick clearance of MIP from the body and no untoward reaction was found. Aerosol route of immunization provided higher protection.

According to the news reporters, the researchers concluded: “Further this study provides evidence that MIP-immunization gives significantly better long term protection as compared to BCG against TB.”

For more information on this research see: Protective efficacy of Mycobacterium indicus pranii against tuberculosis and underlying local lung immune responses in guinea pig model. Vaccine, 2012;30(43):6198-209. (Elsevier - www.elsevier.com; Vaccine - http://www.journals.elsevier.com/vaccine)

Our news journalists report that additional information may be obtained by contacting A. Gupta, Product Development Cell 1, National Institute of Immunology, JNU Complex, Aruna Asaf Ali Marg, New Delhi 110067, India. (2012 Sep 25)

Malaghan Institute of Medical Research, Wellington: Dissecting memory T cell responses to TB: Concerns using adoptive transfer into immunodeficient mice

By a News Reporter-Staff News Editor at Gastroenterology Week – Fresh data on Digestive System Diseases and Conditions are presented in a new report. According to news reporting from Wellington, New Zealand, by NewsRx journalists, research stated, “Several studies have used adoptive transfer of purified T cell subsets into immunodeficient mice to determine the subset of T cells responsible for mediating protection against Mycobacterium tuberculosis. These studies suggested that CD62L(hi) memory CD4(+) T cells from BCG-vaccinated mice are key for protection against tuberculosis.”

The news correspondents obtained a quote from the research from the Malaghan Institute of Medical Research, “Importantly, we observed that transfer of naive CD4(+) T cells into Rag1-/-recipients protected against a mycobacterial challenge as well as transfer of BCG-experienced CD4(+) T cells. We found that transfer of total CD4(+) T cells from naive mice or enriched CD62L(hi)CD4(+) T cells from BCG-vaccinated mice into Rag1-/-recipients induced severe colitis by 3 weeks post cell transfer, whereas transfer of CD62L(lo)CD4(+) T cells from
BCG-vaccinated mice did not. Naive and CD62L(hi)CD4(+) T cells proliferated extensively upon transfer and developed an activated effector phenotype in the lung, even in the absence of infectious challenge. The induction of colitis and systemic cytokine response induced by the transfer and subsequent activation of CD4(+) T cells from naive mice or CD62L(hi)CD4(+) T cells from BCG-vaccinated mice, into immunodeficient recipients, may heighten their ability to protect against mycobacterial challenge.

According to the news reporters, the researchers concluded: “This raises doubts about the validity of this model to study CD4(+) T cell-mediated protection against tuberculosis.”


Our news journalists report that additional information may be obtained by contacting L. Ancelet, Infectious Diseases Group, Malaghan Institute of Medical Research, PO Box 7060, Newtown, Wellington 6242, New Zealand. (2012 Sep 17)

**Fudan University, Shanghai: Novel Recombinant BCG Coexpressing Ag85B, ESAT-6 and Rv2608 Elicits Significantly Enhanced Cellular Immune and Antibody Responses in C57BL/6 Mice**

By a News Reporter-Staff News Editor at Biotech Week – A new study on Mycobacterium Infections is now available. According to news originating from Shanghai, People’s Republic of China, by NewsRx correspondents, research stated, “Tuberculosis (TB) remains an enormous global health problem, and a new vaccine against TB more potent than the current inadequate vaccine, the Bacille Calmette-Guerin (BCG), is urgently needed. BCG has proven to be an effective recombinant delivery vehicle for foreign antigens because of its ability to induce long-lived specific humoral and cellular immunity.”

Our news journalists obtained a quote from the research from Fudan University, “Experimental evidences have revealed that Ag85B, ESAT-6 and Rv2608 are important immunodominant antigens of *Mycobacterium tuberculosis* and are all promising vaccine candidate molecules. In this study, we have constructed a novel recombinant BCG (rBCG) expressing fusion protein Ag85B-ESAT6-Rv2608 and evaluated the immunogenicity of rBCG in C57BL/6 mice. Results show there is strong TB-specific CD4(+) and CD8(+) T lymphocytes proliferative response in mice immunized with rBCG vaccine, especially the cytotoxic CD8(+) T
cells playing an important role in protection against TB. And rBCG immunization has induced a significantly strong Th1 immune response, characterized by the increased ratio of IgG2b/IgG1. Results also show that rBCG immunization could increase the secretion of Th1 cytokines such as TNF-α and IL-2 and could decrease the secretion of Th2 cytokine IL-10. Moreover, it was shown that rBCG immunization induced a strong humoral response in mice, characterized by the elevated IgG titre. Therefore, we conclude that this rBCG immunization could increase both cellular immune response and antigen-specific humoral response significantly as compared to BCG immunization in mice.”

According to the news editors, the researchers concluded: “The above results illustrated that rBCG::Ag85B-ESAT6-Rv2608 is a potential candidate against M. tuberculosis for further study.”


The news correspondents report that additional information may be obtained from Y. Lu, State Key Laboratory of Genetic Engineering, School of Life Sciences, Fudan University, Shanghai, People’s Taiwan. (2012 Sep 12)

IREC, Ciudad Real: Progress in Oral Vaccination against Tuberculosis in Its Main Wildlife Reservoir in Iberia, the Eurasian Wild Boar

By a News Reporter-Staff News Editor at Biotech Week – Investigators publish new report on Mycobacterium Infections. According to news reporting from Ciudad Real, Spain, by NewsRx journalists, research stated, “Eurasian wild boar (Sus scrofa) is the main wildlife reservoir for tuberculosis (TB) in Iberia. This review summarizes the current knowledge on wild boar vaccination including aspects of bait design, delivery and field deployment success; wild boar response to vaccination with Bacillus Calmette-Guerin (BCG) and inactivated Mycobacterium bovis; and wild boar vaccination biosafety issues as well as prospects on future research.”

The news correspondents obtained a quote from the research from IREC, “Oral vaccination with BCG in captive wild boar has shown to be safe with significant levels of protection against challenge with virulent M. bovis. An oral vaccination with a new heat-killed M. bovis vaccine conferred a protection similar to BCG. The study of host-pathogen interactions identified biomarkers of resistance/susceptibility to tuberculosis...
in wild boar such as complement component 3 (C3) and methylmalonyl coenzyme A mutase (MUT) that were used for vaccine development. Finally, specific delivery systems were developed for bait-containing vaccines to target different age groups.”

According to the news reporters, the researchers concluded: “Ongoing research includes laboratory experiments combining live and heat-killed vaccines and the first field trial for TB control in wild boar.”

For more information on this research see: Progress in Oral Vaccination against Tuberculosis in Its Main Wildlife Reservoir in Iberia, the Eurasian Wild Boar. Veterinary Medicine International, 2012;2012():978501. (Hindawi Publishing - www.hindawi.com; Veterinary Medicine International - http://www.hindawi.com/journals/vmi/)

Our news journalists report that additional information may be obtained by contacting B. Beltran-Beck, Instituto de Investigacion de Recursos Cinegeticos, IREC (CSIC-UCLM-JCCM), Ronda de Toledo s, n, 13071 Ciudad Real, Spain. (2012 Sep 12)

Trudeau Institute, Saranac Lake: Protection versus pathology in tuberculosis: recent insights

By a News Reporter-Staff News Editor at Life Science Weekly – Researchers detail new data in Mycobacterium Infections. According to news reporting originating from Saranac Lake, New York, by NewsRx correspondents, research stated, “Recent studies have revisited the roles of prime players in the immune response to tuberculosis (TB) and have highlighted novel functions of these players. Specifically, immunoregulatory mechanisms mediated by IFN? have been delineated as well as a novel role for neutrophils in promoting antigen presentation.”

Our news editors obtained a quote from the research from Trudeau Institute, “New insights into the interaction between the bacterium and phagocyte indicate that the bacterium actively promotes phagocyte necrosis rather than apoptosis and that this impacts generation of the acquired response. There are also many new examples of how the phagocyte responds to the bacteria and how it mediates control. The phenotype of protective T cells is also being re-examined.”

According to the news editors, the researchers concluded: “These developments provide promise for improved vaccine design and highlight the complexity of this disease.”

CHAPTER 8  VACCINES

The news editors report that additional information may be obtained by contacting A.M. Cooper, The Trudeau Institute, Inc 154 Algonquin Ave, Saranac Lake, NY 12983, United States. (2012 Sep 11)

McMaster University, Hamilton: Regulation of TB Vaccine-Induced Airway Luminal T Cells by Respiratory Exposure to Endotoxin

By a News Reporter-Staff News Editor at Vaccine Weekly – Current study results on Mycobacterium Infections have been published. According to news originating from Hamilton, Canada, by NewsRx correspondents, research stated, “Tuberculosis (TB) vaccine-induced airway luminal T cells (ALT) have recently been shown to be critical to host defense against pulmonary TB. However, the mechanisms that maintain memory ALT remain poorly understood.”

Our news journalists obtained a quote from the research from McMaster University, “In particular, whether respiratory mucosal exposure to environmental agents such as endotoxin may regulate the size of vaccine-induced ALT population is still unclear. Using a murine model of respiratory genetic TB vaccination and respiratory LPS exposure, we have addressed this issue in the current study. We have found that single or repeated LPS exposure increases the number of antigen-specific ALT which are capable of robust secondary responses to pulmonary mycobacterial challenge. To investigate the potential mechanisms by which LPS exposure modulates the ALT population, we have examined the role of ALT proliferation and peripheral T cell recruitment. We have found that LPS exposure-increased ALT is not dependent on increased ALT proliferation as respiratory LPS exposure does not significantly increase the rate of proliferation of ALT. But rather, we find it to be dependent upon the recruitment of peripheral T cells into the airway lumen as blockade of peripheral T cell supplies markedly reduces the initially increased ALT. Thus, our data suggest that environmental exposure to airborne agents such as endotoxin has a profound modulatory effect on TB vaccine-elicited T cells within the respiratory tract.”

According to the news editors, the researchers concluded: “Our study provides a new, M.tb antigen-independent mechanism by which the respiratory mucosal anti-TB memory T cells may be maintained.”

For more information on this research see: Regulation of TB Vaccine-Induced Airway Luminal T Cells by Respiratory Exposure to Endotoxin. *Plos One*, 2012;7(7):e41666. (Public Library of Science - www.plos.org; Plos One - www.plosone.org)

The news correspondents report that additional information may be obtained from X. Chen, McMaster Immunology Research Centre and Dept. of Pathology & Molecular Medicine, McMaster University, Hamilton, Ontario, Canada. (2012 Aug 22)
Arizona State University, Tempe: Could changes in national tuberculosis vaccination policies be ill-informed?

By a News Reporter-Staff News Editor at Tuberculosis Week – New research on Mycobacterium Infections is the subject of a report. According to news reporting out of Tempe, Arizona, by NewsRx editors, research stated, “National policies regarding the BCG vaccine for tuberculosis vary greatly throughout the international community and several countries are currently considering discontinuing universal vaccination. Detractors of BCG point to its uncertain effectiveness and its interference with the detection and treatment of latent tuberculosis infection (LTBI).”

Our news journalists obtained a quote from the research from Arizona State University, “In order to quantify the trade-off between vaccination and treatment of LTBI, a mathematical model was designed and calibrated to data from Brazil, Ghana; Germany, India, Mexico, Romania, the United Kingdom and the United States. Country-specific thresholds for when LTBI treatment outperforms mass vaccination were found and the consequences of policy changes were estimated. Our results suggest that vaccination outperforms LTBI treatment in all settings but with greatly reduced efficiency in low incidence countries.”

According to the news editors, the researchers concluded: “While national policy statements emphasize BCG’s interference with LTBI detection, we find that reinfection should be more determinant of a country’s proper policy choice.”


Our news journalists report that additional information may be obtained by contacting D.J. Gerberry, Arizona State University, Sch Math & Stat Sci, Tempe, AZ 85287, United States. (2012 Aug 13)
Toronto General Hospital: The diagnosis of tuberculosis in dialysis patients

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – Research findings on Mycobacterium Infections are discussed in a new report. According to news reporting originating from Toronto, Canada, by NewsRx editors, the research stated, “Tuberculosis is an important issue for nephrologists caring for dialysis patients. Because dialysis patients are immunocompromised, they are at higher risk for reactivation of latent tuberculosis, and they frequently have atypical presentation.”

Our news editors obtained a quote from the research from Toronto General Hospital, “Furthermore, hemodialysis units may foster rapid spread of active pulmonary tuberculosis. The diagnosis of active pulmonary tuberculosis still depends on detection of organisms by smear and culture. Newer nucleic acid detection techniques are more sensitive and specific. Nephrologists should remember that nonspecific presentation of tuberculosis including fever, weight loss, and adenopathy are more common in dialysis patients than in the general population, and diagnosis may require biopsy of extrapulmonary tissue. Detection of latent tuberculosis in dialysis patients should only be undertaken if treatment is planned. Generally, this should apply only to potential transplant candidates and younger dialysis patients with longer life expectancy. Tuberculin skin test is very insensitive in dialysis patients, and false-positives occur in patients born in countries where Bacillus Calmette-Guerin vaccine has been used.”

According to the news editors, the researchers concluded: “Blood tests using stimulation of gamma interferon have been shown to be more sensitive tests of latent tuberculosis and may be used in conjunction with tuberculin skin tests.”


The news editors report that additional information may be obtained by contacting R.M. Richardson, Division of Nephrology, Dept. of Medicine, The Toronto General Hospital, Toronto, Ontario, Canada. (2012 Aug 13)
GlaxoSmithKline, Copenhagen: Immunotherapy for TB

By a News Reporter-Staff News Editor at Biotech Week – New research on Mycobacterium Infections is the subject of a report. According to news reporting originating from Copenhagen, Denmark, by NewsRx editors, the research stated, “Mycobacterium tuberculosis was one of the first human pathogens to be identified as the cause of a specific disease - TB. TB was also one of the first specific diseases for which immunotherapy was attempted.”

Our news editors obtained a quote from the research from GlaxoSmithKline, “In more than a century since, multiple different immunotherapies have been attempted, alongside vaccination and antibiotic treatment, with varying degrees of success. Despite this, TB remains a major worldwide health problem that causes nearly 2 million deaths annually and has infected an estimated 2 billion people. A major reason for this is that M. tuberculosis is an ancient human pathogen that has evolved complex strategies for persistence in the human host. It has thus been long understood that, to effectively control TB, we will need to address the ability of the pathogen to establish a persistent, latent infection in most infected individuals.”

According to the news editors, the researchers concluded: “This review discusses what is presently known about the interaction of M. tuberculosis with the immune system, and how this knowledge has been used to design immunotherapeutic strategies.”

For more information on this research see: Immunotherapy for TB. Immunotherapy, 2012;4(6):629-47.

The news editors report that additional information may be obtained by contacting T.M. Doherty, Medical Affairs, GlaxoSmithKline, Brondby, DK-2605, Copenhagen, Denmark. (2012 Aug 08)

Hvidovre Hospital: Guidelines for screening, prophylaxis and critical information prior to initiating anti-TNF-alpha treatment

By a News Reporter-Staff News Editor at AIDS Vaccine Week – Investigators publish new report on Human Herpes Viruses. According to news originating from Hvidovre, Denmark, by NewsRx correspondents, researchers stated “These national clinical guidelines outlining the screening, prophylaxis and critical information required prior to initiating anti-TNF-alpha treatment have been approved by the Danish Society for Gastroenterology. Anti-TNF-alpha therapy is widely used in gastroenterology (for inflammatory bowel disease), rheumatology (for rheumatoid arthritis, psoriatic arthritis and spondyloarthropathies) and dermatology (for psoriasis).”
Our news journalists obtained a quote from the research from Hvidovre Hospital, “With this background, the Danish Society for Gastroenterology established a group of experts to assess evidence for actions recommended before treatment with anti-TNF-alpha agents. Screening should take place for both active tuberculosis and latent tuberculosis. Screening must evaluate the risk of hepatitis B exposure/infection and that of other viral infections such as human immunodeficiency virus (HIV) and varicella zoster virus (VZV). The assessment should include a history of previous malignancies (cases of malignant disease within 5 years of anti-TNF-alpha treatment should be carefully considered). The physical examination should include lung/heart auscultation and lymph node examination, and the paraclinical investigations should include chest X-rays and laboratory tests, including an interferon gamma release assay, a hepatitis B test, an HIV test and, when prior VZV infection is uncertain, a VZV antibody test. Prophylaxis: Isoniazid should be administered in cases of suspected latent TB infection. Antiviral treatment is recommended in HBsAg-positive patients at the start of anti-TNF-alpha treatment. Before anti-TNF-alpha therapy, vaccination with 23-valent pneumococcal vaccine is recommended, and HBV vaccination may be considered in seronegative patients. Annual vaccination against seasonal influenza is recommended. Human papilloma virus vaccination should be administered in accordance with the guidelines of the National Board of Health of Denmark. In patients without a prior VZV infection, VZV vaccination may be considered. Information for patients: Anti-TNF-alpha treatment results in a generally increased risk of infection and latent tuberculosis flare-up. Women are advised to comply with the national guidelines for screening for cervical cancer, and their HPV immunisation status should be clarified. An increased risk of lymphoma with biological therapy in combination with thiopurines should be mentioned.”

According to the news editors, the researchers concluded: “Patients are advised to seek medical advice in case of herpes zoster infection.”

For more information on this research see: Guidelines for screening, prophylaxis and critical information prior to initiating anti-TNF-alpha treatment. *Danish Medical Journal*, 2012;59(7):C4480.

The news correspondents report that additional information may be obtained from I. Nordgaard-Lassen, Gastrounit, Medical Section, Hvidovre Hospital, 2650 Hvidovre, Denmark. (*2012 Jul 30*)

**Kirikkale University: Association Between Tuberculosis and Atopy: Role of the CD14-159C/T Polymorphism**

By a News Reporter-Staff News Editor at Biotech Week – Researchers detail new data in Obstructive Lung Diseases. According to news reporting originating in Kirikkale, Turkey, by NewsRx journalists, re-
searchers stated “The development of allergic hypersensitivity depends on both genetic and environmental factors. Different amounts of microbial products could affect patients with atopy and different genotypes.”

The news reporters obtained a quote from the research by the authors from Kirikkale University, “We aimed to evaluate the role of varying degrees of exposure to infection by Mycobacterium tuberculosis (tuberculosis) in atopic patients and analyze the association with genetic factors. We performed CD14-159C/T genotyping in atopic patients (n=118) and healthy individuals (n=62) and recorded the following variables: rural lifestyle, exposure to persons with tuberculosis, bacille Calmette-Guerin (BCG) vaccination, tuberculin skin test (TST), skin prick test, and phenotypes of atopy. Blood samples were analyzed for soluble-CD14 (sCD14), interferon (IFN) gamma, total immunoglobulin (Ig) E, and eosinophil levels. A score was used to identify the likelihood of exposure to tuberculosis. Almost all the study participants had had a BCG vaccination, and half had a positive TST result. No differences were observed between atopic patients with high/low tuberculosis scores and CD14 genotypes in terms of atopic phenotypes, allergen sensitization, and levels of total IgE, sCD14, and IFN-gamma. However, the frequency of asthma was higher in atopic patients with a high tuberculosis score and was not associated with CD14 genotypes. Eosinophil counts in blood were higher in atopic patients with a high tuberculosis score and CC+CT genotypes. These results suggest that the C allele of the CD14-159C/T polymorphism has a marked effect on eosinophil levels in atopic patients with increased exposure to tuberculosis.”

According to the news reporters, the researchers concluded: “In addition, the degree of exposure to tuberculosis in atopic patients may modify the development of asthma.”

For more information on this research see: Association Between Tuberculosis and Atopy: Role of the CD14-159C/T Polymorphism. *Journal of Investigational Allergology and Clinical Immunology*, 2012;22(3):201-207. *Journal of Investigational Allergology and Clinical Immunology* can be contacted at: Esmon Publicidad S A, Calle Balmes 209, 3 2, Barcelona, 08006, Spain.

Our news correspondents report that additional information may be obtained by contacting A.B. Kavut, Kirikkale University, Fac Med, Dept. of Infect Dis, Kirikkale, Turkey. (2012 Jul 25)

**Max-Planck-Institute for Infection Biology, Berlin: Tuberculosis vaccine development: strength lies in tenacity**

By a News Reporter-Staff News Editor at Biotech Week – Investigators publish new report on Immunization. According to news originating from Berlin, Germany, by NewsRx editors, the researcher stated “The past decade has witnessed a tremendous increase in the development of
novel vaccines against tuberculosis (TB). In mice, each of these vaccine candidates stimulates an immune response that reduces the bacillary load, reflecting control but not sterilization of infection.”

Our news journalists obtained a quote from the research by the author from Max-Planck-Institute for Infection Biology, “Yet, the immune mechanisms underlying vaccine efficacy are only partially understood. In parallel to clinical assessment of current candidates, the next generation of vaccine candidates still needs to be developed. This requires basic research on how to induce the most efficacious immune response. Equally important is the dissection of immune responses in patients, latently infected healthy individuals, and participants of clinical vaccine trials.”

According to the news editors, the researchers concluded: “Amalgamation of this information will foster the way towards more efficacious vaccination strategies that not only prevent disease, but prevent or abolish infection.”


The news correspondents report that additional information may be obtained from S.H. Kaufmann, Max Planck Institute for Infection Biology, Chariteplatz 1, 10117 Berlin, Germany. (2012 Jul 25)

**McMaster University, Hamilton: Mechanisms of delayed anti-tuberculosis protection in the lung of parenteral BCG-vaccinated hosts: A critical role of airway luminal T cells**

By a News Reporter-Staff News Editor at Life Science Weekly – A new study on Mycobacterium Infections is now available. According to news reporting from Hamilton, Canada, by NewsRx journalists, researchers stated “The immune mechanisms underlying unsatisfactory pulmonary mucosal protection by parenteral Bacillus Calmette-Guerin (BCG) immunization remain poorly understood. We found that parenteral BCG immunization failed to elicit airway luminal T cells (ALT) whereas it induced significant T cells in the lung interstitium.”

The news correspondents obtained a quote from the research by the authors from McMaster University, “After Mycobacterium tuberculosis (M.tb) challenge, ALT remained missing for 10 days. The lack of ALT correlated with lack of lung protection for 14 days post-M.tb challenge. To further investigate the role of ALT, ALT were elicited in BCG-immunized animals by intranasal inoculation of M.tb culture-filtrate (CF) proteins. Installment of ALT by CF restored protection in the early
phases of M.tb infection, which was linked to rapid increases in ALT, but not in lung interstitial T cells. Also, adoptive transfer of T cells to the airway lumen of BCG-immunized animals also accelerated protection.

According to the news reporters, the researchers concluded: “This study thus provides novel evidence that unsatisfactory lung protection by parenteral BCG immunization is due to delayed ALT recruitment after pulmonary M.tb exposure.”

For more information on this research see: Mechanisms of delayed anti-tuberculosis protection in the lung of parenteral BCG-vaccinated hosts: A critical role of airway luminal T cells. Mucosal Immunology, 2012;5(4):420-431. Mucosal Immunology can be contacted at: Nature Publishing Group, 75 Varick St, 9TH Flr, New York, NY 10013-1917, USA. (Nature Publishing Group - http://www.nature.com/; Mucosal Immunology - http://www.nature.com/mi/)

Our news journalists report that additional information may be obtained by contacting C.N. Horvath, McMaster University, Dept. of Pathol & Mol Med, Hamilton, ON, Canada. (2012 Jul 24)

**Colorado State University, Fort Collins: Vaccination of guinea pigs using mce operon mutants of Mycobacterium tuberculosis**

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators publish new report on Vaccines. According to news reporting originating in Fort Collins, Colorado, by NewsRx journalists, researchers stated “The limited efficacy of the BCG vaccine for tuberculosis, coupled with emerging information suggesting that it is poorly protective against newly emerging strains of *Mycobacterium tuberculosis* such as the W-Beijing isolates, makes it paramount to search for more potent alternatives.”

The news reporters obtained a quote from the research by the authors from Colorado State University, “One such class of candidates is attenuated mutants derived from *M. tuberculosis* itself. We demonstrate here, in an initial short term assay, that mutants derived from disruption of the mce genes of the bacillus were highly protective in guinea pigs exposed by low dose aerosol infection with the virulent W-Beijing isolate SA161.”

According to the news reporters, the researchers concluded: “This protection was demonstrated by a significant reduction in the numbers of bacilli harvested from the lungs, and dramatic improvements in lung histopathology.”

For more information on this research see: Vaccination of guinea pigs using mce operon mutants of Mycobacterium tuberculosis. *Vaccine,*
Institute Pasteur, Paris: Strong immunogenicity and cross-reactivity of Mycobacterium tuberculosis ESX-5 type VII secretion: encoded PE-PPE proteins predicts vaccine potential

By a News Reporter-Staff News Editor at Vaccine Weekly – Investigators publish new report on Tuberculosis. According to news reporting originating in Paris, France, by NewsRx journalists, researchers stated “The genome of Mycobacterium tuberculosis (Mtb) encodes five type VII secretion systems, ESX-1 to ESX-5, most of which are associated with genes encoding PE/PPE proteins, named after their N-terminal Pro-Glu (PE) or Pro-Pro-Glu (PPE) motifs. Here, we describe the strong T cell immunogenicity of the ESX-5-encoded PE/PPE proteins, which share a large panel of cross-reactive CD4(+) epitopes with substantial numbers of their ESX-5-nonassociated PE/PPE homologs.”

The news reporters obtained a quote from the research by the authors from Institute Pasteur, “The immunogenicity of these numerous PE/PPE proteins is dependent on their export by a functional EccD(5), the predicted transmembrane channel of the ESX-5 secretion apparatus. The Mtb ?ppe25-pe19 mutant deleted for all ESX-5-associated pe and ppe genes, although highly attenuated in immunocompetent mice, remains able to induce immunity against the ESX-5-associated PE/PPE virulence factors, via cross-reactivity with their numerous homologs, and against the ESX-1 virulence factors ESAT-6/CFP-10.”

According to the news reporters, the researchers concluded: “The ?ppe25-pe19 strain is strongly protective against Mtb infection in mice and represents a potential antituberculosis vaccine candidate.”


Our news correspondents report that additional information may be obtained by contacting F. Sayes, Unite de Regulation Immunitaire et Vaccinologie, Institut Pasteur, Paris, France. (2012 Jul 04)
Cost effectiveness of interferon-gamma release assay for school-based tuberculosis screening

By a News Reporter-Staff News Editor at Life Science Weekly – Researchers detail new data in Tuberculosis. According to news reporting originating from Tokyo, Japan, by NewsRx editors, the researcher stated “To assess the cost effectiveness of school-based tuberculosis (TB) screening using QuantiFERON®-TB Gold In-Tube (QFT) versus the tuberculin skin test (TST) and chest x-ray examination (CXR). We constructed Markov models of first-year high-school and university students, using a societal perspective, and followed them up until the age of 80 years.”

Our news editors obtained a quote from the research by the author, “Three strategies (QFT, TST, and CXR) were modeled. All costs and clinical benefits were discounted at a fixed annual rate of 3%. In the base-case analyses of 16-year-old high-school students and 19-year-old university students, the QFT strategy yielded the greatest benefits at the lowest cost [in year 2009 values] (16-year-olds: $US627.89, 29.69835 quality-adjusted life-years [QALYs]; 19-year-olds: $US646.04, 29.15361 QALYs), compared with the TST strategy (16-year-olds: $US943.50, 29.69767 QALYs; 19-year-olds: $US998.62, 29.15288 QALYs) and the CXR strategy (16-year-olds: $US7286.24, 29.69532 QALYs; 19-year-olds: $US7305.19, 29.14911 QALYs). On one-way sensitivity analyses, the bacillus Calmette-Guerin (BCG) vaccination rate was not sensitive to the TST strategy. On probabilistic sensitivity analysis, the QFT strategy was the most cost effective, with a willingness-to-pay level of $US50?000/QALY gained. The QFT strategy provided the greatest benefits at the lowest cost for school-based TB screening. There appears to be little role for TST or CXR in screening of school populations.”

According to the news editors, the researchers concluded: “Current practices using either TST or CXR screening should be reconsidered on the basis of cost effectiveness.”

For more information on this research see: Cost effectiveness of interferon-gamma release assay for school-based tuberculosis screening. *Molecular Diagnosis & Therapy, 2012;16(3):181-90. Molecular Diagnosis & Therapy* can be contacted at: Adis International LTD, 41 Centorian Dr, Private Bag 65901, Mairangi Bay, Auckland 10, New Zealand.

The news editors report that additional information may be obtained by contacting A. Kowada, Kojiya Haneda Healthcare Service, Ota City Public Health Office, Tokyo, Japan.

Publisher contact information for the journal *Molecular Diagnosis & Therapy* is: Adis International LTD, 41 Centorian Dr, Private Bag 65901, Mairangi Bay, Auckland 10, New Zealand. (2012 Jul 03)
Vaccination of mice with recombinant bacille Calmette-Guerin harboring Rv1357c protects similarly to native BCG

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – Current study results on Tuberculosis have been published. According to news reporting originating in Mexico City, Mexico, by NewsRx journalists, researchers stated “Despite the availability of a Mycobacterium bovis bacille Calmette Guerin (BCG) vaccine, tuberculosis (TB) remains a global public health problem.”

The news reporters obtained a quote from the research by the authors, “In this study, we introduced the c-di-GMP phosphodiesterase gene Rv1357c, implicated in regulating mycobacterial replication within macrophages, into BCG Pasteur, and tested the resulting strain for capacity to serve as a vaccine against TB in a murine model.”

According to the news reporters, the researchers concluded: “Modified BCG was more phagocytosed than its parental strain, but halted bacterial replication, and protected against M. tuberculosis challenge similarity to unmodified BCG.”

For more information on this research see: Vaccination of mice with recombinant bacille Calmette-Guerin harboring Rv1357c protects similarly to native BCG. *International Journal of Tuberculosis and Lung Disease*, 2012;16(6):774-776. *International Journal of Tuberculosis and Lung Disease* can be contacted at: Int Union Against Tuberculosis Lung Disease (I U A T L D), 68 Boulevard Saint-Michel, 75006 Paris, France.

Our news correspondents report that additional information may be obtained by contacting M.A. Flores-Valdez, Inst Nacl Nutr & Ciencias Med Salvador Zubiran, Mexico City, DF, Mexico. (2012 Jul 02)

Tulane National Primate Research Center, Covington: The non-human primate model of tuberculosis

By a News Reporter-Staff News Editor at Vaccine Weekly – Current study results on Tuberculosis have been published. According to news reporting from Covington, Louisiana, by NewsRx journalists, researchers stated “Non-human primates (NHPs) are used to model human disease owing to their remarkably similar genomes, physiology, and immune systems. Recently, there has been an increased interest in modeling tuberculosis (TB) in NHPs.”

The news correspondents obtained a quote from the research by the authors from Tulane National Primate Research Center, “Macaques are
susceptible to infection with different strains of Mycobacterium tuberculosis (Mtbc), producing the full spectrum of disease conditions, including latent infection, chronic progressive infection, and acute TB, depending on the route and dose of infection. Clearly, NHPs are an excellent model of human TB. While the initial aim of the NHP model was to allow preclinical testing of candidate vaccines and drugs, it is now also being used to study pathogenesis and immune correlates of protection. Recent advances in this field are discussed in this review.”

According to the news reporters, the researchers concluded: “Key questions such as the effect of hypoxia on the biology of Mtbc and the basis of reactivation of latent TB can now be investigated through the use of this model.”


Our news journalists report that additional information may be obtained by contacting D. Kaushal, Tulane Natl Primate Res Center, Div Comparat Pathol, Covington, LA 70433, United States. (2012 Jun 27)

**Colombia National University, Bogota: Peptides derived from Mycobacterium tuberculosis Rv2301 protein are involved in invasion to human epithelial cells and macrophages**

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators discuss new findings in Tuberculosis. According to news originating from Bogota, Colombia, by NewsRx correspondents, researchers stated “The specific function of putative cut2 protein (or CFP25), encoded by the gene from H37Rv, has not been identified yet. The aim of this study was to assess some of CFP25 characteristics and its possible biological role in H37Rv invasion process to target cells.”

Our news journalists obtained a quote from the research by the authors from Colombia National University, “Molecular assays indicated that the gene encoding Rv2301 is present and transcribed in complex strains. The presence of Rv2301 protein over the bacilli surface was confirmed by Western blot and immunoelectron microscopy analyses, using goats sera inoculated with synthetic peptides derived from Rv2301 protein. Receptor-ligand binding assays with carcinomic human alveolar basal epithelial cells (A549) and macrophages derived from human histolytic lymphoma monocytes (U937) allowed us to identify five high activity binding peptides (HABPs) in both cell lines, and two additional
HABPs only in A549 cells. U937 HABPs binding interactions were characterized by saturation assays, finding dissociation constants (d) within the nanomolar range and positive cooperativity (H > 1). Inhibition assays were performed to assess the possible biological role of Rv2301 identified HABPs, finding that some of them were able to inhibit invasion at a 5 μM concentration, compared with the cytochalasin control. On the other hand, HABPs, and especially HABP 36507 located at the N-terminus of the protein, facilitated the internalization of fluorescent latex beads into A549 cells.

According to the news editors, the researchers concluded: “These findings are of vital importance for the rational selection of Rv2301 HABPs, to be included as components of an antituberculosis vaccine.”

For more information on this research see: Peptides derived from Mycobacterium tuberculosis Rv2301 protein are involved in invasion to human epithelial cells and macrophages. Amino Acids, 2012;42(6):2067-2077. Amino Acids can be contacted at: Springer, 233 Spring St, New York, NY 10013, USA. (Springer - www.springer.com; Amino Acids - http://www.springerlink.com/content/0939-4451/)

The news correspondents report that additional information may be obtained from M. Ocampo, Colombia National University, Bogota, Colombia. (2012 Jun 26)

Indian Institute of Science, Bangalore: Distinct mechanisms of DNA repair in mycobacteria and their implications in attenuation of the pathogen growth

By a News Reporter-Staff News Editor at Biotech Week – Data detailed on Tuberculosis Vaccines have been presented. According to news reporting originating from Bangalore, India, by NewsRx correspondents, researchers stated “About a third of the human population is estimated to be infected with Mycobacterium tuberculosis. Emergence of drug resistant strains and the protracted treatment strategies have compelled the scientific community to identify newer drug targets, and to develop newer vaccines.”

Our news editors obtained a quote from the research by the authors from the Indian Institute of Science, “In the host macrophages, the bacterium survives within an environment rich in reactive nitrogen and oxygen species capable of damaging its genome. Therefore, for its successful persistence in the host, the pathogen must need robust DNA repair mechanisms. Analysis of M. tuberculosis genome sequence revealed that it lacks mismatch repair pathway suggesting a greater role for other DNA repair pathways such as the nucleotide excision repair, and base excision repair pathways. In this article, we summarize the
“outcome of research involving these two repair pathways in mycobacteria focusing primarily on our own efforts.”

According to the news editors, the researchers concluded: “Our findings, using Mycobacterium smegmatis model, suggest that deficiency of various DNA repair functions in single or in combinations severely compromises their DNA repair capacity and attenuates their growth under conditions typically encountered in macrophages.”


The news editors report that additional information may be obtained by contacting K. Kurthkoti, Dept. of Microbiology and Cell Biology, Indian Institute of Science, Bangalore 560012, India. (2012 Jun 13)

**Pohang University of Science and Technology (POSTECH): Mtb32 is a promising tuberculosis antigen for DNA vaccination in pre- and post-exposure mouse models**

By a News Reporter-Staff News Editor at Biotech Week – A new study on Gene Therapy is now available. According to news originating from Pohang, South Korea, by NewsRx correspondents, researchers stated “Identification of antigens that provide protective immunity via prophylactic and therapeutic vaccination against *Mycobacterium tuberculosis* is critical for the development of subunit vaccines for tuberculosis (TB). In this study, we performed a head-to-head comparison of seven well-known TB antigens delivered by DNA vaccine, and evaluated their respective immunogenicities and protective efficacies in pre-and post-exposure mouse models.”

Our news journalists obtained a quote from the research by the authors from the Pohang University of Science and Technology (POSTECH), “All TB antigens were designed as a chimeric fusion with Flt3-L to enhance antigen-specific T-cell immunity upon vaccination. Prophylactic vaccination with the Flt3L (F)-Mtb32 DNA vaccine elicited significant protection in both the spleen and lungs against *M. tuberculosis* challenge, comparable to the Bacillus Calmette-Guerin vaccine. F-Ag85A and F-Mtb32 DNA vaccines, in combination with chemotherapy, reduced the bacterial burden to undetectable levels in the lungs of all mice infected with *M. tuberculosis*.”

According to the news editors, the researchers concluded: “These data collectively indicate that the F-Mtb32 DNA vaccine confers the most efficient protective immunity that suppresses bacterial growth in the active or latent status of M.”
CHAPTER 8  VACCINES


The news correspondents report that additional information may be obtained from S.S. Ahn, Division of Molecular and Life Sciences, Postech Biotech Center, Pohang University of Science and Technology, Pohang, South Korea. *(2012 Jun 13)*

**Patent Issued for Mycobacterial Mutants Affecting Host Apoptosis**

By a News Reporter-Staff News Editor at AIDS Weekly – From Alexandria, Virginia, NewsRx journalists report that a patent by the inventors Jacobs, Jr., William R. (Pelham, NY); Porcelli, Steven A. (Bronx, NY); Briken, Volker (Burtonsville, MD); Braunstein, Miriam (Chapel Hill, NC), filed on January 12, 2006, was cleared and issued on March 12, 2013.

The patent’s assignee for patent number 8394388 is Albert Einstein College of Medicine of Yeshiva University (Bronx, NY).

News editors obtained the following quote from the background information supplied by the inventors: “(1). Field of the Invention

“The present invention generally relates to mutants of Mycobacterium tuberculosis. More particularly, the invention is directed to M. tuberculosis mutants that affect host cell apoptosis.

“(2). Description of the Related Art

“References


necrosis in monocytes from patients with tuberculosis and healthy control subjects. J Infect Dis 189: 2120-2128.


“Mycobacterium tuberculosis, the etiological agent of tuberculosis, is responsible for more deaths each year than any other single pathogen (Corbett et al., 2003). The emergence of drug resistant strains of M. tuberculosis and HIV co-infection has contributed to the worsening impact of this disease. The pathogen exhibits extraordinary capacity to subvert and resist bactericidal responses of its infected host. M. tuberculosis virulence has been associated with its initial survival within macrophages by evading the host response in many different ways. The tubercle bacilli reside in endocytic vacuoles (Armstrong and Hart, 1975; Clemens and Horwitz, 1995), which fail to fuse to lysosomes due to M. tuberculosis mediated retention of a host protein TACO on the membrane of these vacuoles (Gatfield and Pieters, 2000). Similarly, M. tuberculosis can downregulate the expression of MHC-II (Noss et al.,
and costimulatory molecules (Stenger et al., 1998; Wadde et al., 1995), modulate the cytokine environment in its vicinity (VanHeyningen et al., 1997) and inhibit apoptosis of the host cell (Keane et al., 1997). Although M. tuberculosis evades many host responses to maintain itself in a habitable environment, the bacterial effectors mediating such effects need to be delineated. On invading the host cell, a capsule-like structure is formed outside the membrane and the cell wall of the tubercle bacilli (Daffe and Etienne, 1999), and this interface contains important surface proteins involved in the pathogenesis and immune responses to TB. The secreted and cell envelope associated proteins, located at the interface between the mycobacterium and its eukaryotic host mediate host-pathogen interactions. Therefore, such proteins are candidate virulence factors and warrants further study (Finlay and Falkow, 1997).

“The exported and secreted proteins of M. tuberculosis have been proposed to play a role in virulence and indeed contribute to the immune responses to TB (Abou-Zeid et al., 1988; Johansen et al., 1996; Nagai et al., 1991; Zhang et al., 1992). Research on several bacterial pathogens has revealed that the majority of virulence factors are secreted (Finlay and Falkow, 1997). Studies have also emphasized the importance of the secreted and exported proteins of M. tuberculosis in the generation of a protective immune response. The most striking demonstration of this property comes from experiments in which mice or guinea pigs were immunized with extracellular proteins and significant protective immunity elicited (Andersen, 1994; Hubbard et al., 1992; Pal and Horwitz, 1992; Roberts et al., 1995). Recently, the exported ERP (exported repetitive protein) protein was shown to contribute to the virulence of M. tuberculosis (Berthet et al., 1998). Likewise, superoxide dismutase (SOD), a culture filtrate component was shown to be associated with virulence by interfering with host apoptosis (Edwards et al., 2001). While many secreted proteins have been studied, the study of the cell surface proteins is still lacking due to technological constraints in isolating samples of membrane proteins.

“Host cell apoptosis has been implicated in Mycobacterium spp. virulence and protective immunity (e.g., Aleman et al., 2002; Balcewicz-Sablinska et al., 1998; Ciaramella et al., 2000; Duan et al., 2001, 2002; Duarte et al., 1997; Eddine et al., 2005; Grode et al., 2005; Keane et al., 2000; Kornfeld et al., 1999; Lopez et al., 2003; Protalés-Perez et al., 2002; Sly et al., 2003; Spira et al., 2003). However, there is need for more information on Mycobacterium host genes that affect host cell apoptosis. The present invention addresses that need.”
mutants that do not express the proteins are useful for inducing immunity to virulent mycobacteria.

"Thus, the present invention is directed to recombinant mycobacteria having a mutation in an nlaA gene. The mutation in these mycobacteria increases the ability of the mycobacteria to induce apoptosis of a mammalian macrophage infected by the mycobacteria.

"The invention is also directed to recombinant mycobacteria having a mutation in a nuoG gene. The mutation in these mycobacteria also increases the ability of the mycobacteria to induce apoptosis of a mammalian macrophage infected by the mycobacteria.

"The present invention is additionally directed to isolated and purified nlaA proteins from a mycobacterium. These nlaA proteins have an amino acid sequence at least 85% identical to SEQ ID NO:1. These nlaA proteins prevent the mycobacterium from inducing apoptosis in a mammalian macrophage.

"The invention is further directed to isolated and purified nuoG proteins from a mycobacterium. These nuoG proteins have an amino acid sequence at least 85% identical to SEQ ID NO:3. These nuoG proteins also prevent the mycobacterium from inducing apoptosis in a mammalian macrophage.

"The present invention is also directed to isolated and purified nucleic acids comprising a recombinant nlaA gene having a nucleotide sequence at least 85% identical to SEQ ID NO:2.

"Additionally, the invention is directed to isolated and purified nucleic acids comprising a recombinant nuoG gene having a nucleotide sequence at least 85% identical to SEQ ID NO:4.

"The current invention is further directed to methods of inducing an immune response in a mammal. The methods comprise inoculating the mammal with any of the above-described mycobacteria.

"The invention is additionally directed to methods of making a recombinant mycobacterium. The methods comprise eliminating expression of the nlaA gene in the mycobacterium.

"The present invention is further directed to additional methods of making a recombinant mycobacterium. The methods comprise eliminating expression of the nuoG gene in the mycobacterium."

Patent Issued for Bioassay and Peptides for Use Therein

By a News Reporter-Staff News Editor at Life Science Weekly – According to news reporting originating from Alexandria, Virginia, by NewsRx journalists, a patent by the inventors Sharma, Ram P. (Southampton, GB); Mehrotra, Amit P. (Southampton, GB), filed on December 22, 2006, was cleared and issued on February 12, 2013.

The assignee for this patent, patent number 8372412, is Rapid Biosensor Systems Limited (Cambridge, GB).

Reporters obtained the following quote from the background information supplied by the inventors: “Tuberculosis is an infection caused by the bacterium Mycobacterium tuberculosis. Tuberculosis is a major problem in many countries, especially in the developing world, and is on the increase in many developed countries. Whilst tuberculosis often presents as a lung infection, it can also affect other parts of the body such as lymph nodes, skin and bones.

“Diagnosis of tuberculosis, so allowing treatment, is the major weapon against the spread of the disease. Diagnosis may be made using a combination of clinical signs, sputum cultures, chest X-ray, histology of tissue and bronchial lavage fluid, and the use of the tuberculin skin test (also known as the Purified Protein Derivative Standard, or PPD skin test) such as the Mantoux test and Heaf Test. The tests rely on an immune reaction to M. tuberculosis protein, revealing the presence of antibodies of M. tuberculosis in the patient’s blood.

“The tests require administration of an immunological challenge to a patient, and a subsequent follow-up examination to determine the test result. These steps make the test difficult to apply for mass screening operations.

“The present invention attempts to provide a solution to some of these problems.”

In addition to obtaining background information on this patent, NewsRx editors also obtained the inventors’ summary information for this patent: “In a broad first aspect, the invention comprises a peptide of fewer than 18 amino acids comprising the sequence NSPAX where X is Methionine (SEQ ID 18), Leucine (SEQ ID 17), Alanine (SEQ ID 15) or Valine (SEQ ID 10) wherein the peptide is capable of binding to an antibody raised against the peptide GRDIKVQFQSGGNNSPAV (SEQ ID 11). In particularly preferred embodiments, the peptide binds to such an antibody.

“In practical terms, such an antibody would be raised against this peptide (SEQ ID 11) supplemented by an additional C amino acid at the C-terminal end, i.e. raised against GRDIKVQFQSGGNNSPAVC (SEQ ID 27).
“In a second aspect, therefore, the peptide comprises up to 6 additional amino acids at the C and/or N terminal end of the sequence NSPAX (SEQ ID 28).

“Preferably, therefore, the peptide of the first or second aspect comprises the sequence NNSPAX (SEQ ID 29), and more preferably the peptide comprises the sequence NNSPAV (SEQ ID 14).

“In a further preferred aspect, the peptide comprises the sequence SGGNNSPAX (SEQ ID 26), where X is Methionine (SEQ ID 18), Leucine (SEQ ID 17), Alanine (SEQ ID 15) or Valine (SEQ ID 10).

“In any aspect of the invention it is preferred that the peptide is not GRIKQFQSGGNNSPAV (SEQ ID 11).

“Also in any aspect of the invention it is preferable that the peptide consists of the sequence SGGNNSPAX (SEQ ID 26), where X is Methionine (SEQ ID 18), Leucine (SEQ ID 17), Alanine (SEQ ID 15) or Valine (SEQ ID 10).

“Also in any peptide of the invention it is preferable that X is Methionine (SEQ ID 18), Leucine (SEQ ID 17) or Alanine (SEQ ID 15). Especially preferred are peptides wherein X is Methionine (SEQ ID 18) or Alanine (SEQ ID 15). These particular substitutions are found to have particularly good Leu-heat stability, making them suitable for field use in hot countries.

“Particularly preferred peptides according to any aspect of the invention further comprise a label. The use of a labelled peptide facilitates its use in an assay for the detection of Mycobacterium tuberculosis. Suitable labels might include radio-labels (e.g. by the addition of a radioactive species or the substitution of one or more atoms of the peptide by its radioactive equivalent) thereby allowing the presence or concentration of the peptide, or a complex comprising the peptide, to be readily detected, e.g. by scintillation counting or the like. Other labels such as an enzyme-mediated chromogenic label might also be used. Particularly preferred labels would be fluorescent labels, including binding of the peptide to a fluorescent protein. A fluorescent label such as Alexa Fluor (e.g. Alexa Fluor 633) is, however, particularly suitable.

“Preferably also, any of the above peptides are in an isolated form, i.e. essentially free of proteins of native (e.g. bacterial, fungal or mammalian) origin.

“Peptides described above have application in assays for the detection of Mycobacterium tuberculosis.

“Included within the scope of the invention is a nucleotide sequence encoding any of the above peptides. Such a sequence has application in the biosynthesis of the peptides of the present invention.

“Included within the scope of the invention is an antibody raised against SEQ ID 11. The antibodies of the invention may be polyclonal or monoclonal, or may be recombinant antibodies, such as chimeric antibodies wherein the murine constant regions on light and heavy chains
are replaced by human sequences, or CDR-grafted antibodies wherein only the complementary determining regions are e.g. of murine origin. Antibodies of the invention may also be human antibodies prepared, for example, by immunization of transgenic animals capable of producing human antibodies (see, for example, PCT Application No. WO93/12227).

“Also included within the scope of the invention is a displacement ELISA (Enzyme-Linked Immuno-Sorbent) assay for determining the presence of Mycobacterium tuberculosis comprising a peptide as described herein. A suitable procedure for carrying out such an assay will be described below. Preferably, such a displacement assay further comprises an antibody raised against SEQ ID 11, or a fragment of such an antibody having affinity for SEQ ID 11.

“Also included within the scope of the invention is an ELISA assay for determining the presence of Mycobacterium tuberculosis comprising an antibody raised against SEQ ID 11, or a fragment of such an antibody having affinity for SEQ ID 11.

“Further included within the scope of the invention is a displacement assay for determining the presence of Mycobacterium tuberculosis comprising a peptide according to the invention and a peptide according to SEQ ID 11.”


By a News Reporter-Staff News Editor at Biotech Week – A patent application by the inventors Benjamin, Rodney L. (Vancouver, WA); Keller, Anthony L. (Medford, OR); Varelman, Jeffrey (Moyie Springs, ID), filed on April 27, 2012, was cleared for further review on October 25, 2012, according to news reporting originating from Washington, D.C., by NewsRx correspondents.

Patent serial number 458907 is assigned to Biogenic Innovations, LLC.

The following quote was obtained by the news editors from the background information supplied by the inventors: “Embodiments of the invention relate generally to formulations comprising dimethyl sulfoxide
(DMSO) alone or in combination with methylsulfonylmethane (MSM) to treat infectious diseases. Certain embodiments relate to sensitizing drug-resistant microbes to drugs. Several formulations disclosed herein are useful for treating drug-resistant tuberculosis.

“Infectious diseases are diseases caused by pathogenic microbial agents, including viruses, bacteria, fungi, parasites, and prions, among others. The pathogenic agents may be primary or opportunistic pathogens. Primary pathogens cause infection as a direct result of their virulence, while opportunistic pathogens typically require a compromised host defense system to produce an infection. Examples of common infectious diseases include HIV/AIDS, measles, tetanus, tuberculosis, malaria, upper and lower respiratory infections, and hepatitis. While modern medicine has reduced the prevalence of many infectious diseases, particularly in developed countries, they still account for a large degree of morbidity and mortality.

“Tuberculosis, malaria, HIV/AIDS, and diarrhoeal diseases are the leading killers among the infectious diseases. Tuberculosis (tubercle bacillus) is caused by mycobacteria, primarily Mycobacterium tuberculosis. Tuberculosis primarily infiltrates the lungs (pulmonary tuberculosis), but has also been documented as affecting the central nervous system, the lymphatic system, and the circulatory system, among others. Other mycobacteria may also cause tuberculosis, for example, Mycobacterium bovis, Mycobacterium africanum, Mycobacterium canetti, and Mycobacterium microti. However, these species are less common in humans.

“Dimethyl sulfoxide (DMSO; (CH$_3$)$_2$(SO)) is a polar, aprotic solvent widely used as a solvent. It is frequently used in various chemical and biological reactions and as a cryoprotectant for cell storage. The strong unpleasant odor of DMSO (or metabolites), among other side effects, has adversely impacted the use of DMSO in medical applications.

“Methylsulfonylmethane (MSM; (CH$_3$)$_2$SO$_2$), also known as dimethyl sulfone, is an organosulfur compound that is a metabolite
of DMSO and certain sulfur-containing amino acids. MSM has been marketed primarily as a dietary supplement.”

In addition to the background information obtained for this patent application, NewsRx journalists also obtained the inventors’ summary information for this patent: “There exists a need for an effective and easily administered therapy against infectious diseases, particularly those that are developing or have developed some degree of antimicrobial resistance.

“Tuberculosis classically presents as a chronic cough with blood-tinged sputum, fever, night sweats, and weight loss. Tuberculosis may also infect other organ systems, leading to a diverse set of symptoms. Diagnosis of tuberculosis is typically achieved through radiology, tuberculin skin test, blood tests, as well as microscopic examination and microbiological culture of bodily fluids. Current tuberculosis treatment requires long courses of multiple antibiotics. One course of treatment for tuberculosis is isoniazid, rifampicin, pyrazamide, and ethambutol for about two months, followed by only isoniazid and rifampicin for a further four months. The patient is considered cured at six months (although there is still a relapse rate of 2 to 3%). Latent tuberculosis therapy involves six to nine months of isoniazid alone.

“Drug-resistant tuberculosis includes tuberculosis that is resistant to at least one anti-tuberculosis drug. Multidrug-resistant tuberculosis (MDR tuberculosis) includes tuberculosis that is resistant to more than one first line anti-tuberculosis drug.

“In several embodiments, formulations comprising DMSO alone or DMSO in combination with MSM, and a therapeutic agent are provided to treat tuberculosis, including drug-resistant tuberculosis.

“In several embodiments, formulations comprising DMSO alone or in combination with MSM are provided as an inhalant to treat drug-resistant tuberculosis. In some embodiments, formulations comprising DMSO alone or in combination with MSM are formulated as solids, while in several other embodiments, formulations comprising DMSO and MSM are formulated as liquids. In some embodiments, the formulations are consumed orally to treat drug-resistant tuberculosis, while in some other embodiments, the formulations are applied topically. In several embodiments, drug-resistant diseases other than tuberculosis are treated with formulations comprising DMSO alone or in combination with MSM.

“In yet other embodiments, non-drug-resistant diseases are treated with formulations comprising DMSO alone or DMSO in combination with MSM. In such embodiments, DMSO or a combination of DMSO and MSM is combined with a therapeutic agent to enhance the effects of the therapeutic agent.

“In several embodiments, subjects with drug-resistant tuberculosis are treated with a DMSO formulation, an MSM formulation, or
combination of DMSO and MSM, together with isoniazid, rifampicin, pyrazinamide, and ethambutol for a time period (e.g., two weeks-two months), then isoniazid and rifampicin alone for another time pe-
riod (e.g., four weeks-four months). In some embodiments, subjects
with drug-resistant tuberculosis are treated with a DMSO formulation,
alone or in combination with MSM, together with isoniazid, rifampicin,
pyrazinamide, and/or ethambutol. In one embodiment, DMSO alone or
in combination with MSM formulations sensitize drug-resistant tuber-
culosiss to antibiotics, and therefore isoniazid, rifampicin, pyrazinamide,
and/or ethambutol become lethal to sensitized tuberculosis bacteria.
In other embodiments, subjects with drug-resistant tuberculosis are

treated with a DMSO formulation, alone or in combination with MSM,
together with one or more of the following: isoniazid, rifampicin, pyraz-
imamide, ethambutol, lamprene, mycobutin, seromycin, streptomycin,
myambutol, priftin and rifamate.

“In several embodiments, a system for treating drug-resistant tuber-
culosiss is provided. In one embodiment, the system comprises a ther-
apeutic agent and DMSO alone, or a combination of DMSO and MSM.
The concentration of the DMSO and/or MSM ranges from about 15% to
about 95% in a total volume of about two to about six milliliters. The
therapeutic agent is selected from one or more compounds selected from
the group consisting of: isoniazid, rifampicin, pyrazinamide, and etham-
butol. In one embodiment, the system includes an inhalant device,
wherein the inhalant device is constructed from a material adapted for
contacting DMSO and/or MSM and wherein the inhalant device is con-
figured for administering the formulation to a subject. The inhalant
device is configured to deliver the formulation to directly contact drug-
resistant tuberculosis bacteria in the subject’s lung tissue. In one em-
bodyment, the DMSO and/or MSM sensitizes the drug-resistant tuber-
culosiss bacteria to at least one of isoniazid, rifampicin, pyrazinamide, and
ethambutol to generate sensitized tuberculosis bacteria. The sensitized
tuberculosis bacteria are lethally inhibited by exposure to least one of
isoniazid, rifampicin, pyrazinamide, and ethambutol.

“In several embodiments, the invention comprises a method for
treating drug-resistant tuberculosis. In one embodiment, the method
comprises providing a formulation comprising a therapeutic agent and
DMSO alone, or a combination of DMSO and MSM. In one embark-
dent, the concentration of DMSO and/or MSM ranges from about 15%
to about 95% in a total volume of about two to about six milliliters. In
one embodiment, the therapeutic agent is selected from one or more
compounds selected from the group consisting of: isoniazid, rifampicin,
pyrazinamide, and ethambutol. In some embodiments, the method fur-
ther includes providing an inhalant device and administering the for-
mulation via the inhalant device to a subject having drug-resistant tu-
berculosis. The inhalant device is configured to deliver the formula-
tion to directly contact drug-resistant tuberculosis bacteria in the subject’s lung tissue. The drug-resistant tuberculosis bacteria are sensitized (with the DMSO) to at least one of isoniazid, rifampicin, pyrazamide, and ethambutol to generate sensitized tuberculosis bacteria, and lethally inhibited by at least one of isoniazid, rifampicin, pyrazamide, and ethambutol. In one embodiment, a method of treating drug-resistant tuberculosis in the field is provided. In one embodiment, a test for tuberculosis is performed within hours of seeing a subject, a test for INH and RRP is given within hours, the subject is treated with DMSO alone or in combination with MSM (e.g., intravenously), and then treated with a inhaled formulation of DMSO alone or in combination with MSM, provided with mask and trained to use an inhalant device in the field. Methods of treating drug-resistant diseases other than tuberculosis with DMSO alone or in combination with MSM are also provided according to several embodiments.

"In several embodiments, the invention comprises a formulation for sensitizing drug-resistant microorganisms to a therapeutic agent. In one embodiment, the formulation comprises a therapeutic agent and DMSO alone or a combination of DMSO and MSM. The concentration of the DMSO and/or MSM ranges from about 15% to about 95% in a total volume or weight of the formulation. The DMSO or combination of DMSO and MSM is configured for contacting a drug-resistant microbe, wherein the drug-resistant microbe is resistant to the therapeutic agent. After contact with the DMSO or combination of DMSO and MSM the drug-resistant microbes are sensitized to the therapeutic agent and are transformed into sensitized microbes, wherein the sensitized microbes are inhibited by the therapeutic agent. The drug-resistant microorganism contacted with DMSO or a combination of DMSO and MSM includes, but is not limited to, tuberculosis, malaria, MRSA and streptococcus.

"In some embodiments, the inhalant device is an inhaler, nebulizer or ventilator. According to several embodiments, the inhalant device is constructed from a material adapted for contacting DMSO and/or MSM without degrading into the subject’s airway, trachea, bronchial tubes, or lung tissue, or without rupturing. In one embodiment, the formulation is pre-dosed in the inhalant device.

"In some embodiments, the total formulation volume is about 2-8 ml, e.g., about 3 ml for an inhaler or 7 ml for a nebulizer. According to some embodiments, the formulations described herein also comprise urea. Urea may be provided in a dose about 1 mg to about 10 grams or higher in several embodiments. In one embodiment, formulations disclosed herein are configured for delivery at least three times daily.

"In one embodiment, the formulation comprises a daily dose of: rifampicin in an amount ranging from about 500 mg to about 700 mg, isoniazid in an amount ranging from about 200 mg to about 400 mg,
pyrazinamide in an amount ranging from about 2.0 g to about 3.0 g, and ethambutol in an amount ranging from about 1.0 g to about 2.0 g. In another embodiment, the formulation comprises a total daily dose or a daily dose per kg of body weight of: rifampicin in an amount ranging from about 1 mg to about 100000 mg, isoniazid in an amount ranging from about 2 mg to about 10000 mg, pyrazinamide in an amount ranging from about 0.02 g to about 10.0 g, and ethambutol in an amount ranging from about 0.01 g to about 10.0 g. In one embodiment, the formulation comprises a daily dose of about 600 mg rifampicin, 300 mg isoniazid, 2.4 g pyrazinamide, and 1.2 g ethambutol. Streptomycin or other therapeutic agents are included in several embodiments. In one embodiment, streptomycin is provided in a total daily dose or a daily dose per kg of body weight of about 10 mg to about 200 g.

“A system according to any one of the preceding claims, further comprising a pretreatment composition, wherein the pretreatment composition comprises about 50 mg to about 60 mg DMSO and is configured for intravenous administration to the subject.

“In several embodiments, wherein the inhalant device is configured to generate particles of the formulation that range in size from about 0.5 micron (µ.m) to about 5 µ.m.

“In one embodiment, the invention comprises a kit for treating drug-resistant tuberculosis, comprising: a system according to any one of the embodiments described herein; and instructions for administering the formulation via the inhalant device at least three times daily. The kit may also include a mask, a battery charger and/or a battery pack.”


**Patent Issued for Compositions and Methods for Stabilizing Lipid Based Adjuvant Formulations Using Glycolipids**

By a News Reporter-Staff News Editor at Biotech Week – From Alexandria, Virginia, NewsRx journalists report that a patent by the inventors Davidsen, Jesper (Solroed Strand, DK); Andersen, Peter (Brenshoej, DK); Rosenkrands, Ida (Vaeloese, DK), filed on May 21, 2010, was cleared and issued on October 2, 2012.

The patent’s assignee for patent number 8277823 is Statens Serum Institut (Copenhagen S, DK).
News editors obtained the following quote from the background information supplied by the inventors: “The present invention relates to liposome formulations that are physically stable. In particular the present invention relates to steric stabilization of cationic liposomes by an unique film method whereby glycolipids are incorporated into the liposomes. The stabilized liposomes can be used either as an adjuvant for antigenic components or as a drug delivery system. In particular the invention relates to vaccines with adjuvants in aqueous media for immunization, where the final product is stable.

“The first vaccines used in humans to produce immunity against infectious diseases consisted of live, attenuated pathogens. The attenuated forms were either naturally occurring closely related organisms or obtained through serial passages in culture. One example is tuberculosis that is combated by vaccination with attenuated but living strains of Mycobacterium bovis (BCG vaccine). However, the efficacy of this procedure does not always provide satisfactory resistance to human tuberculosis in every population. There is therefore a need for new and efficient ways of producing immunity against tuberculosis and other infectious diseases. A particular promising approach has been to isolate and use recombinant forms of immunodominant antigens such as the early secretory antigenic target (ESAT-6) and antigen 85 (Ag85) as a vaccine. These vaccines are well-defined and side-reactions are minimized. Unfortunately, many highly purified substances, e.g., purified recombinant proteins, are not very immunogenic and do not produce an effective immune response protective against the real infectious disease. This fact is well known and many attempts have been made to increase the immunogenic properties by combining the substance in question with so-called adjuvants. Depending on the pathogen, protection may require that either a humoral or a cell-mediated response predominate. The development of a specific kind of immune response (humoral or cell-mediated) can be determined by the choice of adjuvant.

“Protective immunity against an intracellular pathogen like M. tuberculosis requires a cell-mediated immune response, and a suitable adjuvant for a subunit vaccine directed against TB should enhance a Th1 response (Lindblad et. al., 1997). It is generally believed that antibodies do not play an important role in immunity to TB whereas cell-mediated release of IFN-gamma (interferon gamma) is the most important cytokine involved in protection (Collins & Kaufmann, 2001).

“A large number of adjuvants that induce a cell mediated immune response have been suggested but in general without any being ideal in all respects.

“One particular effective type of adjuvant that promotes a cell-mediated immune response is quaternary ammonium compounds, such as dimethyldioctadecylammonium (DDA) (Hilgers and Snippe, 1992). DDA is a synthetic amphiphile comprising a hydrophilic positively
charged dimethylammonium head-group and two long hydrophobic alkyl chains. In an aqueous environment DDA self-assemble to form vesicular bilayers similar to liposomes made from natural phospholipids. Combinations of DDA and other immunomodulating agents have been described. Administration of Arquad 2HT, which comprises DDA, in humans was promising and did not induce apparent side effects (Stanfield et. al., 1973). An experimental vaccine based on culture filtrate proteins from M. tuberculosis and DDA generated a protective immune response against TB in mice (Andersen, 1994). Vaccination of mice with a fusion protein of M. tuberculosis proteins ESAT-6 and Ag85B, and DDA/MPL as adjuvant, provides protection similar to that obtained by BCG vaccination (Olsen et. al., 2001). These studies demonstrate that, in contrast to e.g., alum, DDA-based adjuvants are able to induce a protective immune response against TB in mice. Moreover, DDA has been used as an adjuvant for a DNA vaccine against pseudorabies virus leading to enhanced T-cell responses is and antiviral immunity (van Rooij et. al., 2002).

“Addition of TDM (alpha,alpha’-trehalose 6,6’-dimycolate) oil emulsions to DDA solutions was investigated by Woodard et. al. (1980) as adjuvants for Brucella abortus vaccines based on heat killed bacteria. Neither DDA alone nor the mixtures of DDA and TDM was able to induce protection. In another study of a Brucella abortus subunit vaccine based on a soluble protein extract, a combination of DDA and TDM was also used as adjuvant (Dzata et. al., 1991), and the mixture was found to enhance the immune responses (antibody levels, skin test response, and IL-2 levels) observed compared to DDA alone. Holten-Andersen et. al. (2004) studied a combination of DDA liposomes and a suspension of TDB (alpha,alpha’-trehalose 6,6’-dibehenate), and administration of the ESAT-6 antigen with this adjuvant mixture was found to induce a strong protective immune response against tuberculosis which was significantly higher than when ESAT-6 was administered in DDA liposomes.

“Unfortunately, suspensions of amphiphilic quaternary ammonium compounds such as DDA alone or mixtures of DDA and MPL, TDM or TDB as described above are physically unstable and prolonged storage at 4.degree. C. is not possible without the occurrence of aggregation and precipitates. As precipitation will prevent clinical use of the formulation, the lack of stability of DDA formulations has so far been a major obstacle for any application in humans.

“In Great Britain Pat. No. 2147263-A, Takahashi and Tsujii describe stabilization of vesicles from quaternary ammonium compounds by mixing two quaternary ammonium compounds together or adding various detergents to the quaternary ammonium compound.
“In U.S. Pat. No. 5,026,546, Hilgers and Weststrate describe stabilization of an adjuvant suspension of DDA with a polymer of acrylic acid crosslinked with polyallyl sucrose.

“Lyophilization of cationic lipid-protamin-DNA complexes for transfection of cells was described by Li et. al. (2000). The effect of adding traditional cryoprotectants like monosaccharides and disaccharides was evaluated, and disaccharides were found to preserve particle size better than monosaccharides. Also non-lyophilized lipid-protamin-DNA complexes stabilised with 10% sucrose maintained a stable particle size after 8 weeks storage at 4° C., but the transfection efficiency was higher in lyophilized than in non-lyophilized samples.

“U.S. Pat. No. 5,922,350 describes a method for extending storage of liposomes e.g., based on phospholipids by adding sugars like trehalose and sucrose before the dehydration of the liposomes. Furthermore, the patent describes that delayed loading of the preformed, stored liposomes is feasible by a combination of concentration gradients and the dehydration-rehydration process.

“Liposomes of phospholipids for drug delivery (fusogenic liposomes) stabilized with a polyethylene glycol derivative are described in WO 96/10392. Another drug delivery formulation described in WO 02/03959 discloses a formulation comprising cationic liposomes and neutral liposomes where each liposome group either carries the same or different therapeutic agents.

“Preferred methods for making liposome preparations are described by Bangham (Bangham et. al., 1965). This preparation involves dissolving phospholipids in an organic solvent which is then evaporated to dryness leaving a thin lipid film on the inside of the test tube. The dry lipid film is then hydrated in an appropriate amount of aqueous phase and the mixture is heated to above the phase transition temperature of the lipids and allowed to ‘swell’. The resulting liposomes which consist of multilamellar vesicles (MLV’s) are dispersed by shaking the test tube. The lipids constituting the vesicular bilayer membranes are organized such that the hydrophobic hydrocarbon ‘tails’ are oriented toward the center of the bilayer while the hydrophilic ‘heads’ orient towards the in- and outside aqueous phase, respectively. This preparation provides the basis for producing unilamellar vesicles (UV) by methods such as sonication (Papahadjopoulos et. al., 1967) or extrusion as described by Cullis et. al. in U.S. Pat. No. 5,008,050.

“Other techniques used to prepare vesicles are reverse-phase evaporation introduced by Szoka and Papahadjopoulos (Szoka and Papahadjopoulos, 1978; U.S. Pat. No. 4,235,871). This technique consists of forming a water-in-oil emulsion of lipids in an organic solvent and an aqueous buffer solution containing a substance to be encapsulated. Removal of the organic solvent under reduced pressure produces a viscous
When this gel collapses an aqueous suspension of lipid vesicles are formed.

"Another method described by Carmona-Ribeiro and Chaimovich (Carmona-Ribeiro and Chaimovich, 1983) involves injecting an organic e.g., chloroform, methanol, ethanol, solution of the desired lipids into an aqueous buffer where the lipids spontaneously forms liposomes as the solvent evaporates.

"The liposomes can also be prepared by the aqueous heat method as described for DDA by Holten-Andersen et. al. (2004) by which a suspension of the liposome forming compound in aqueous buffer is heated to e.g., 80.degree. C. by intermittent shaking for 20 minutes followed by cooling to room temperature.

"Above mentioned 'aqueous heat method', used and described by Woodard et. al. (1980), Dzata et. al. (1991) and Holten-Andersen et. al. (2004) does not stabilize solutions of DDA and TDB.

"In one particular preferred method protein antigens are entrapped within preformed vesicles by the dehydration-rehydration method (Kirby and Gregoriadis, 1984) in which an oligonucleotide, peptide or protein present in the aqueous phase is entrapped by freeze drying followed by rehydration of the lyophilized liposomes.

"Alternatively the antigen is incorporated using the freeze and thaw technique described by Pick (Pick, 1981) and by Bally et. al. in U.S. Pat. No. 4,975,282. In this technique vesicles are mixed with the protein antigen and repeatedly snap frozen in liquid nitrogen and warmed to temperatures above the main phase transition temperature of the relevant lipids. The vesicles may be further processed to remove any non-entrapped antigen e.g., by washing and centrifuging.

"It has been shown that acylated glycosides such as TDB and cord factor isolated from the mycobacterial cell wall, TDM, inhibits fusion between phospholipid vesicles (Spargo et. al., 1991 and Crowe et. al., 1994). The hydrophilic trehalose moiety is likely to be immobilized at the surface of the vesicles, thus increasing the hydration force that is an important primary barrier to fusion. Alternatively the immobilized trehalose moiety might act as a steric barrier to fusion (Spargo et. al., 1991).

"Liposomes from phospholipids (without TDB) are presently used experimentally as adjuvants in e.g., influenza vaccine (Ben-Yehuda et. al., 2003). Another example is IMUXEN.TM. liposomal vaccine against influenza (Lipoxen Technologies Ltd.; Gregoriadis et. al., 1999).

"As quaternary ammonium compounds and especially DDA is a very promising candidate for an effective vaccine adjuvant but has the major disadvantage of being physically un-stable in aqueous solution forming aggregates and precipitates during storage it is much needed to stabilise the vesicles formed. The present invention describes a new method of stabilizing adjuvant formulations composed of cationic lipids.
such as DDA. Additionally, by this method the adjuvant effect of the formulation is enhanced.”

As a supplement to the background information on this patent, NewsRx correspondents also obtained the inventors’ summary information for this patent: “The present invention discloses compositions and methods for stabilizing cationic liposome suspensions by incorporating glycolipids e.g., acylated glycosides such as alpha alpha’-trehalose 6,6’-dibehenate (TDB) or alpha alpha’-trehalose 6,6’-dimycolate (TDM) into liposomal bilayers made from amphiphilic quaternary ammonium compounds such as DDA, DODA, DOTAP, DODAP or DOTMA. The strongly hydrated sugar head-groups of the glycolipids increases the overall hydration of the liposomal bilayers, which prevents dehydration of the quaternary ammonium head-groups and aggregation caused by reduced charge repulsion of the cationic vesicles. This stabilization of DDA is not obtained alone by adding the sugar, e.g., trehalose or sucrose or by a simple mixing of the quaternary ammonium compounds and glycolipids. The present invention also discloses the use of these stabilized liposomes as vaccine adjuvants.

“The present invention discloses compositions and methods for stabilizing cationic liposome suspensions by incorporating glycolipids e.g., acylated glycosides such as alpha alpha’-trehalose 6,6’-dibehenate (TDB) or alpha alpha’-trehalose 6,6’-dimycolate (TDM) into liposomal bilayers made from amphiphilic quaternary ammonium compounds such as DDA, DODA, DOTAP, DODAP or DOTMA. The strongly hydrated sugar head-groups of the glycolipids increases the overall hydration of the liposomal bilayers, which prevents dehydration of the quaternary ammonium head-groups and aggregation caused by reduced charge repulsion of the cationic vesicles. This stabilization of DDA is not obtained alone by adding the sugar, e.g., trehalose or sucrose or by a simple mixing of the quaternary ammonium compounds and glycolipids. The present invention also discloses the use of these stabilized liposomes as vaccine adjuvants.”

Patent Issued for Hypoxia Inducible Factor Inducer and Methods for Using the Same

By a News Reporter-Staff News Editor at Life Science Weekly – From Alexandria, Virginia, NewsRx journalists report that a patent by the inventors Basaraba, Randall Joseph (Fort Collins, CO); Bielefeldt-Ohmann, Helle (Brisbane, AU), filed on March 19, 2008, was cleared and issued on September 18, 2012.

The patent’s assignee for patent number 8268330 is Colorado State University Research Foundation (Fort Collins, CO).

News editors obtained the following quote from the background information supplied by the inventors: “Traditionally, vaccines have been based on live attenuated, or inactivated microorganisms. However, in many instances these strategies are inefficient due to factors such as antigenic variability of microorganisms such as bacteria or fungi. Peptide vaccines that consist of antigenic peptides or peptide fragments of microorganisms have been developed. Conserved peptide fragments are less likely to exhibit antigenic variability, and can overcome some of the problems associated with traditional peptides. Accordingly, subunit vaccines have been developed that target conserved regions of microorganisms. However, synthetic peptide vaccines tend to be poorly immunogenic, and also tend to induce humoral antibody responses, but are less able to induce cell-mediated responses.

“With the emergence of drug resistant and/or virulent strains of microorganisms, there is a need for a more effective vaccine against a wide variety of infectious microorganisms.”

As a supplement to the background information on this patent, NewsRx correspondents also obtained the inventors’ summary information for this patent: “Generally, the invention provides vaccines for a microorganism (i.e., microbe) and methods for using the same. In some aspects, vaccines for microorganisms that produce HIF inducing compound is provided. Typically, the vaccine comprises at least a portion of an HIF inducing compound that is produced by the microorganism, a precursor of the HIF inducing compound, or a combination thereof.

“In some embodiments, the microorganism is a bacteria. The vaccine can also include one or more siderophores or bacterial product that is capable of binding or chelating one or more metal cations. Exemplary metal cations include iron, copper, magnesium, zinc, manganese, and nickel. Exemplary siderophores include, but are not limited to, Mycobacterial spp. siderophores mycobactin, carboxymycobactin, and exochelins.

“In some embodiments, the microorganism is any bacteria that produce similar chelators or siderophores.

“Still in other embodiments, the microorganism is Mycobacterium tuberculosis, or related mycobacteria or other members of the
Actinobacteria, including, but not limited to, pathogenic and non-pathogenic Mycobacterium spp.

“Exemplary HIF inducing compounds include, but are not limited to, siderophores, or iron chelators, such as mycobactin, carboxymycobactin and exochelins disclosed above.

“In some embodiments, the siderophore comprises mycobactin, carboxymycobactin, exochelins, or a combination thereof.

“Yet in other embodiments, the vaccine comprises a fragment of the HIF inducing compound. In particular, those fragments that are recognized by the immune system of the subject.

“The vaccine can also include an epitope of the microorganism to elicit immune response from the subject.

“In some embodiments, the vaccine includes an attenuated or inactivated microorganism. Alternatively, the vaccine can include any conventional compositions known to one skilled in the art. For example, a vaccine composition for M. tuberculosis can be BCG-vaccine which includes an HIF inducing compound such as those disclosed herein.

“Other aspects of the invention provide a method for vaccinating a subject against a microorganism infection. Such methods generally comprises administering to the subject a vaccine composition comprising at least a portion of an HIF inducing compound that is produced by the microorganism, a precursor of the HIF inducing compound, or a combination thereof.

“In some embodiments, the vaccine includes an epitope of the microorganism.

“In other embodiments, the vaccine includes an attenuated or inactivated microorganism.

“Methods of the invention are applicable for vaccinating against a wide variety of microorganism including various bacteria or fungi. Generally, methods of the invention are suited for vaccinating a subject against a microorganism that produces an HIF inducing compound. In some embodiments, the microorganism is a bacteria. Within these embodiments, in some instances, the microorganism is Mycobacterium tuberculosis, other pathogenic and non-pathogenic mycobacterium spp. or other members of the Actinobacteria family.

“In some embodiments, the HIF inducing compound is a siderophore or a cation chelator, for example, mycobactin, carboxymycobactin or exochelins. Within these embodiments, in some instances, the siderophore comprises mycobactin, carboxymycobactin, exochelins, or a combination thereof.

“Yet in other embodiments, the vaccine comprises a fragment of the HIF inducing compound.

“Still other aspects of the invention provide a method for stimulating an immune response against Mycobacterium tuberculosis in a subject.
Such methods generally include administering a composition comprising mycobactin, carboxymycobactin, exochelins, a fragment thereof, or a combination thereof to the subject.

“In some embodiments, the composition includes and epitope of Mycobacterium tuberculosis.

“Still in other embodiments, the composition includes an attenuated or inactivated Mycobacterium tuberculosis.

“Yet in some embodiments, the composition includes those of BCG vaccine.”

Chapter 9

Additional Research

Division of Nephrology, Istanbul: Tuberculosis in dialysis patients: a nine-year retrospective analysis

By a News Reporter-Staff News Editor at Life Science Weekly – Research findings on Infection Research are discussed in a new report. According to news reporting out of Istanbul, Turkey, by NewsRx editors, research stated, “Diagnosis of tuberculosis (TB) among dialysis patients may be difficult because of increased frequency of extra-pulmonary presentations, atypical clinical manifestations, and non-specific symptoms. This study aimed to investigate the spectrum of clinical presentations and outcome in dialysis patients during a nine-year period.”

Our news journalists obtained a quote from the research from the Division of Nephrology, “A total of 651 patients undergoing hemodialysis (HD) and peritoneal dialysis (PD) for at least three months in our unit between 2001 and 2010 were studied. Dialysis and follow-up were performed in our tertiary care center located in the eastern region of Turkey. Diagnosis of TB was established by combining clinical, radiological, biochemical, microbiological, and histological findings. Choice of anti-TB drug used, the results of therapy, and patient outcome were noted. Out of 651 dialysis patients studied, 322 (49.4%) were on PD and the remainder on HD (50.6%). Twenty-six (4%) of the 651 dialysis patients were diagnosed with TB (15 PD, 11 HD), 5 of whom were diagnosed by microbiological assessment, 9 by pathological assessment, and 12 by clinical and radiological findings. Mean age at diagnosis was 41.5 +/- 16.5 years and the female/male ratio was 1.18. Three patients had a history of pulmonary TB. Extra-pulmonary involvement was observed in 17 (65.4%) patients. All patients were treated with rifampicin isoniazid, ethambutol, pyrazinamide and pyridoxine. Four patients died during the study. TB occurred in dialysis patients and extra-pulmonary TB was more commonly identified than pulmonary TB.”
According to the news editors, the research concluded: “Tuberculous lymphadenitis was the most frequent form of extra-pulmonary TB in our cohort.”

For more information on this research see: Tuberculosis in dialysis patients: a nine-year retrospective analysis. *Journal of Infection in Developing Countries*, 2013;7(3):208-213. *Journal of Infection in Developing Countries* can be contacted at: J Infection Developing Countries, Jidc Cent Off Porto Conte Ricerche Res Ctr, S P 55, Porto Conte Capo Caccia Km 8.400 Loc, Tramaniglio, 07041, Italy.

Our news journalists report that additional information may be obtained by contacting A. Unsal, Sisli Etfal Res & Educ Hosp, Div Nephrol, TR-80650 Istanbul, Turkey. (2013 Apr 23)

**University of Delhi: Development of a Novel PCR Restriction Analysis of the hsp65 Gene as a Rapid Method To Screen for the Mycobacterium tuberculosis Complex and Nontuberculous Mycobacteria in High-Burden Countries**

By a News Reporter-Staff News Editor at Tuberculosis Week – Investigators publish new report on Clinical Microbiology. According to news originating from Delhi, India, by NewsRx correspondents, research stated, “The limitations of conventional methods of identification of *Mycobacterium tuberculosis* have led to the development of several nucleic acid amplification techniques which have the advantage of being rapid, sensitive, and specific. However, their expense or the need for technical expertise makes it difficult to use them in regions in which tuberculosis is endemic.”

Our news journalists obtained a quote from the research from the University of Delhi, “A novel PCR restriction analysis (PRA) of the hsp65 gene was therefore developed for rapid screening of clinical isolates to identify Mycobacterium spp. The restriction enzymes NruI and BamHI were selected to obtain a limited number of restriction patterns to further differentiate between *Mycobacterium tuberculosis* complex (MTBC) and nontuberculous mycobacteria (NTM). Three hundred ten isolates from clinical specimens and 24 reference strains were tested. The assay correctly identified 295 of the 310 culture isolates as MTBC, while the remaining 15 isolates were identified as NTM. Of the isolates tested, 135 MTBC strains and all 15 NTM were also confirmed by PRA using Sau96I and CfoI. Thirty-eight randomly selected MTBC strains and all 15 NTM were further confirmed by sequencing. The NruI/BamHI PRA was simple, as it did not require any elaborate analyses. It was cost-effective, rapid, highly sensitive, and specific and did not require technical expertise.”
According to the news editors, the research concluded: “The assay can, therefore, be used as a simple screening test not only to detect Mycobacterium spp. but also to differentiate MTBC from NTM in peripheral laboratories with minimal availability of funds.”

For more information on this research see: Development of a Novel PCR Restriction Analysis of the hsp65 Gene as a Rapid Method To Screen for the Mycobacterium tuberculosis Complex and Nontuberculous Mycobacteria in High-Burden Countries. *Journal of Clinical Microbiology*, 2013;51(4):1165-70.

The news correspondents report that additional information may be obtained from M. Varma-Basil, Dept. of Microbiology, Vallabhbhai Patel Chest Institute, University of Delhi, Delhi, India. *(2013 Apr 15)*

**Radboud University Medical Center, Nijmegen: A predictive signature gene set for discriminating active from latent tuberculosis in Warao Amerindian children**

By a News Reporter-Staff News Editor at Pediatrics Week – Fresh data on Mycobacterium Infections are presented in a new report. According to news reporting originating from Nijmegen, Netherlands, by Vertical-News correspondents, research stated, “Tuberculosis (TB) continues to cause a high toll of disease and death among children worldwide. The diagnosis of childhood TB is challenged by the paucibacillary nature of the disease and the difficulties in obtaining specimens.”

Our news editors obtained a quote from the research from Radboud University Medical Center, “Whereas scientific and clinical research efforts to develop novel diagnostic tools have focused on TB in adults, childhood TB has been relatively neglected. Blood transcriptional profiling has improved our understanding of disease pathogenesis of adult TB and may offer future leads for diagnosis and treatment.”

According to the news editors, the research concluded: “No studies applying gene expression profiling of children with TB have been published so far.”


The news editors report that additional information may be obtained by contacting L.M. Verhagen, Laboratory of Pediatric Infectious Diseases, Radboud University Medical Centre, PO Box 9101 (internal post 224), Nijmegen, 6500 HB, Netherlands. *(2013 Apr 13)*
University of Pennsylvania, Philadelphia: Info-gap management of public health Policy for TB with HIV-prevalence and epidemiological uncertainty

By a News Reporter-Staff News Editor at Ivy League Week – Research findings on Public Health are discussed in a new report. According to news reporting from Philadelphia, Pennsylvania, by NewsRx journalists, research stated, “Formulation and evaluation of public health policy commonly employs science-based mathematical models. For instance, epidemiological dynamics of TB is dominated, in general, by flow between actively and latently infected populations.”

The news correspondents obtained a quote from the research from the University of Pennsylvania, “Thus modelling is central in planning public health intervention. However, models are highly uncertain because they are based on observations that are geographically and temporally distinct from the population to which they are applied. We aim to demonstrate the advantages of info-gap theory, a non-probabilistic approach to severe uncertainty when worst cases cannot be reliably identified and probability distributions are unreliable or unavailable.

Info-gap is applied here to mathematical modelling of epidemics and analysis of public health decision-making. Applying info-gap robustness analysis to tuberculosis/HIV (TB/HIV) epidemics, we illustrate the critical role of incorporating uncertainty in formulating recommendations for interventions. Robustness is assessed as the magnitude of uncertainty that can be tolerated by a given intervention. We illustrate the methodology by exploring interventions that alter the rates of diagnosis, cure, relapse and HIV infection. We demonstrate several policy implications. Equivalence among alternative rates of diagnosis and relapse are identified. The impact of initial TB and HIV prevalence on the robustness to uncertainty is quantified. In some configurations, increased aggressiveness of intervention improves the predicted outcome but also reduces the robustness to uncertainty. Similarly, predicted outcomes may be better at larger target times, but may also be more vulnerable to model error. The info-gap framework is useful for managing model uncertainty and is attractive when uncertainties on model parameters are extreme.”

According to the news reporters, the research concluded: “When a public health model underlies guidelines, info-gap decision theory provides valuable insight into the confidence of achieving agreed-upon goals.”

Research Hospital, Ankara: Spinal Tuberculosis (Pott’s disease) Mimicking Paravertebral Malignant Tumor in a Child Presenting with Spinal Cord Compression

By a News Reporter-Staff News Editor at Pain & Central Nervous System Week – Investigators publish new report on Life Science. According to news reporting from Ankara, Turkey, by NewsRx journalists, research stated, “Paravertebral tumors may interfere with the radiological and clinical features of spinal tuberculosis. We report a case of a 3-year-old boy with spinal tuberculosis who was initially misdiagnosed as having a paraspinal tumor.”

The news correspondents obtained a quote from the research from Research Hospital, “The diagnosis of tuberculosis was made on the basis of intraoperative findings and confirmed by histopathology. This case highlights the importance of awareness of the different radiographic features of spinal tuberculosis, which can mimic a spinal malignancy.”

According to the news reporters, the research concluded: “In order to avoid delayed diagnosis, pediatricians and radiologists must be aware of spinal tuberculosis, which may interfere with other clinical conditions.”


Our news journalists report that additional information may be obtained by contacting S. Emir, Dept. of Pediatric Hematology Oncology, SB Ankara Children’s Hematology Oncology Training and Research Hospital, Ankara, Turkey. (2013 Mar 18)
Murdoch Children’s Research Institute, Melbourne: Evaluation Of An Interferon-gamma Release Assay In Children With Suspected Tuberculosis In Papua New Guinea

By a News Reporter-Staff News Editor at Pediatrics Week – New research on Mycobacterium Infections is the subject of a report. According to news reporting out of Melbourne, Australia, by Vertical-News editors, research stated, “There are few data from tuberculosis (TB) endemic settings of the performance and outcome predictors of the QuantiFERON-TB Gold in Tube assay (QFT) in children with suspected TB. A prospective cross-sectional study was conducted in Papua New Guinea children with suspected TB evaluated at Port Moresby General Hospital (Port Moresby, Papua New Guinea).”

Our news journalists obtained a quote from the research from Murdoch Children’s Research Institute, “Two hundred sixteen children were enrolled including 106 probable TB, 87 possible TB and 23 without TB. Concordance between QFT and tuberculin skin test results was 86% (P < 0.001, kappa = 0.70). QFT was significantly more likely to be positive than tuberculin skin test, overall and within the probable or possible TB categories, with no difference in prevalence of positivity between these 2 categories.”

According to the news editors, the research concluded: “The role of QFT in supporting the clinical diagnosis of TB in endemic settings, where resources are limited, remains uncertain especially as cost and technical requirements remain considerable.”


Our news journalists report that additional information may be obtained by contacting T. Uluk, Royal Children’s Hospital, Murdoch Childrens Res Inst, Melbourne, Vic, Australia. (2013 Mar 09)
Research Institute, Houston: Test Variability of the QuantiFERON-TB Gold In-Tube Assay in Clinical Practice

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – Investigators publish new report on Respiratory Research. According to news reporting out of Houston, Texas, by NewsRx editors, research stated, “Although IFN-gamma release assays (IGRAs) are widely used to screen for Mycobacterium tuberculosis infection in high-income countries, published data on repeatability are limited. To determine IGRA repeatability.”

Our news journalists obtained a quote from the research from Research Institute, “The study population included consecutive patients referred to The Methodist Hospital (Houston, TX) between August 1, 2010 and July 31, 2011 for latent tuberculosis (TB) infection screening with an IGRA (QuantiFERON-TB Gold In-Tube; Cellestis, Carnegie, Australia). We performed multiple IGRA tests using leftover stimulated plasma according to a prospectively formulated quality control protocol. We analyzed agreement in interpretation of test results classified according to manufacturer-recommended criteria and repeatability of quantitative TB response. During the study period, 1,086 test results were obtained from 543 subjects. Per the manufacturer’s cutpoint, the result of the second test was discordant from that of the first in 28 (8%) of 366 patients with valid test results, including 13 with an initial negative result and 15 with an initial positive result. Although agreement between repeat test results was high (kappa = 0.84; 95% confidence interval, 0.79-0.90), the normal expected range of within-subject variability in TB response on retesting included differences of +/- 0.60 IU/ml for all individuals (coefficient of variation, 14%), and +/- 0.24 IU/ml (coefficient of variation, 27%) for individuals whose initial TB response was between 0.25 and 0.80 IU/ml. There is substantial variability in TB response when IGRAs are repeated using the same patient sample.”

According to the news editors, the research concluded: “IGRA results should be interpreted cautiously when TB response is near interpretation cut-points.”


Our news journalists report that additional information may be obtained by contacting J.Z. Metcalfe, Methodist Hosp, Res Inst, Dept. of Pathol & Genom Med, Houston, TX 77030, United States. (2013 Mar 04)
Yokohama City University, Kanagawa: Development and validation of a tuberculosis prognostic score for smear-positive in-patients in Japan

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators publish new report on Tuberculosis and Lung Disease. According to news reporting out of Kanagawa, Japan, by NewsRx editors, research stated, “No scoring system has ever been used to estimate the prognosis of individual tuberculosis (TB) patients. To develop and validate a tuberculosis prognostic score.”

Our news journalists obtained a quote from the research from Yokohama City University, “This retrospective cohort study conducted in Japan comprised the development (n = 179; mean age 65.9 +/- 18.8 years) and validation (n = 244; mean age 64.3 +/- 20.1 years) of a tuberculosis prognostic score among patients with newly diagnosed smear-positive non-multidrug-resistant pulmonary tuberculosis without human immunodeficiency virus infection. The score (raw score) was defined by modifying a logistic regression formula using known risk factors as independent variables and in-patient death as a dependent variable. The raw score was calculated as follows: age (years) + (oxygen requirement, 10 points) -20 x albumin (g/dl) + (activity of daily living: independent, 0 point; semi-dependent, 5 points; totally dependent, 10 points). The raw scores were grouped into risk groups 1 (raw score &lt; -30) to 5 (raw score &gt;= 60) using 30-point intervals. Every increase in risk group was equivalent to a 7.3-fold increase in the odds ratio for in-hospital death (P &lt; 0.001). The area under the receiver operating characteristics curve by risk group for in-patient death was 0.875 (P &lt; 0.001).”

According to the news editors, the research concluded: “In this study we were able to develop and validate a tuberculosis prognostic score.”

For more information on this research see: Development and validation of a tuberculosis prognostic score for smear-positive in-patients in Japan. International Journal of Tuberculosis and Lung Disease, 2013;17(1):54-60. International Journal of Tuberculosis and Lung Disease can be contacted at: Int Union Against Tuberculosis Lung Disease (I U A T L D), 68 Boulevard Saint-Michel, 75006 Paris, France.

Our news journalists report that additional information may be obtained by contacting N. Horita, Yokohama City University, Medical Center, Resp Dis Center, Yokohama, Kanagawa 2360004, Japan. (2013 Feb 19)
Hacettepe University, Ankara: Abdominal Tuberculosis Leading To Portal Vein Thrombosis, Mimicking Peritoneal Carcinomatosis And Liver Cirrhosis

By a News Reporter-Staff News Editor at Hematology Week – Current study results on Health and Medicine have been published. According to news reporting from Ankara, Turkey, by NewsRx journalists, research stated, “Abdominal tuberculosis is a rare infectious disease that can involve the peritoneum and lead to portal vein thrombosis and mimic peritoneal carcinomatosis. We report on a 43-year-old male patient with fatigue and progressive weight loss for two years.”

The news correspondents obtained a quote from the research from Hacettepe University, “Ascites was the only pathologic finding in his physical examination and laboratory findings revealed only a mild anaemia with Ca-125 elevation. The ascitic fluid Adenosine deaminase (ADA) level was also elevated. Computed tomography revealed splenomegaly, a mesenteric mass measuring 3.5 cm and intra-abdominal lymphadenopathies at the hepatic hilum. Oesophagogastroduodenoscopy (EGD) revealed oesophageal varices which was also consistent with portal hypertension.”

According to the news reporters, the research concluded: “Diagnostic laparotomy and biopsies obtained from the omentum and the lymph nodes revealed acid-fast staining tuberculosis bacilli.”

For more information on this research see: Abdominal Tuberculosis Leading To Portal Vein Thrombosis, Mimicking Peritoneal Carcinomatosis And Liver Cirrhosis. Acta Clinica Belgica, 2012;67(2):137-139. Acta Clinica Belgica can be contacted at: Acta Clinica Belgica, Univ Hospital Gent, De Pintelaan 185, Renal Division, B-9000 Ghent, Belgium.

Our news journalists report that additional information may be obtained by contacting B. Ozseker, Hacettepe University, Fac Med, Dept. of Gen Surg, TR-06100 Ankara, Turkey. (2013 Jan 28)

Federal University, Curitiba: Detection of RD(Rio) strain of Mycobacterium tuberculosis in tapirs (Tapirus terrestris) from a zoo in Brazil

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators publish new report on Zoo and Wildlife Medicine. According to news originating from Curitiba, Brazil, by NewsRx correspondents, research stated, “Tuberculosis is a chronic infection caused by strains of the Mycobacterium tuberculosis complex and occurs in both animal and human populations. The death of a tapir showing purulent material and a hard mass in the lungs at necropsy raised suspicion of a potential disease caused by mycobacteria species in a Brazilian zoo.”
Our news journalists obtained a quote from the research from Federal University, “Later, two other tapirs with similar signs died and were further investigated. Polymerase chain reaction (PCR) from bronco-alveolar lavages was performed, and both animals tested positive for the RD(Rio) strain of \textit{M. tuberculosis}, which is a recently discovered Latin American-Mediterranean sublineage and the main cause of human tuberculosis in Rio de Janeiro, Brazil. To investigate the possibility of human infection and the source of transmission, all 50 zoo employees underwent tuberculin skin testing; four were reactive, but radiographic exams and direct sample staining did not suggest tuberculosis. Thus, direct human to animal transmission was not proven.”

According to the news editors, the research concluded: “However, the presence of RD(Rio) \textit{M. tuberculosis} in tapirs highlights the lack of attention to diseases that human beings may transmit to wildlife.”

For more information on this research see: Detection of RD(Rio) strain of Mycobacterium tuberculosis in tapirs (Tapirus terrestris) from a zoo in Brazil. \textit{Journal of Zoo and Wildlife Medicine}, 2012;43(4):872-5. \textit{Journal of Zoo and Wildlife Medicine} can be contacted at: Amer Assoc Zoo Veterinarians, 6 North Pennell Road, Media, PA 19063, USA.

The news correspondents report that additional information may be obtained from P.S. Murakami, Dept. of Veterinary Medicine, Federal University of Parana, Curitiba, Parana 80035, Brazil.

The publisher’s contact information for the \textit{Journal of Zoo and Wildlife Medicine} is: Amer Assoc Zoo Veterinarians, 6 North Pennell Road, Media, PA 19063, USA. (2013 Jan 22)

\textbf{All India Institute of Medical Sciences, New Delhi: mRNA and DNA PCR tests in cutaneous tuberculosis}

By a News Reporter-Staff News Editor at Tuberculosis Week – Current study results on Tuberculosis have been published. According to news reporting originating from New Delhi, India, by NewsRx correspondents, research stated, “The microbiologic diagnosis of cutaneous tuberculosis is difficult because most lesions harbor only a small number of mycobacteria that cannot usually be detected by staining for the organism or by culture. Nucleic acid amplification tests based on the polymerase chain reaction (PCR) are potentially useful in this situation.”

Our news editors obtained a quote from the research from the All India Institute of Medical Sciences, “To evaluate the utility of mRNA PCR and DNA PCR in the diagnosis of cutaneous tuberculosis. Biopsies from 28 cases of cutaneous tuberculosis and 19 controls with other diseases were subjected to microbiologic tests including direct smears for mycobacteria, culture and both mRNA PCR and DNA PCR. The laboratory was blinded to the clinical diagnosis. None of the patients or
controls showed a positive reaction on mRNA PCR test. Seven of 28 cases and 5 out of 19 controls showed a positive result on DNA PCR test yielding a sensitivity of 25% and a specificity of 73.7%.

According to the news editors, the research concluded: “The results of PCR tests in cutaneous tuberculosis should be interpreted in the light of clinical and histopathological findings.”


The news editors report that additional information may be obtained by contacting C. Suthar, Dept. of Dermatology and Venereology, All India Institute of Medical Sciences, New Delhi, India. (2013 Jan 14)

**University Hospital, Granada: Evaluation of the Speed-oligo Direct Mycobacterium tuberculosis Assay for Molecular Detection of Mycobacteria in Clinical Respiratory Specimens**

By a News Reporter-Staff News Editor at Tuberculosis Week – A new study on Clinical Microbiology is now available. According to news originating from Granada, Spain, by NewsRx correspondents, research stated, “We present the first evaluation of a novel molecular assay, the Speed-oligo Direct *Mycobacterium tuberculosis* (SO-DMT) assay, which is based on PCR combined with a dipstick for the detection of mycobacteria and the specific identification of *M. tuberculosis* complex (MTC) in respiratory specimens. A blind evaluation was carried out in two stages: first, under experimental conditions on convenience samples comprising 20 negative specimens, 44 smear-and culture-positive respiratory specimens, and 11 sputa inoculated with various mycobacterium-related organisms; and second, in the routine workflow of 566 fresh respiratory specimens (4.9% acid-fast bacillus [AFB] smear positives, 7.6% MTC positives, and 1.8% nontuberculous mycobacteria [NTM] culture positives) from two Mycobacterium laboratories.”

Our news journalists obtained a quote from the research from University Hospital, “SO-DMT assay showed no reactivity in any of the mycobacterium-free specimens or in those with mycobacterium-related organisms. Compared to culture, the sensitivity in the selected smear-positive specimens was 0.91 (0.92 for MTC and 0.90 for NTM), and there was no molecular detection of NTM in a tuberculosis case or vice versa. With respect to culture and clinical data, the sensitivity, specificity, and positive and negative predictive values for the SO-DMT system in routine specimens were 0.76 (0.93 in smear positives [1.0 for MTC and 0.5 for NTM] and 0.56 in smear negatives [0.68 for MTC and 0.16 for NTM]),
0.99, 0.85 (1.00 in smear positives and 0.68 in smear negatives), and 0.97, respectively. Molecular misidentification of NTM cases occurred when testing 2 gastric aspirates from two children with clinically but not microbiologically confirmed lung tuberculosis.

According to the news editors, the research concluded: “The SO-DMT assay appears to be a fast and easy alternative for detecting mycobacteria and differentiating MTC from NTM in smear-positive respiratory specimens.”


The news correspondents report that additional information may be obtained from A. Lara-Oya, Dept. of Microbiology, University Hospital Virgen de las Nieves, Granada, Spain. (2013 Jan 14)

A modified acid-fast staining method for rapid detection of Mycobacterium tuberculosis

By a News Reporter-Staff News Editor at Tuberculosis Week – Fresh data on Microbiology are presented in a new report. According to news reporting originating in Shenzhen, People’s Republic of China, by NewsRx journalists, research stated, “A modified add-fast staining method was developed for rapid detection of Mycobacterium tuberculosis and its L forms, wherein carbol fuchsin and dioxogen were mixed into the sputum smear. With this method, the dyeing time is shortened and heating is not required.”

The news reporters obtained a quote from the research, “The sensitivity, specificity, positive predictive value, negative predictive value, positive rate, and diagnostic efficiency of the new method were compared to those obtained by PCR using 50 clinical samples. Further, 468 clinical samples were analyzed using the new method, the modified intensified Kinyoun (IK) acid-fast staining method, and the traditional Ziehl-Neelsen acid-fast staining method. Differences among the positive detection rates of the three methods were analyzed using Student’s t-test, and no significant differences were found between the new method and the modified IK acid-fast staining method, while the rates of both these methods were higher than that of the traditional acid-fast staining method.”

According to the news reporters, the research concluded: “Additionally, the dyeing time in the new method was markedly less than that in the modified IK acid-fast staining method (5 min and 24 h, respectively).”

For more information on this research see: A modified acid-fast staining method for rapid detection of Mycobacterium tuberculosis.
Department of Laboratory Medicine, Weifang: Proteomic analysis of sputum in patients with active pulmonary tuberculosis

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – Investigators discuss new findings in Mycobacterium Infections. According to news reporting from Weifang, People’s Republic of China, by NewsRx journalists, research stated, “The protein composition of sputum most faithfully reflects the state of the lungs. The aim of this study was to determine whether relative qualitative and quantitative differences in protein expression of sputum could be related to active pulmonary tuberculosis.”

The news correspondents obtained a quote from the research from the Department of Laboratory Medicine, “Sputum samples were collected from 65 patients with active pulmonary tuberculosis and 38 healthy controls. Comprehensive proteomic approaches were used to profile the proteome changes of host sputum in response to Mycobacterium tuberculosis infection using two-dimensional electrophoresis in combination with matrix-assisted laser desorption ionization time-of-flight/time-of-flight mass spectrometry. Mascot software was used to identify proteins from protein databases. Enzyme-linked immunosorbent assay was used to confirm the proteomic results. A total of 62 differentially expressed proteins were identified, among which, 15 proteins were up-regulated and 47 proteins were down-regulated in the tuberculosis sputum compared with the controls. Bacterial protein UqhC was the most increased protein, whereas serum albumin was the most decreased protein in the tuberculosis sputum compared with the controls. The enzyme-linked immunosorbent assay analysis was consistent with proteomic data. Bioinformatics analysis suggested that multiple host cell pathways were involved in the tuberculosis infection processes, including acute phase response, signal transduction, cytoskeleton structure, immune response and so on. In all, for the first time, our results revealed that a number of proteins were differentially expressed during active pulmonary tuberculosis infection.”
According to the news reporters, the research concluded: “These data will provide valuable clues for further investigation of tuberculosis pathogenesis and biomarkers for detection of active pulmonary tuberculosis infection.”


Our news journalists report that additional information may be obtained by contacting Y.R. Fu, Chest Special Hosp Weifang, Dept. of Lab Med, Weifang, People’s Republic of China. (2012 Dec 31)

**Institute for Biology Research, Taipei: Identification of the Mycobacterium marinum Apa antigen O-mannosylation sites reveals important glycosylation variability with the M. tuberculosis Apa homologue**

By a News Reporter-Staff News Editor at Proteomics Weekly – Investigators publish new report on Proteomics. According to news reporting from Taipei, Taiwan, by NewsRx journalists, research stated, “The 45/47 kDa Apa, an immuno-dominant antigen secreted by Mycobacterium tuberculosis is O-mannosylated at multiple sites. Glycosylation of Apa plays a key role in colonization and invasion of the host cells by M. tuberculosis through interactions of Apa with the host immune system C-type lectins.”

The news correspondents obtained a quote from the research from Institute for Biology Research, “Mycobacterium marinum (M.ma) a fish pathogen, phylogenetically close to M. tuberculosis, induces a granulomatous response with features similar to those described for M. tuberculosis in human. Although M.ma possesses an Apa homologue, its glycosylation status is unknown, and whether this represents a crucial element in the pathophysiology induced by M.ma remains to be addressed. To this aim, we have identified two concanavalin A-reactive 45/47 kDa proteins from M.ma, which have been further purified by a two-step anion exchange chromatography process. Advanced liquid chromatography-nanoESI mass spectrometry-based proteomic analyses of peptides, derived from either trypptic digestion alone or in combination with the Asp-N endoproteinase, established that M.ma Apa possesses up to seven distinct O-mannosylated sites with mainly single mannose substitutions, which can be further extended at the Ser/Thr/Pro rich region near the N-terminus.”
According to the news reporters, the research concluded: “This opens the way to further studies focusing on the involvement and biological functions of Apa O-mannosylation using the http://M.ma/zebrafish model.”


Our news journalists report that additional information may be obtained by contacting B. Coddeville, Academy Sinica, Inst Biol Chem, Taipei 115, Taiwan. (2012 Dec 31)

Catholic University of Korea, Seoul: Atypical Disseminated Skeletal Tuberculosis Mimicking Metastasis on PET-CT and MRI

By a News Reporter-Staff News Editor at Tuberculosis Week – Investigators discuss new findings in Internal Medicine. According to news reporting from Seoul, South Korea, by NewsRx journalists, research stated, “Multifocal skeletal tuberculosis is a very rare manifestation of tuberculous infection. The multiple bone lesions of multifocal skeletal tuberculosis are difficult to differentiate from metastasis, even when performing 2-[fluorine-18]-fluoro-2-deoxy-D-glucose (FDG) positron emission tomography (FDG PET/CT) or magnetic resonance imaging (MRI).”

The news correspondents obtained a quote from the research from the Catholic University of Korea, “A 25-year-old man presented with an abnormal chest X-ray. Radiologically, there were extensive osteolytic lesions on the skull, along the entire spine and on the ribs and both iliac bones, suggesting a diagnosis of bone metastasis. On FDG PET/CT, intensely increased F-18 FDG lesions were observed. A bone biopsy with a microbiologic study revealed a tuberculous infection.”

According to the news reporters, the research concluded: “Follow-up PET/CT performed after treatment showed marked improvement in the extensive FDG uptake lesions.”

For more information on this research see: Atypical Disseminated Skeletal Tuberculosis Mimicking Metastasis on PET-CT and MRI. Internal Medicine, 2012;51(20):2961-2965. Internal Medicine can be contacted at: Japan Soc Internal Medicine, 34-3 3-Chome Hongo Bunkyo-Ku, Tokyo, 113, Japan. (Wiley-Blackwell - http://www.wiley.com/;
MEMORIAL HOSPITAL, BUSAN: A CASE OF Sigmoid Colon Tuberculosis Mimicking Colon Cancer

By a News Reporter-Staff News Editor at Tuberculosis Week – Current study results on Mycobacterium Infections have been published. According to news reporting originating in Busan, South Korea, by NewsRx journalists, research stated, “Tuberculosis of the sigmoid colon is a rare disorder. An 80-year-old man visited Bongseng Memorial Hospital for medical examination.”

The news reporters obtained a quote from the research from Memorial Hospital, “A colonoscopy was performed, and a lesion in the sigmoid colon that was suspected to be colon cancer was found. A biopsy was performed, and tuberculous enteritis with chronic granulomatous inflammation was diagnosed. Intestinal tuberculosis is most frequent in the ileocecal area, followed by the ascending colon, transverse colon, duodenum, stomach, and sigmoid colon, in descending order.”

According to the news reporters, the research concluded: “Hence, we report a case of intestinal tuberculosis in the sigmoid colon, which is rare and almost indistinguishable from colon cancer.”


Our news correspondents report that additional information may be obtained by contacting S.M. Yu, Dept. of Internal Medicine, Bongseng Memorial Hospital, Busan, South Korea. (2012 Dec 24)
University Hospital, Pisa: Evaluation of underreporting tuberculosis in Central Italy by means of record linkage

By a News Reporter-Staff News Editor at Tuberculosis Week – Investigators discuss new findings in Public Health. According to news reporting from Pisa, Italy, by NewsRx journalists, research stated, “Tuberculosis (TB) surveillance systems have some pitfalls outside of a National Tuberculosis Program and lack of efficient surveillance hampers accurate epidemiological quantification of TB burden. In the present study we assessed the quality of surveillance at the University Hospital in Pisa (UHP), Italy, and TB incidence rates over a ten year period (1999-2008).”

The news correspondents obtained a quote from the research from University Hospital, “Assessment of underreporting was done by record-linkage from two sources: databases of TB diagnoses performed in the UHP and the Italian Infectious Disease Surveillance (IIDS) system. Two different databases were examined: a) TB diagnoses reported in the Hospital Discharge Records (HDR) from three Units of UHP (Respiratory Pathophysiology, Pulmonology and Infectious Diseases Units) (TB database A); b) TB diagnoses reported in HDR of all Units of UHP plus TB positive cases obtained by the Laboratory Register (LR) of UHP (TB database B). For the TB database A, the accuracy of TB diagnosis in HDR was assessed by direct examination of the Clinical Record Forms of the cases. For the TB database B, clinical and population data were described, as well as the trend of incidence and underreporting over 10 yrs. In the first study 293 patients were found: 80 patients (27%) with a confirmed TB diagnosis were underreported, 39 of them were microbiologically confirmed. Underreporting was related to age (Reported vs Non Reported, mean age: 49.27 +/- 20 vs 55 +/- 19, p< 0.005), diagnosis (smear positive vs negative cases 18.7 vs 81.2%, p = 0.001), microbiological confirmation (49% vs 51%, p< 0.05), X-ray findings (cavitary vs non-cavitary cases: 12.5 vs 87.5%, p = 0.001) but not to nationality. In the second study, 666 patients were found. Mean underreporting rate was 69.4% and decreased over time (68% in 1999, 48% in 2008). Newly diagnosed TB cases were also found to decrease in number whereas immigration rate increased. Underreporting was related to nationality (Immigrants vs Italians: 18% vs 68%, p< 0.001), diagnosis (microbiological confirmation: 25% vs 75%, p< 0.01), kind of hospital regimen (hospitalized patients vs Day Hospital: 70% vs 16%, p< 0.001), and position of TB code in the HDR (TB code in first position vs in the following position: 39.5% vs 45% p< 0.001). TB is underreported in Pisa, particularly in older patients and those without microbiological confirmation.”
According to the news reporters, the research concluded: “The TB code in first position of HDR seems fairly accurate in confirming TB diagnosis.”


Our news journalists report that additional information may be obtained by contacting L. Melosini, University Hospital, Medical Direct, Pisa, Italy. (2012 Dec 24)

Keck Graduate Institute of Applied Life Sciences, Claremont: Nucleic acid testing for tuberculosis at the point-of-care in high-burden countries

By a News Reporter-Staff News Editor at Life Science Weekly – New research on Molecular Diagnostics is the subject of a report. According to news reporting originating in Claremont, California, by NewsRx journalists, research stated, “Early diagnosis of tuberculosis (TB) facilitates appropriate treatment initiation and can limit the spread of this highly contagious disease. However, commonly used TB diagnostic methods are slow, often insensitive, cumbersome and inaccessible to most patients in TB endemic countries that lack necessary resources.”

The news reporters obtained a quote from the research from the Keck Graduate Institute of Applied Life Sciences, “This review discusses nucleic acid amplification technologies, which are being developed for rapid near patient TB diagnosis, that are in the market or undergoing clinical evaluation. They are based on PCR or isothermal methods and are implemented as manual assays or partially/fully integrated instrument systems, with associated tradeoffs between clinical performance, cost, robustness, quality assurance and usability in remote settings by minimally trained personnel.”

According to the news reporters, the research concluded: “Unmet needs prevail for the identification of drug-resistant TB and for TB diagnosis in HIV-positive and pediatric patients.”

For more information on this research see: Nucleic acid testing for tuberculosis at the point-of-care in high-burden countries. *Expert Review of Molecular Diagnostics*, 2012;12(7):687-701.

Our news correspondents report that additional information may be obtained by contacting A. Niemz, Keck Graduate Institute of Applied Life Sciences, 535 Watson Drive, Claremont, CA 91711, United States. (2012 Dec 18)
Institute of Materials, Beijing: Identification of antituberculosis agents that target ribosomal protein interactions using a yeast two-hybrid system

By a News Reporter-Staff News Editor at Tuberculosis Week – Investigators publish new report on Mycobacterium Infections. According to news reporting originating from Beijing, People’s Republic of China, by NewsRx correspondents, research stated, “Mycobacterium tuberculosis kills about 2 million people annually and antibiotic resistance is a cause of increased mortality. Therefore, development of new antituberculosis drugs is urgent for the control of widespread tuberculosis infections.”

Our news editors obtained a quote from the research from the Institute of Materials, “For this purpose, we performed an innovative screen to identify new agents that disrupt the function of ribosomes in M. tuberculosis. Two bacterial ribosomal proteins L12 and L10 interact with each other and constitute the stalk of the 50S ribosomal subunit, which recruits initiation and elongation factors (EFs) during translation. Therefore, the L12-L10 interaction should be essential for ribosomal function and protein synthesis. We established a yeast two-hybrid system to identify small molecules that block the interaction between L12 and L10 proteins from M. tuberculosis. Using this system, we identified two compounds T766 and T054 that show strong bactericidal activity against tuberculosis but with low toxicity to mice and other bacterial strains. Moreover, using surface plasmon resonance (SPR) assay, we have demonstrated that these compounds bind specifically to L12 to disrupt L12-L10 interaction. Overproduction of L12 protein, but not L10, lowers the antibacterial activity of T766 and T054, indicating that the ribosome is likely the cellular target.”

According to the news editors, the research concluded: “Therefore, our data demonstrate that this yeast two-hybrid system is a useful tool to identify unique antituberculosis agents targeting the ribosomal protein L12-L10 interaction.”


The news editors report that additional information may be obtained by contacting Y. Lin, Chinese Academy Med Sci, Inst Mat Med, State
Protecting the tuberculosis drug pipeline: stating the case for the rational use of fluoroquinolones

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – A new study on Respiratory Research is now available. According to news reporting originating in The Hague, Netherlands, by NewsRx journalists, research stated, “The use of fluoroquinolones (FQs) to treat lower respiratory tract infections (LRTI) other than tuberculosis (TB) allows selection of Fa-resistant TB when TB is misdiagnosed. This study maps national guidelines on the use of FQs for LRTI in Europe and determines the risk of Fa-resistant TB upon FQ treatment before TB diagnosis.”

The news reporters obtained a quote from the research, “A questionnaire was developed to map existing national LRTI and community-acquired pneumonia (CAP) guidelines. A systematic review and meta-analysis were performed to determine the risk of Fa-resistant TB if prescribed FQs prior to TB diagnosis. 15 (80%) out of 24 responding European Respiratory Society national delegates reported having national LRTI management guidelines, seven including recommendations on FQ use and one recommending FQs as the first-choice drug. 18 out of 24 countries had national CAP management guidelines, two recommending FQ as the drug of choice. Six studies investigating FQ exposure and the risk of FQ-resistant TB were analysed. TB patients had a three-fold higher risk of having Fa-resistant TB when prescribed FQs before TB diagnosis, compared to non FQ-exposed patients (OR 2.81, 95% CI 1.47-5.39). Although the majority of European countries hold national LRTI/CAP guidelines, our results suggest that a risk of developing FQ resistance exists.”

According to the news reporters, the research concluded: “Further strengthening of, and adherence to, guidelines is needed to ensure rational use of FQs.”


Our news correspondents report that additional information may be obtained by contacting G.B. Migliori, KNCV TB Fdn, The Hague, Netherlands. (2012 Nov 26)
Catholic University, Taegu: Spontaneously Healed Asymptomatic Pulmonary Tuberculosis: Prevalence of Airflow Obstruction, and Correlation Between High-Resolution CT Findings and Pulmonary Function Tests

By a News Reporter-Staff News Editor at Computer Weekly News – Investigators discuss new findings in Computer-Assisted Tomography. According to news reporting out of Taegu, South Korea, by VerticalNews editors, research stated, “We investigated the relationships between spontaneously healed asymptomatic pulmonary tuberculosis (SHAPTB), airflow obstruction (AFO), and high-resolution computed tomography (HRCT) findings. We selected 82 participants with SHAPTB diagnosed by interferon-gamma release assay and 8044 with normal chest radiographs (CXR).”

Our news journalists obtained a quote from the research from Catholic University, “We applied a CT scoring system for the extent of tuberculous sequelae to correlate the HRCT findings with pulmonary function test. We compared the AFO prevalence between subjects with and without SHAPTB. The subjects with SHAPTB diagnosed by interferon-gamma release assay had a significantly higher prevalence of AFO (13.4% [11/82]) than those with normal CXR (7.4% [595/8044]). The important HRCT findings that correlated with AFO were the number of lung segments with TB sequelae and the CT score for emphysema.”

According to the news editors, the research concluded: “The subjects with SHAPTB had a higher AFO prevalence than those with normal CXR, and the important HRCT findings correlated with AFO were the extent of tuberculous sequelae and emphysema.”


Our news journalists report that additional information may be obtained by contacting K.Y. Lee, Catholic Univ Daegu, Dept. of Radiol Sci, Taegu, South Korea. (2012 Nov 22)
University Hospital, Caen: Pulmonary botryomycosis on a lung cavity: a rare pulmonary infection mimicking cancer

By a News Reporter-Staff News Editor at Tuberculosis Week – A new study on Mycobacterium Infections is now available. According to news reporting originating from Caen, France, by NewsRx correspondents, research stated, “Lung botryomycosis is a rare disease. We report what is to our knowledge the first case occurring on a lung cavity.”

Our news editors obtained a quote from the research from University Hospital, “In a 42-year-old man suffering asthenia and cough, a chest radiograph revealed a right upper lobe opacity. Computed tomography scan showed a necrotic mass which was also spiculated. Repeated research for Mycobacterium tuberculosis was negative. The patient underwent a lobectomy. Histological and bacteriological examinations made the diagnosis of botryomycosis, because the cavity presented numerous colonies of pyogenic Fusobacterium nucleatum bacteria. Botryomycosis is a difficult diagnosis that clinically mimics actinomycosis, tuberculosis or cancer.”

According to the news editors, the research concluded: “In most cases, surgery is necessary to assess diagnosis and treatment.”


The news editors report that additional information may be obtained by contacting M. Heyndrickx, Dept. of Thoracic Surgery, University Hospital Center of Caen, 14000 Caen, France.

Publisher contact information for the journal General Thoracic and Cardiovascular Surgery is: Springer, 233 Spring Street, New York, NY 10013, USA. (2012 Nov 19)

University of Cambridge: Estimating the hidden burden of bovine tuberculosis in great britain

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators publish new report on Computational Biology. According to news reporting from Cambridge, United Kingdom, by NewsRx journalists, research stated, “The number of cattle herds placed under movement restrictions in Great Britain (GB) due to the suspected presence of bovine tuberculosis (bTB) has progressively increased over the past
25 years despite an intensive and costly test-and-slaughter control program. Around 38% of herds that clear movement restrictions experience a recurrent incident (breakdown) within 24 months, suggesting that infection may be persisting within herds.

The news correspondents obtained a quote from the research from the University of Cambridge, “Reactivity to tuberculin, the basis of diagnostic testing, is dependent on the time from infection. Thus, testing efficiency varies between outbreaks, depending on weight of transmission and cannot be directly estimated. In this paper, we use Approximate Bayesian Computation (ABC) to parameterize two within-herd transmission models within a rigorous inferential framework. Previous within-herd models of bTB have relied on ad-hoc methods of parameterization and used a single model structure (SORI) where animals are assumed to become detectable by testing before they become infectious. We study such a conventional within-herd model of bTB and an alternative model, motivated by recent animal challenge studies, where there is no period of epidemiological latency before animals become infectious (SOR). Under both models we estimate that cattle-to-cattle transmission rates are non-linearly density dependent. The basic reproductive ratio for our conventional within-herd model, estimated for scenarios with no statutory controls, increases from 1.5 (0.26-4.9; 95% CI) in a herd of 30 cattle up to 4.9 (0.99-14.0) in a herd of 400. Under this model we estimate that 50% (33-67) of recurrent breakdowns in Britain can be attributed to infection missed by tuberculin testing. However this figure falls to 24% (11-42) of recurrent breakdowns under our alternative model. Under both models the estimated extrinsic force of infection increases with the burden of missed infection.”

According to the news reporters, the research concluded: “Hence, improved herd-level testing is unlikely to reduce recurrence unless this extrinsic infectious pressure is simultaneously addressed.”

For more information on this research see: Estimating the hidden burden of bovine tuberculosis in great britain. Plos Computational Biology, 2012;8(10):e1002730. (Public Library of Science - www.plos.org; Plos Computational Biology - www.ploscompbiol.org)

Our news journalists report that additional information may be obtained by contacting A.J. Conlan, Disease Dynamics Unit (DDU), Dept. of Veterinary Medicine, University of Cambridge, Cambridge, UK. (2012 Nov 13)
Tohoku University Graduate School of Medicine, Sendai: Usefulness of postmortem computed tomography before forensic autopsy for alerting forensic personnel to tuberculosis infection

By a News Reporter-Staff News Editor at Life Science Weekly – Research findings on Mycobacterium Infections are discussed in a new report. According to news reporting from Sendai, Japan, by NewsRx journalists, research stated, “Since May 2009, we have performed multislice computed tomography (MSCT) prior to forensic autopsy for cases of suspicious death. In the present case, innumerable widely scattered nodules in both pulmonary fields on MSCT were indicative of miliary tuberculosis (TB).”

The news correspondents obtained a quote from the research from the Tohoku University Graduate School of Medicine, “At autopsy, both lungs were submerged in formalin fluid immediately after removal from the body. Miliary TB was finally diagnosed based on microscopic findings. TB is a disease that autopsy room workers need to be aware of to protect themselves. Unfortunately, because little medical information about deceased individuals is usually available before forensic autopsy, the diagnosis of TB is frequently not made until autopsy. This leads to a much higher incidence of TB in autopsy room staff members even if they wear protective clothing.”

According to the news reporters, the research concluded: “Therefore, MSCT before forensic autopsy may identify suspected cases of miliary TB in advance and thus help to prevent TB infection in forensic autopsy personnel.”


Our news journalists report that additional information may be obtained by contacting A. Usui, Diagnostic Image Analysis, Tohoku University Graduate School of Medicine, 2-1 Seiryo-machi, Sendai 980-8575, Japan. (2012 Nov 06)
Department of Clinical Microbiology, Auckland: An evaluation of the Xpert MTB/RIF assay and detection of false-positive rifampicin resistance in Mycobacterium tuberculosis

By a News Reporter-Staff News Editor at Tuberculosis Week – New research on Microbiology is the subject of a report. According to news reporting out of Auckland, New Zealand, by NewsRx editors, research stated, “Recent reports suggest that false-positive rifampicin resistance may be assigned by the Xpert MTB/RIF assay.”

Our news journalists obtained a quote from the research from the Department of Clinical Microbiology, “We analysed 169 specimens using the MTB/RIF assay. Using culture as the gold standard, we found that the assay had 100% sensitivity and specificity for detecting M. tuberculosis.”

According to the news editors, the research concluded: “However, we found that the assay incorrectly assigned rifampicin resistance in 4/13 (31%) of cases.”

For more information on this research see: An evaluation of the Xpert MTB/RIF assay and detection of false-positive rifampicin resistance in Mycobacterium tuberculosis. Diagnostic Microbiology and Infectious Disease, 2012;74(2):207-209. Diagnostic Microbiology and Infectious Disease can be contacted at: Elsevier Science Inc, 360 Park Ave South, New York, NY 10010-1710, USA. (Elsevier - www.elsevier.com; Diagnostic Microbiology and Infectious Disease - http://www.elsevier.com/wps/product/cws_home/505759)

Our news journalists report that additional information may be obtained by contacting D.A. Williamson, Auckland Dist Hlth Board, Dept. of Clin Microbiol, Auckland, New Zealand. (2012 Nov 05)

Prince of Songkla University, Songkhla: Physicians’ practices regarding management of antituberculosis drug-induced hepatotoxicity

By a News Reporter-Staff News Editor at Tuberculosis Week – Fresh data on Mycobacterium Infections are presented in a new report. According to news reporting out of Songkhla, Thailand, by NewsRx editors, research stated, “To investigate the practices of physicians regarding the diagnosis and management of antituberculosis drug-induced hepatotoxicity (ATH), a cross sectional descriptive survey using a self-administered questionnaire with multiple choice questions was conducted among physicians who treated adult tuberculosis (TB) patients at 74 public hospitals in southern Thailand. Of the 272 questionnaires mailed, 204 (75%) were returned.”
Our news journalists obtained a quote from the research from the Prince of Songkla University, “Sixty-two physicians (31.0%) said they used alanine aminotransferase (ALT), aspartate aminotransferase (AST) and bilirubin concurrently to diagnose ATH. Only 9.0% of physicians adhered to the American Thoracic Society (ATS) guidelines of using either an ALT or AST level. Nearly all physicians (96.6%) withheld suspected antituberculosis (anti-TB) drugs in their management of ATH patients. While waiting for normalization of liver enzyme, the alternative combination regimen of ethambutol, ofloxacin, and streptomycin (EOS) was used by most physicians (99/197). Of the 197 physicians who withheld anti-TB drugs, 175 (88.8%) decided to reintroduce them. Among these, 169 (96.6%) used a sequential rechallenge method (16.6% prescribed a full dosage, 71.4% prescribed an increasing dosage) and 1 (0.6%) used a simultaneous rechallenge method. Isoniazid was prescribed as the first drug for rechallenge in 77.5% of physicians. Only 6.5% of physicians complied with the ATS guidelines by prescribing rifampicin as the first agent. The reported practices of physicians in the diagnosis and management of ATH noticeably diverged from ATS guidelines.”

According to the news editors, the research concluded: “However, alternative regimen selection and rechallenge method complied with ATS guidelines.”

For more information on this research see: Physicians’ practices regarding management of antituberculosis drug-induced hepatotoxicity. The Southeast Asian Journal of Tropical Medicine and Public Health, 2012;43(3):724-34.

Our news journalists report that additional information may be obtained by contacting W. Thongraung, Dept. of Clinical Pharmacy, Faculty of Pharmaceutical Sciences, Prince of Songkla University, Hat Yai, Songkhla, Thailand. (2012 Nov 05)

Eradication of bovine tuberculosis at a herd-level in Madrid, Spain: study of within-herd transmission dynamics over a 12 year period

By a News Reporter-Staff News Editor at Life Science Weekly – Researchers detail new data in Veterinary Research. According to news reporting originating from Madrid, Spain, by NewsRx correspondents, research stated, “Eradication of bovine tuberculosis (bTB) through the application of test-and-cull programs is a declared goal of developed countries in which the disease is still endemic. Here, longitudinal data from more than 1,700 cattle herds tested during a 12 year-period in the eradication program in the region of Madrid, Spain, were analyzed to quantify the within-herd transmission coefficient (beta) depending on the herd-type (beef/dairy/bullfighting).”
Our news editors obtained a quote from the research, “In addition, the probability to recover the officially bTB free (OTF) status in infected herds depending on the type of herd and the diagnostic strategy implemented was assessed using Cox proportional hazard models. Overall, dairy herds showed higher beta (median 4.7) than beef or bullfighting herds (2.3 and 2.2 respectively). Introduction of interferon-gamma (IFN-gamma) as an ancillary test produced an apparent increase in the beta coefficient regardless of production type, likely due to an increase in diagnostic sensitivity. Time to recover OTF status was also significantly lower in dairy herds, and length of bTB episodes was significantly reduced when the IFN-gamma was implemented to manage the outbreak. Our results suggest that bTB spreads more rapidly in dairy herds compared to other herd types, a likely cause being management and demographic-related factors. However, outbreaks in dairy herds can be controlled more rapidly than in typically extensive herd types.”

According to the news editors, the researchers concluded: “Finally, IFN-gamma proved its usefulness to rapidly eradicate bTB at a herd-level.”

For more information on this research see: Eradication of bovine tuberculosis at a herd-level in Madrid, Spain: study of within-herd transmission dynamics over a 12 year period. *BMC Veterinary Research*, 2012;8():1-8. *BMC Veterinary Research* can be contacted at: Biomed Central Ltd, 236 Grays Inn Rd, Floor 6, London WC1X 8HL, England. (BioMed Central - http://www.biomedcentral.com/; BMC Veterinary Research - http://www.biomedcentral.com/bmcvetres/)

The news editors report that additional information may be obtained by contacting J. Alvarez, Consejería Medio Ambiente Vivienda & Ordenac Terr, Direcc Gen Medio Ambiente, Area Ganaderia, Madrid 28012, Spain. (2012 Oct 16)

**College of Nursing, Pingtung: Association between gallium-67 uptake by lung foci and sputum smear status in patients with pulmonary tuberculosis**

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – Research findings on Mycobacterium Infections are discussed in a new report. According to news reporting from Pingtung, Taiwan, by NewsRx journalists, research stated, “Rapid determination of the inflammatory and sputum smear status in patients with pulmonary tuberculosis (PTB) is crucial for clinical decision making. The purpose of this study was to assess the relationship between gallium-67 (Ga-67) uptake by lung foci and sputum smear status in patients with PTB.”

The news correspondents obtained a quote from the research from the College of Nursing, “We also attempted to predict the patients with
acid-fast bacilli (AFB) smear-positive PTB by means of a semiquantitative measurement of Ga-67 uptake ratio using single-photon emission computed tomography images. Ninety-five patients with PTB were enrolled in this retrospective study. A volume-of-interest method was used to quantify Ga-67 uptake in single-photon emission computed tomography images. The Ga-67 uptake ratio was defined as the maximum voxel value of the pulmonary lesion divided by the maximum voxel value of normal lung tissue. The Ga-67 uptake ratio was higher in patients with active PTB than in those with inactive PTB (3.11 +/- 1.52 vs. 1.42 +/- 0.14, P< 0.01). In active PTB, the Ga-67 uptake ratio was higher in smear-positive patients than in smear-negative patients (3.41 +/- 1.60 vs. 2.16 +/- 0.61, P< 0.01). In patients with AFB smear grades 1+, 2+, and 3+, the Ga-67 uptake ratios were 2.51 +/- 0.81, 3.30 +/- 1.57, and 4.23 +/- 1.73, respectively. The correlation between Ga-67 uptake ratio and AFB smear grading was statistically significant (Spearman’s p=0.60, P< 0.01). In receiver operating characteristic curve analyses, the area under the curve for the Ga-67 uptake ratio was 0.95 +/- 0.02 (P< 0.01) for predicting active PTB and 0.87 +/- 0.04 (P< 0.01) for predicting smear-positive active PTB. In patients with active PTB, more-intense Ga-67 uptake was associated with more AFB load in the sputum - that is a greater potential to transmit PTB.”

According to the news reporters, the researchers concluded: “This finding might facilitate clinical decision making for immediate isolation and treatment to reduce transmission of PTB.”

For more information on this research see: Association between gallium-67 uptake by lung foci and sputum smear status in patients with pulmonary tuberculosis. Nuclear Medicine Communications, 2012;33(9):941-946. Nuclear Medicine Communications can be contacted at: Lippincott Williams & Wilkins, 530 Walnut St, Philadelphia, PA 19106-3621, USA. (Lippincott Williams and Wilkins - www.lww.com; Nuclear Medicine Communications - http://journals.lww.com/nuclearmedicinecomm/pages/default.aspx)

Our news journalists report that additional information may be obtained by contacting C.C. Hsu, Meiho Univ, Coll Nursing & Hlth, Dept. of Nursing, Pingtung, Taiwan. (2012 Sep 24)

National Taiwan University, Taipei: Epidemiologic surveillance to detect false-positive Mycobacterium tuberculosis cultures

By a News Reporter-Staff News Editor at Tuberculosis Week – Current study results on Microbiology have been published. According to news reporting from Taipei, Taiwan, by NewsRx journalists, research
stated, “This study was aimed to investigate the ability of potential indices from epidemiologic surveillance to detect false-positive cultures of Mycobacterium tuberculosis (MTB). All clinical specimens for mycobacterial culture from April 1 to August 31, 2010, were reviewed.”

The news correspondents obtained a quote from the research from National Taiwan University, “Single-positive cultures without relevant clinical and pathologic information were categorized as suspected false-positive cultures. Genotyping methods were used to confirm false-positive cultures. The performance of epidemiologic surveillance indices to detect potential false-positive cultures was evaluated. A total of 14,462 specimens were sent to the laboratory and 214 batches were processed in 107 work days (average 67.6 specimens per batch, ranging from 21 to 130 specimens per batch). Seventy-one single-positive cultures were identified, among which 5 cultures of multidrug-resistant MTB in 1 batch were false-positive, confirmed by genotyping methods. Epidemiologic surveillance with statistical process control charts for single-positive cultures per day showed good performance in epidemiologic surveillance. The false-positive rate was 38.5% in the 13 potential false-positive cultures according to the statistical process control chart for single-positive cultures per day. Although the incidence of tuberculous disease is high in Taiwan, clustering of multidrug-resistant MTB in 1 batch or clustering of single-positive cultures still suggested the occurrence of false-positive MTB cultures.”

According to the news reporters, the researchers concluded: “Therefore, epidemiologic surveillance for the clustering of single-positive cultures with the statistical process control chart could be used to monitor the occurrence of false-positive results.”

For more information on this research see: Epidemiologic surveillance to detect false-positive Mycobacterium tuberculosis cultures. Diagnostic Microbiology and Infectious Disease, 2012;73(4):343-349. Diagnostic Microbiology and Infectious Disease can be contacted at: Elsevier Science Inc, 360 Park Ave South, New York, NY 10010-1710, USA. (Elsevier - www.elsevier.com; Diagnostic Microbiology and Infectious Disease - http://www.elsevier.com/wps/product/cws_home/505759)

Our news journalists report that additional information may be obtained by contacting M.R. Lee, National Taiwan University, Coll Med, Dept. of Clin Lab Sci & Med Biotechnol, National Taiwan University, Taipei 10764, Taiwan. (2012 Sep 24)
Knowledge as a factor in vulnerability to tuberculosis among nursing students and professionals

By a News Reporter-Staff News Editor at Computer Weekly News – Current study results on Mycobacterium Infections have been published. According to news reporting originating in Jundiai, Brazil, by Vertical-News journalists, research stated, “The objective of this study was to identify vulnerability to tuberculosis (TB) related to knowledge about the disease among 76 nursing students and professionals. A quantitative descriptive study was conducted using a closed questionnaire for the collection of data regarding transmission, preventive and biosafety measures, diagnosis, and prejudice regarding the disease.”

The news reporters obtained a quote from the research, “The SAS software version 9.1.3 was used for data analysis, with the level of significance set at 5% (p <0.05). Nursing students and professionals showed a vulnerability to TB related to knowledge about transmission, preventive and biosafety measures, and diagnosis of the disease. With respect to transmission, vulnerability was higher among nursing professionals.”

According to the news reporters, the researchers concluded: “The results indicate the need for investment by healthcare institutions surrounding this topic in view of the important role of nursing in the establishment of strategies for prevention and control of the disease.”

For more information on this research see: Knowledge as a factor in vulnerability to tuberculosis among nursing students and professionals. *Revista Da Escola De Enfermagem Da U.S.P*, 2012;46(3):696-703.

Our news correspondents report that additional information may be obtained by contacting T.V. Mussi, Nursing Department, Faculdade de Medicina de Jundiai, Jundiai, Brazil. *(2012 Sep 20)*

Bovine tuberculosis surveillance alternatives in Belgium

By a News Reporter-Staff News Editor at Life Science Weekly – New research on Mycobacterium Infections is the subject of a report. According to news reporting originating in Brussels, Belgium, by NewsRx journalists, research stated, “Belgium obtained the bovine tuberculosis (bTB) officially free status in 2003 (EC Decision 2003/467/EC). This study was carried out to evaluate the components of the current bTB surveillance program in Belgium and to determine the sensitivity of this program.”

The news reporters obtained a quote from the research, “Secondly, alternatives to optimize the bTB surveillance in accordance with European legislation (Council Directive 64/432/EEC) were evaluated. Separate scenario trees were designed for each active surveillance component of the bTB surveillance program. Data from 2005 to 2009 regarding cattle population, movement and surveillance were collected to feed
the stochastic scenario tree simulation model. A total of 7,403,826 cattle movement history records were obtained for the 2,678,020 cattle from 36,059 cattle herds still active in 2009. The current surveillance program sensitivity as well as the impact of alternative surveillance protocols was simulated in a stochastic model using 10,000 iterations per simulation. The median (50% percentile) of the component sensitivities across 10,000 iterations was 0.83, 0.85, 0.99, 0.99, respectively, for (i) testing the cattle only during the winter screening, (ii) testing only imported cattle, (iii) testing only purchased cattle and (iv) testing only all slaughtered cattle. The sensitivity analysis showed that the most influential input parameter explaining the variability around the output came from the uncertainty distribution around the sensitivity of the diagnostic tests used within the bTB surveillance. Providing all animals are inspected and post mortem inspection is highly sensitive, slaughterhouse surveillance was the most effective surveillance component. If these conditions were not met, the uncertainty around the mean sensitivity of this component was important.”

According to the news reporters, the researchers concluded: “Using an antibody ELISA at purchase and an interferon gamma test during winter screening and at import would increase greatly the sensitivity and the confidence level of Belgium’s freedom from bTB infection status.”

For more information on this research see: Bovine tuberculosis surveillance alternatives in Belgium. Preventive Veterinary Medicine, 2012;106(2):152-61. (Elsevier - www.elsevier.com; Preventive Veterinary Medicine - http://www.elsevier.com/wps/product/cws_home/503315)

Our news correspondents report that additional information may be obtained by contacting S. Welby, Unit for Co-ordination of Veterinary Diagnostics, Epidemiology and Risk Analysis (CVD-ERA), Groeselberg 99, B-1180 Brussels, Belgium. (2012 Sep 18)

Department of Radiology, Kolhapur: Tuberculosis of the parotid gland

By a News Reporter-Staff News Editor at Tuberculosis Week – A new study on Mycobacterium Infections is now available. According to news originating from Kolhapur, India, by NewsRx correspondents, research stated, “Parotid gland involvement is extremely rare, even in countries in which tuberculosis is endemic. Clinically, it usually presents as a slow-growing mass indistinguishable from a malignancy.”

Our news journalists obtained a quote from the research from the Department of Radiology, “On imaging too, tuberculosis of the parotid may mimic neoplasm. The diagnosis of parotid tuberculosis needs a high degree of clinical suspicion.”
According to the news editors, the researchers concluded: “This paper highlights the clinical presentation, imaging findings, and importance of FNAC in diagnosis of this rare entity.”

For more information on this research see: Tuberculosis of the parotid gland. *Case Reports In Radiology*, 2012;2012():278793. (Hindawi Publishing - www.hindawi.com; Case Reports In Radiology - http://www.hindawi.com/crim/radiology/)

The news correspondents report that additional information may be obtained from V. Gupta, Dept. of Radiology, Apple Hospital, Kolhapur 416001, India. *(2012 Sep 17)*

**University of Pittsburgh Medical Center: Cytomorphology of unusual infectious entities in the Pap test**

By a News Reporter-Staff News Editor at Clinical Oncology Week – Research findings on Mycobacterium Infections are discussed in a new report. According to news reporting from Pittsburgh, Pennsylvania, by NewsRx journalists, research stated, “Rare entities in the Pap test, including neoplastic and non-neoplastic conditions, pose challenges due to their infrequent occurrence in the daily practice of cytology. Furthermore, these conditions give rise to important diagnostic pitfalls.”

The news correspondents obtained a quote from the research from the University of Pittsburgh Medical Center, “Infections such as tuberculosis cervicitis may be erroneously diagnosed as carcinoma, whereas others, such as schistosomiasis, are associated with squamous cell carcinoma. These cases include granuloma inguinale (donovanosis), tuberculosis, coccidioidomycosis, schistosomiasis, taeniasis, and molluscum contagiosum diagnosed in Pap tests. Granuloma inguinale shows histiocytes that contain intracytoplasmic bacteria (Donovan bodies). Tuberculosis is characterized by necrotizing granulomatous inflammation with Langhans-multinucleated giant cells. Coccidioidomycosis may show large intact or ruptured fungal spherules associated with endospores. Schistosoma haematobium is diagnosed by finding characteristic ova with a terminal spine. Molluscum contagiosum is characterized by the appearance of squamous cells with molluscum bodies.”

According to the news reporters, the researchers concluded: “This article reviews the cytomorphology of selected rare infections and focuses on their cytomorphology, differential diagnosis, and role of ancillary diagnostic studies.”


Our news journalists report that additional information may be obtained by contacting W.E. Khalbuss, Dept. of Pathology, University of
Department of Biochemistry and Molecular Biology, Dalian: Identification of amino acids involved in catalytic process of *M. tuberculosis* GlmU acetyltransferase

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators publish new report on Enzymes and Coenzymes. According to news reporting out of Dalian, People’s Republic of China, by NewsRx editors, research stated, “*M. tuberculosis* GlmU is a bifunctional enzyme with acetyltransferase activity in C-terminus and uridyltransferase activity in N-terminus, and it is involved in the biosynthesis of glycosyl donor UDP-N-acetylglucosamine (UDP-GlcNAc). The crystal structure of *M. tuberculosis* GlmU clearly determines the active site and catalytic mechanism of GlmU uridyltransferase domain but not succeed in GlmU acetyltransferase domain.”

Our news journalists obtained a quote from the research from the Department of Biochemistry and Molecular Biology, “Sequence comparison analysis revealed highly conserved amino acid residues in the C-terminus between *M. tuberculosis* GlmU and GlmU enzymes from other bacteria. To find the essential amino acids related to *M. tuberculosis* GlmU acetyltransferase activity, we substituted 10 conserved amino acids in the acetyltransferase domain of *M. tuberculosis* GlmU by site-directed mutagenesis. All the mutant GlmU proteins were largely expressed in soluble and purified by affinity chromatography. Enzyme assays showed that K362A, H374A, Y398A and W460A mutants abolished more than 90 % activity of *M. tuberculosis* GlmU acetyltransferase and totally lost the affinity with two substrates, suggesting the potential substrate-binding functions.”

According to the news editors, the researchers concluded: “However, K403A, S416A, N456A and E458A mutants exhibited decreased GlmU acetyltransferase activity and lower kinetic parameters, probably responsible for substrate releasing by conformation shifting.”


Our news journalists report that additional information may be obtained by contacting Y. Zhou, Dept. of Biochemistry and Molecular Biology, Dalian Medical Universtiy, Dalian, 116044, People’s Taiwan.

Publisher contact information for the *Glycoconjugate Journal* is: Springer, 233 Spring Street, New York, NY 10013, USA. (2012 Sep 11)
Department of Biochemistry and Molecular Biology, Liaoning: Identification of M. tuberculosis Rv3441c and M. smegmatis MSMEG_1556 and Essentiality of M. smegmatis MSMEG_1556

By a News Reporter-Staff News Editor at Tuberculosis Week – A new study on Mycobacterium Infections is now available. According to news reporting out of Liaoning, People’s Republic of China, by NewsRx editors, research stated, “The normal growth of mycobacteria attributes to the integrity of cell wall core which consists of peptidoglycan (PG), arabinogalactan (AG) and mycolic acids. N-acetyl glucosamine (GlcNAc) is an essential component in both PG and AG of mycobacterial cell wall.”

Our news journalists obtained a quote from the research from the Department of Biochemistry and Molecular Biology, “The biosynthetic pathway for UDP-N-acetylglucosamine (UDP-GlcNAc), as a sugar donor of GlcNAc, is different in prokaryotes and eukaryotes. The conversion of glucosamine-6-phosphate to glucosamine-1-phosphate, which is catalyzed by phosphoglucomutase (GlmM), is unique to prokaryotes. Bioinformatic analysis showed that Msm MSMEG_1556 and Mtb Rv3441c are homologous to Ec GlmM. In this study, soluble Msm MSMEG_1556 protein and Mtb Rv3441c protein were expressed in E. coli BL21(DE3) and their phosphoglucomutase activity were detected. In order to further investigate the essentiality of MSMEG_1556 for the growth of M. smegmatis, we generated a conditional MSMEG_1556 knockout mutant, which harbored thermo-sensitive rescue plasmid carrying Mtb Rv3441c. As the rescue plasmid was unable to complement MSMEG_1556 deficiency at 42°C, MSMEG_1556 knockout mutant did not grow. The dramatic morphological changes of MSMEG_1556 knockout mutant after temperature shift from 30°C to 42°C have been observed by scanning electron microscope. These results demonstrated that MSMEG_1556 is essential for growth of M. smegmatis.”

According to the news editors, the researchers concluded: “This study provided evidence that GlmM enzyme could be as a potential target for developing anti-tuberculosis drugs.”

For more information on this research see: Identification of M. tuberculosis Rv3441c and M. smegmatis MSMEG_1556 and Essentiality of M. smegmatis MSMEG_1556. Plos One, 2012;7(8):e42769. (Public Library of Science - www.plos.org; Plos One - www.plosone.org)

Our news journalists report that additional information may be obtained by contacting S. Li, Dept. of Biochemistry and Molecular Biology, Dalian Medical University, Dalian, Liaoning, People’s Taiwan. (2012 Sep 10)
Western Michigan University, Kalamazoo: Pouched rats’ detection of tuberculosis in human sputum: comparison to culturing and polymerase chain reaction

By a News Reporter-Staff News Editor at Tuberculosis Week – Investigators discuss new findings in Mycobacterium Infections. According to news reporting originating in Kalamazoo, Michigan, by NewsRx journalists, research stated, “Tanzania. To compare microscopy as conducted in direct observation of treatment, short course centers to pouched rats as detectors of *Mycobacterium tuberculosis*.”

The news reporters obtained a quote from the research from Western Michigan University, “Ten pouched rats were trained to detect tuberculosis in sputum using operant conditioning techniques. The rats evaluated 910 samples previously evaluated by smear microscopy. All samples were also evaluated through culturing and multiplex polymerase chain reaction was performed on culture growths to classify the bacteria. The patientwise sensitivity of microscopy was 58.0%, and the patient-wise specificity was 97.3%. Used as a group of 10 with a cutoff (defined as the number of rat indications to classify a sample as positive for *Mycobacterium tuberculosis*) of 1, the rats increased new case detection by 46.8% relative to microscopy alone. The average samplewise sensitivity of the individual rats was 68.4% (range 61.1-73.8%), and the mean specificity was 87.3% (range 84.7-90.3%).”

According to the news reporters, the researchers concluded: “These results suggest that pouched rats are a valuable adjunct to, and may be a viable substitute for, sputum smear microscopy as a tuberculosis diagnostic in resource-poor countries.”

For more information on this research see: Pouched rats’ detection of tuberculosis in human sputum: comparison to culturing and polymerase chain reaction. *Tuberculosis Research and Treatment*, 2012;2012():716989. (Hindawi Publishing - www.hindawi.com; Tuberculosis Research and Treatment - http://www.hindawi.com/journals/trt/)

Our news correspondents report that additional information may be obtained by contacting A. Mahoney, Dept. of Psychology, Western Michigan University, Kalamazoo, MI 49008-5200, United States. (2012 Sep 10)
University of Washington, Seattle: TB infection in the nonhuman primate biomedical model: Tip of the iceberg?

By a News Reporter-Staff News Editor at Tuberculosis Week – Investigators discuss new findings in Mycobacterium Infections. According to news originating from Seattle, Washington, by NewsRx correspondents, research stated, “Biomedical research in the 21st century increasingly relies on pathogen-free nonhuman primates (NHPs) to model human pathophysiology. Despite adherence to protocols designed to maintain pathogen-free colonies, reports of tuberculosis regularly appear.”

Our news journalists obtained a quote from the research from the University of Washington, “We hypothesize that, undetected by standard screening protocols, mycobacteria of the Mycobacterium tuberculosis complex (MTBC) continue to circulate in established NHP colonies and may, in addition, be periodically reintroduced with newly imported animals. The tuberculin skin test (TST), the accepted standard screening test for tuberculosis, relies on the host’s immune response to detect infection, but empirical data suggest that TST lacks both specificity and, particularly in certain NHP species and in immune compromised animals, sensitivity. In order to improve the detection of MTBC infection in NHP colonies we propose new screening protocols that incorporate molecular methods to detect mycobacteria. These new tests do not rely on the host’s immune response and may allow for strain typing of the pathogens -enhancing our ability to elucidate patterns of disease transmission.”

According to the news editors, the researchers concluded: “Moreover, the ability to rapidly and noninvasively collect specimens could lead to an improved appreciation of the burden of MTBC circulating in populations of NHPs and humans, including drug-resistant strains, data that are invaluable to public health efforts.”


The news correspondents report that additional information may be obtained from A.K. Wilbur, University of Washington, National Primate Research Center, Evolutionary Emergence of Infectious Diseases Laboratory, 1705 Pacific St NE, HSB, I-039, Seattle, WA, United States. (2012 Aug 27)
Ondokuz Mayis University, Samsun: Comparative evaluation of the microplate nitrate reductase assay and the rezasurin microtitre assay for the rapid detection of multidrug resistant Mycobacterium tuberculosis clinical isolates

By a News Reporter-Staff News Editor at Tuberculosis Week – Data detailed on Mycobacterium Infections have been presented. According to news originating from Samsun, Turkey, by NewsRx correspondents, research stated, “The microplate nitrate reductase assay (MNRA) and the rezasurin microtitre assay (REMA) were used for the susceptibility testing of 73 clinical isolates and the results were compared with those that were obtained using the Bactec 460 TB and Bactec MGIT 960 systems. The REMA and the MNRA were performed in 96-well plates.”

Our news journalists obtained a quote from the research from Ondokuz Mayis University, “For the REMA, the concentrations of isoniazid (INH) and rifampicin (RIF) ranged from 1.0-0.01 g/mL and 2.0-0.03 g/mL, respectively. For the MNRA, the INH concentration was between 1.0-0.03 g/mL and the RIF concentration was between 2.0-0.06 g/mL. For the MNRA, the sensitivity, specificity, positive predictive value, negative predictive value and INH/RIF agreement were 100/95.6, 97.6/100, 96.8/100, 100/98 and 98.6/98.6, respectively, and for the REMA, they were 100/91.3, 90.4/100, 88.5/100, 100/96.1 and 94.5/97.2, respectively.”

According to the news editors, the researchers concluded: “Our data suggest that these two rapid, low-cost methods may be inexpensive, alternative assays for the rapid detection of multidrug resistant tuberculosis in low-income countries.”

For more information on this research see: Comparative evaluation of the microplate nitrate reductase assay and the rezasurin microtitre assay for the rapid detection of multidrug resistant Mycobacterium tuberculosis clinical isolates. Memorias Do Instituto Oswaldo Cruz, 2012;107(5):578-81.

The news correspondents report that additional information may be obtained from A.Y. Coban, Dept. of Medical Microbiology, Medical School, Ondokuz Mayis University, Samsun, Turkey. (2012 Aug 20)
Seoul National University: Positive Tuberculin Skin Test or Interferon-Gamma Release Assay in Patients with Radiographic Lesions Suggesting Old Healed Tuberculosis

By a News Reporter-Staff News Editor at Tuberculosis Week – Fresh data on Mycobacterium Infections are presented in a new report. According to news reporting out of Seoul, South Korea, by NewsRx editors, research stated, “Radiographic lesions suggesting old healed tuberculosis (TB) is considered a risk factor for the subsequent development of active TB. The aim of this study was to estimate the positive rates of tuberculin skin test (TST) and interferon-gamma release assay (IGRA) in persons with old healed TB.”

Our news journalists obtained a quote from the research from Seoul National University, “Participants with lesions suggesting old healed TB on chest images and controls without such lesions were prospectively enrolled between January 1, 2010, and January 31, 2011. TST and the QuantiFERON-TB Gold In-Tube test (QFT-GIT) were performed. In total, 193 participants with old healed TB and 126 controls were recruited. The rates of positive TST and QFT-GIT among patients with old healed TB were 54.6% and 77.7%, respectively. The rates of positive TST and QFT-GIT among patients without old healed TB were 38.9% and 61.9%. Sixteen percent of participants with old healed TB showed negative results by both TST and QFT-GIT. The positive rate of TST waned among participants with old healed TB who were older than 60 yr, whereas QFT-GIT positivity was unaffected by age. The positive rates of TST and IGRA among participants with radiographic lesions suggesting old healed TB was higher than without those lesions.”

According to the news editors, the researchers concluded: “In addition, IGRA may be more accurate than TST for the detection of latent TB infection, especially in populations of individuals older than 60 yr.”

For more information on this research see: Positive Tuberculin Skin Test or Interferon-Gamma Release Assay in Patients with Radiographic Lesions Suggesting Old Healed Tuberculosis. Journal of Korean Medical Science, 2012;27(7):761-766. Journal of Korean Medical Science can be contacted at: Korean Acad Medical Sciences, 302 75 Dong Du Ichon, Dong Yongsan Ku, Seoul 140 031, South Korea.

Our news journalists report that additional information may be obtained by contacting Y.J. Jeong, Seoul National University, Dept. of Radiol, Coll Med, Seoul 110744, South Korea. (2012 Aug 20)
Seoul National University College of Medicine: Positive tuberculin skin test or interferon-gamma release assay in patients with radiographic lesion suggesting old healed tuberculosis

By a News Reporter-Staff News Editor at Tuberculosis Week – Current study results on Mycobacterium Infections have been published. According to news reporting from Seoul, South Korea, by NewsRx journalists, research stated, “Radiographic lesions suggesting old healed tuberculosis (TB) is considered a risk factor for the subsequent development of active TB. The aim of this study was to estimate the positive rates of tuberculin skin test (TST) and interferon-gamma release assay (IGRA) in persons with old healed TB.”

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For more information on this research see: Positive tuberculin skin test or interferon-gamma release assay in patients with radiographic lesion suggesting old healed tuberculosis. *Journal of Korean Medical Science*, 2012;27(7):761-6.

Our news journalists report that additional information may be obtained by contacting Y.J. Jeong, Division of Pulmonary and Critical Care Medicine, Dept. of Internal Medicine, Seoul National University College of Medicine, Seoul, South Korea. (2012 Aug 06)
Columbia University, New York City: Assessing capacity for diagnosing tuberculosis in children in sub-Saharan African HIV care settings

By a News Reporter-Staff News Editor at Ivy League Week – Research findings on Mycobacterium Infections are discussed in a new report. According to news originating from New York City, New York, by NewsRx correspondents, researchers stated “Research on the prevalence of pediatric-specific tuberculosis (TB) diagnostics in sub-Saharan Africa is scarce. We assessed the availability of pediatric TB diagnostic tests at 651 pediatric human immunodeficiency virus care and treatment sites across nine African countries: 54% of the sites had access to sputum culture capacity and 51% to chest X-ray services.”

Our news journalists obtained a quote from the research from Columbia University, “While 87% of sites had access to smear microscopy, only 6% had the capacity to perform sputum induction and 5% to perform gastric aspirate. These findings confirm that diagnostic resources for the accurate diagnosis of pediatric TB are limited.”

According to the news editors, the researchers concluded: “Capacity-building initiatives to improve sputum collection in children are urgently required.”


The news correspondents report that additional information may be obtained from M.J.A. Reid, Columbia University, Mailman Sch Public Hlth, Int Center AIDS Care & Treatment Programs, New York, NY, United States. *(2012 Jul 31)*

Aga Khan University Hospital, Karachi: Laryngeal tuberculosis presenting as laryngeal carcinoma

By a News Reporter-Staff News Editor at Gastroenterology Week – Current study results on Mycobacterium Infections have been published. According to news reporting from Karachi, Pakistan, by NewsRx journalists, researchers stated “Tuberculosis (TB) accounts for the highest number of mortalities among infectious diseases worldwide. Laryngeal TB is an extremely rare presentation of TB.”

The news correspondents obtained a quote from the research from Aga Khan University Hospital, “It has many similarities to laryngeal carcinoma, one of the three most common cancers among males in the city, with an age standardized rate of 8.6. The associated risk factors
of laryngeal carcinoma i.e. smoking, paan, betel nut usage and alcohol use also tend to be concentrated in the same demographic background as that of TB, creating a diagnostic dilemma. We present a case of granulomatous laryngeal TB, in a 40 year old male, with characteristic presenting features of laryngeal carcinoma i.e. persistent hoarseness and weight loss. He had no associated symptoms of fever, night sweats, cough or dysphagia, nor did he have any history of tobacco or irritant use. There was no history of tuberculosis (TB) contact. He was initially worked up for laryngeal carcinoma; however laryngoscopic biopsy revealed laryngeal TB.”

According to the news reporters, the researchers concluded: “We present this case to emphasize the point that although primary laryngeal tuberculosis is a rarity, it must not be overlooked as a possibility when evaluating dysphonia and/or considering laryngeal carcinoma.”


Our news journalists report that additional information may be obtained by contacting A. Suhail, Dept. of Otorhinolaryngology, Head & Neck Surgery, Aga Khan University Hospital, Karachi, Pakistan. (2012 Jul 30)

**Institute of Biophysics and Biomedical Engineering, Sofia: Structure-activity relationships of pyrrole hydrazones as new anti-tuberculosis agents**

By a News Reporter-Staff News Editor at Drug Week – Data detailed on Medicinal Chemistry have been presented. According to news reporting originating in Sofia, Bulgaria, by NewsRx journalists, researchers stated “Preliminary investigations of our research team have shown that some pyrrole hydrazones posses strong inhibitory activity against the tuberculosis bacilli, and thus represent a new perspective for development of anti-tuberculosis agents. In this work the anti-tuberculosis activity of an in-house series of pyrrole hydrazones was investigated by quantitative structure-activity relationships (QSAR) analysis and by pharmacophore modelling.”

The news reporters obtained a quote from the research by the authors from the Institute of Biophysics and Biomedical Engineering, “Different constitutional, topological, physicochemical, and quantum-mechanical descriptors of the chemical structure were calculated. The QSAR models included the number of chlorine, fluorine and nitrogen atoms, molecular flexibility and shape indexes, and magnitudes of charged molecular surfaces areas and hydrophobic volumes, suggesting importance of these structural characteristics for the activity. Next, a pharmacophore analysis was applied.”
According to the news reporters, the researchers concluded: “A possible pharmacophore responsible for the compound interactions with their biological target in the 3D space consisted of five features, including hydrophobic centres, a potential H-bond acceptor and a potential metal ligator.”


Our news correspondents report that additional information may be obtained by contacting I. Lessigiaraska, Institute of Biophysics and Biomedical Engineering, Bulgarian Academy of Sciences, Acad G Bonchev Str, bl 105, 1113 Sofia, Bulgaria. (2012 Jul 27)

**Clinical Microbiology Laboratory, Palo Alto: Can a Simple Flotation Method Lower the Limit of Detection of *Mycobacterium tuberculosis* in Extrapulmonary Samples Analyzed by the GeneXpert MTB/RIF Assay?**

By a News Reporter-Staff News Editor at Tuberculosis Week – Researchers detail new data in Clinical Microbiology. According to news reporting originating from Palo Alto, California, by NewsRx correspondents, researchers stated “The rapid and accurate diagnosis of tuberculosis (TB) in children and extrapulmonary TB in adults continues to be a challenge. In this study, we determined the lower limit of detection (LOD) of the GeneXpert MTB/RIF assay with nonrespiratory specimens and investigated the utility of flotation procedures for concentrating the bacilli.”

Our news editors obtained a quote from the research by the authors from Clinical Microbiology Laboratory, “Clinical specimens (9 cerebrospinal fluid [CSF], 13 gastric aspirate, 8 tissue, and 17 stool) were spiked with single-celled *Mycobacterium tuberculosis*, and the LOD of the GeneXpert assay was determined. Flotation studies were conducted with sucrose and NaCl, and the cycle thresholds of the MTB/RIF assay were compared between treated and untreated samples. There was no significant difference between the LODs of the GeneXpert assay with saline solution (median, 33 CFU/ml) and CSF (median, 25 CFU/ml) (p >0.05) or gastric aspirate samples (median, 58 CFU/ml) (p >0.05). The LOD with spiked tissue (median, 1,525 CFU/ml) and stool samples (median, 6,800 CFU/ml) was significantly elevated compared to that determined with saline solution (p=0.05 and=0.0005, respectively). Flotation studies with sucrose or NaCl did not consistently result in lowered cycle thresholds in stool or gastric aspirates, but a cycle reduction of
&gt;10 was achieved in two of the three pooled CSF samples. Unlike the results seen with tissue and stool samples, there was no significant PCR inhibition in the MTB/RIF assay with CSF and gastric aspirates.”

According to the news editors, the researchers concluded: “Although preconcentration of CSF samples with sucrose and NaCl may enhance detection of *M. tuberculosis* by PCR, further advances are needed to concentrate the bacilli and eliminate PCR inhibitors in paucibacillary nonrespiratory samples.”


The news editors report that additional information may be obtained by contacting N. Taylor, Clinical Microbiology Laboratory, Stanford Hospital and Clinics, Palo Alto, California, United States. (2012 Jul 16)

**Kyungpook National University, Daegu:** Clinical value of whole-blood interferon-gamma assay in patients with suspected pulmonary tuberculosis and AFB smear- and polymerase chain reaction-negative bronchial aspirates

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – Current study results on Mycobacterium Infections have been published. According to news reporting originating in Daegu, South Korea, by NewsRx journalists, researchers stated “Combining a polymerase chain reaction (PCR) test with bronchoscopy is frequently performed to allow a rapid diagnosis of smear-negative pulmonary tuberculosis (PTB). However, limited data are available concerning clinical judgment in patients with suspected PTB and AFB smear-and PCR-negative bronchial aspirates (BA).”

The news reporters obtained a quote from the research by the authors from Kyungpook National University, “The present study evaluated the usefulness of whole-blood QuantiFERON-TB Gold In-Tube (QFT) testing in these patients. Of 166 patients with suspected PTB who had undergone bronchoscopy because of smear-negative sputum or inadequate sputum production, 93 (56%) were diagnosed with culture-positive PTB. Seventy-four patients were either AFB smear-or PCR-positive. In the 75 patients whose BA AFB smear and PCR results were both negative, 19 were finally diagnosed with PTB by culture. The QFT test had a negative predictive value of 91% for PTB.”

According to the news reporters, the researchers concluded: “The QFT test may be useful for excluding PTB in patients with suspected PTB whose BA AFB smear and PCR results are both negative.”

Our news correspondents report that additional information may be obtained by contacting J. Lee, Dept. of Internal Medicine, Kyungpook National University, School of Medicine, Daegu, South Korea. (2012 Jul 16)

**Biosciences Institute, Antrim: Fasciola hepatica is associated with the failure to detect bovine tuberculosis in dairy cattle**

By a News Reporter-Staff News Editor at Life Science Weekly – A new study on General Science is now available. According to news reporting originating in Antrim, United Kingdom, by NewsRx journalists, researchers stated “Bovine tuberculosis (BTB) is a significant and intractable disease of cattle caused by Mycobacterium bovis. In the United Kingdom, despite an aggressive eradication programme, the prevalence of BTB is increasing with an unexplained, exponential rise in cases year on year.”

The news reporters obtained a quote from the research by the authors from Biosciences Institute, “Here we show in a study involving 3,026 dairy herds in England and Wales that there is a significant negative association between exposure to the common, ubiquitous helminth parasite, Fasciola hepatica and diagnosis of BTB. The magnitude of the single intradermal comparative cervical tuberculin test used to diagnose BTB is reduced in cattle experimentally co-infected with M. bovis and F. hepatica. We estimate an under-ascertainment rate of about one-third (95% confidence interval 27-38%) among our study farms, in the hypothetical situation of no exposure to F. hepatica.”

According to the news reporters, the researchers concluded: “This finding may in part explain the continuing spread of BTB and the failure of the current eradication programme in the United Kingdom.”

University of Toronto: From the Mouths of Monkeys: Detection of Mycobacterium tuberculosis Complex DNA From Buccal Swabs of Synanthropic Macaques

By a News Reporter-Staff News Editor at Life Science Weekly – Fresh data on Tuberculosis are presented in a new report. According to news originating from Toronto, Canada, by NewsRx correspondents, researchers stated “Although the Mycobacterium tuberculosis complex (MTBC) infects a third of all humans, little is known regarding the prevalence of mycobacterial infection in nonhuman primates (NHP). For more than a century, tuberculosis has been regarded as a serious infectious threat to NHP species.”

Our news journalists obtained a quote from the research by the authors from the University of Toronto, “Advances in the detection of MTBC open new possibilities for investigating the effects of this poorly understood pathogen in diverse populations of NHP. Here, we report results of a cross-sectional study using well-described molecular methods to detect a nucleic acid sequence (IS6110) unique to the MTBC. Sample collection was focused on the oral cavity, the presumed route of transmission of MTBC. Buccal swabs were collected from 263 macaques representing 11 species in four Asian countries and Gibraltar. Contexts of contact with humans included free ranging, pets, performing monkeys, zoos, and monkey temples. Following DNA isolation from buccal swabs, the polymerase chain reaction (PCR) amplified IS6110 from 84 (31.9%) of the macaques. In general, prevalence of MTBC DNA was higher among NHP in countries where the World Health Organization reports higher prevalence of humans infected with MTBC. This is the first demonstration of MTBC DNA in the mouths of macaques. Further research is needed to establish the significance of this finding at both the individual and population levels.”

According to the news editors, the researchers concluded: “PCR of buccal samples holds promise as a method to elucidate the mycobacterial landscape among NHP, particularly macaques that thrive in areas of high human MTBC prevalence. Am. J. Primatol. 74:676-686, 2012.”

For more information on this research see: From the Mouths of Monkeys: Detection of Mycobacterium tuberculosis Complex DNA From Buccal Swabs of Synanthropic Macaques. American Journal of Primatology, 2012;74(7):676-686. American Journal of Primatology can be contacted at: Wiley-Blackwell, 111 River St, Hoboken 07030-5774, NJ,

The news correspondents report that additional information may be obtained from A.K. Wilbur, Univ Toronto Scarborough, Toronto, ON, Canada. (2012 Jul 03)

**World Health Organization, New Delhi: Capilia test for identification of Mycobacterium tuberculosis in MGIT &#8482;-positive cultures**

By a News Reporter-Staff News Editor at Respiratory Therapeutics Week – New research on Tuberculosis is the subject of a report. According to news reporting originating in New Delhi, India, by NewsRx journalists, researchers stated “The performance of the Capilia test for rapid identification of Mycobacterium tuberculosis complex (MTC) in Mycobacterium Growth Indicator Tube (MGIT) positive samples with contaminating organisms is not well documented. To assess the diagnostic yield of the Capilia test in the rapid identification of MTC in MGIT-positive cultures.”

The news reporters obtained a quote from the research by the authors from World Health Organization, “A total of 459 selected sputum samples were cultured using BACTEC &#8482; MGIT &#8482; 960. Tubes flagged positive by the MGIT instrument (MGIT-positive) were examined for acid-fast bacilli and cording in smears, spotted on blood agar (BA), subcultured for biochemical tests and tested using the Capilia test. Based on smear and growth on BA, MGIT-positive tubes were grouped into MGIT true-positive, MGIT-positive with contamination and MGIT contamination. Performance parameters of Capilia test such as sensitivity, specificity, efficiency, and positive and negative predictive values (PPV, NPV) for each of these groups were determined against biochemical tests as gold standard. Of the 346 MGIT-positives, respectively 233, 73 and 40 were MGIT true-positive, MGIT-positive with contamination and MGIT contamination. For the three groups, the PPV and NPV of the Capilia test were respectively 97%, 96% and 100%, and 32%, 27% and 60%.”

According to the news reporters, the researchers concluded: “In settings with high contamination of MGIT cultures, the performance of the Capilia test is diminished.”

For more information on this research see: Capilia test for identification of Mycobacterium tuberculosis in MGIT &#8482;-positive cultures. *International Journal of Tuberculosis and Lung Disease*, 2012;16(6):788-792. *International Journal of Tuberculosis and Lung Disease* can be contacted at: Int Union Against Tuberculosis Lung Disease (I U A T L D), 68 Boulevard Saint-Michel, 75006 Paris, France.
Our news correspondents report that additional information may be obtained by contacting N.S. Gomathi, Off World Hlth Organization Representat India, New Delhi, India. (2012 Jul 02)

**Eskisehir Osmangazi University: Peritoneal tuberculosis mimicking ovarian cancer**

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators discuss new findings in Tuberculosis. According to news reporting out of Eskisehir, Turkey, by NewsRx editors, researchers stated “To evaluate the characteristics of 20 patients diagnosed as tuberculous peritonitis (TBP) mimicking ovarian cancer during a 10-year period at a single center. Among 612 operations for ovarian malignancy we retrospectively reviewed the surgical and pathological reports of 20 patients suspected preoperatively as having ovarian malignancy but whose pathological results revealed TBP, between 2000 and 2011 in a university clinic.”

Our news journalists obtained a quote from the research by the authors from Eskisehir Osmangazi University, “Demographic characteristics, physical and pelvic examination, laboratory investigations and radiological imaging of the patients were evaluated retrospectively. Diagnostic laparotomy, laparoscopy and ultrasound guided tru-cut biopsy were performed in 11, 2 and 7 of the 20 patients, respectively. The mean age of the patients was 37.5 +/- 17.3 years (range 16-70 years). The most common symptoms were abdominal pain (n = 14%, 70%) and abdominal distension (n = 13%, 65%). Serum CA 125 was elevated in 16 (80%) cases and the average CA 125 level was 289 +/- 186.2 IU/ml. During ultrasonographic imaging and CT scans, ascites and a pelvic mass were detected in 19 (85%) and 12 (60%) patients respectively. TBP was suspected in 7 (35%) patients and ultrasound guided tru-cut biopsy was preferred as a first-line approach. Surgery was performed in 11 patients (55%) and during exploration widespread miliary nodules (n = 9%, 81%), widespread adhesion (n = 5%, 45%), adnexal mass (n = 8%, 72%) and caseous necrotic substance (n = 4%, 36%) were observed. Patients underwent unilateral (n = 3% 27%) or bilateral (n = 4%, 36%) salpingo-oophorectomy in seven (63%) cases. Since ovarian cancer is a serious condition and preoperative diagnosis of TBP is difficult, laparotomy is usually mandatory to distinguish these two entities.”

According to the news editors, the researchers concluded: “Ultrasound guided tru-cut biopsy is useful in selected patients and frozen section analysis avoids hazardous radical surgery at operation.”

Military Medical College, Shanghai: Clinical data and CT findings of pulmonary infection caused by different pathogens after kidney transplantation

By a News Reporter-Staff News Editor at Life Science Weekly – Investigators publish new report on Tuberculosis. According to news originating from Shanghai, People's Republic of China, by NewsRx correspondents, researchers stated “The overall objective was to review clinical data and CT findings of pulmonary infection caused by different pathogens after kidney transplantation in an attempt to help early clinical qualitative diagnosis. 446 cases of clinically confirmed pulmonary infection after kidney transplantation in recent 10 years were evaluated with respect to the time of occurrence and 89 cases with complete CT data and pathogenic diagnosis were further analyzed for pathogen types and CT manifestations.”

Our news journalists obtained a quote from the research by the authors from Military Medical College, “Statistical analysis was performed using Fisher’s exact test. Pulmonary infection reached the peak in 3 months after transplantation. Bacterial infection and mixed infection were predominant between 1 and 6 months. And most tuberculosis occurred after one year. Bacterial (38.2%) and mixed infections (38.2%) were the common types. The next was fungal infection, tuberculosis and viral infection (10.1%, 7.9% and 5.6%, respectively). CT manifestations of pulmonary infections after kidney transplantation were diverse and complex, lacking characteristic signs. More than 3/4 of pulmonary infections after kidney transplantation can be attributed to bacteria and mixed pathogens.”

According to the news editors, the researchers concluded: “The combination of time course, clinical data and CT manifestations plays an important role in the early clinical qualitative diagnosis.”

For more information on this research see: Clinical data and CT findings of pulmonary infection caused by different pathogens after kidney transplantation. European Journal of Radiology, 2012;81(6):1347-1352. European Journal of Radiology can be contacted at: Elsevier Ireland Ltd, Elsevier House, Brookvale Plaza, East Park Shannon, Co,
Indian Council for Medical Research, Tamil Nadu: Phage lysin as a substitute for antibiotics to detect Mycobacterium tuberculosis from sputum samples with the BACTEC MGIT 960 system

By a News Reporter-Staff News Editor at Biotech Week – Data detailed on Tuberculosis have been presented. According to news originating from Tamil Nadu, India, by NewsRx correspondents, researchers stated “Phage lysin was evaluated as a substitute for antibiotics in sputum samples processed by a modified Petroff’s method for the detection of Mycobacterium tuberculosis with the MGIT similar to 960 system. One hundred and fifty sputum samples were processed, inoculated onto two slopes of LowensteinJensen medium, and divided in to two aliquots of 0.5 mL each.”

Our news journalists obtained a quote from the research by the authors from Indian Council for Medical Research, “One aliquot was added to 7 mL of MGIT medium containing polymyxin similar to B, amphotericin similar to B, nalidixic acid, trimethoprim and azlocillin (PANTA) (MGIT-PANTA) and the other was added to 7 mL of MGIT medium containing 0.8 mL of lysin (MGIT-Lysin). The samples were randomized and incubated at 37 degrees C in the MGIT similar to 960 system. The sensitivity and specificity of MGIT-Lysin were 97% and 88%, respectively, as compared with MGIT-PANTA. The average times to detection with MGIT-Lysin and MGIT-PANTA were 9.3 and 8.6 similar to days, respectively. The rate of contamination with MGIT-PANTA and MGIT-Lysin were 16% and 7.3%, respectively.”

According to the news editors, the researchers concluded: “Phage lysin can be substituted for antibiotics in processed sputum samples for the detection of M. similar to tuberculosis.”

The news correspondents report that additional information may be obtained from B. Subramanyam, Indian Council Med Res, TB Res Center, Dept. of Bacteriol, Madras 600031, Tamil Nadu, India. (2012 Jun 06)

**Veterinary Laboratories Agency, Exeter: Controlling tuberculosis in a llama (Lama glama) herd using clinical signs, tuberculin skin testing and serology**

By a News Reporter-Staff News Editor at Veterinary Week – Data detailed on Tuberculosis have been presented. According to news reporting from Exeter, United Kingdom, by VerticalNews journalists, researchers stated “An outbreak of tuberculosis (TB), caused by *Mycobacterium bovis*, was investigated in a small herd of llamas (Lama glama).”

The news correspondents obtained a quote from the research by the authors from Veterinary Laboratories Agency, “Based on three ante-mortem diagnostic methods (clinical signs, tuberculin skin test reactions, and ‘Rapid Test’ serology), 12 llamas were selected for examination post-mortem. Grossly visible lesions suspicious of TB were observed in eight animals, four of which had exhibited clinical signs, one was a skin test ‘reactor’, and three had been seropositive. *M. bovis* was isolated from seven of these eight animals.”

According to the news reporters, the researchers concluded: “Clinical signs combined with serology were found to be useful in identifying infected animals, but tuberculin skin testing had limited negative predictive value as four llamas that were subsequently confirmed as infected were not detected using this assay.”


Our news journalists report that additional information may be obtained by contacting D.F. Twomey, Veterinary Laboratories Agency, Staplake Mount, Starcross, Exeter, Devon EX6 8PE, UK. (2012 Jun 04)

By a News Reporter-Staff News Editor at Politics & Government Week – A patent application by the inventors Shah, Jyotsna S. (Santa Clara, CA); Weltman, Helena (Los Altos, CA); Narciso, Patricia (Union City, CA), filed on February 13, 2012, was cleared for further review on October 25, 2012, according to news reporting originating from Washington, D.C., by VerticalNews correspondents.

Patent application serial number 371711 has not been assigned to a company or institution.

The following quote was obtained by the news editors from the background information supplied by the inventors: “The century old sputum microscopy test using Ziehl-Neelsen stained smears form unconcentrated sputum (direct smears) remains the primary tool for diagnosing tuberculosis (TB) in low-income countries. However direct smear microscopy has poor sensitivity (range 20-80%) particularly in HIV-coinfected patients (Steingart, K. R., V. Ng, M. Henry, P. C. Hopewell, A. Ramsay, J. Cunningham, R. Urbanczik, M. D. Perkins, M. A. Aziz, and M. Pai. 2006. Sputum processing methods to improve the sensitivity of smear microscopy for tuberculosis: a systematic review. Lancet Infect. Dis. 6:664-674). Therefore, the Stop TB Partnership Retooling Task Force identified bleach sedimentation as one of the 3 promising approaches to improving the sensitivity of sputum smear microscopy in high burden countries (World Health Organization. 2008. New laboratory diagnostic tools for tuberculosis control. Stop TB Partnership Retooling Task Force. WHO Press, Geneva, Switzerland). The biggest problem with this technique is that mycobacteria become non-viable and, therefore, cannot be cultured from the bleach treated sputum.


“In middle and high income countries processing of sputum by chemical and/or physical methods is commonly used to increase diagnostic sensitivity. The most commonly used methods use sodium hydroxide alone or a combination of sodium hydroxide and N-acetyl-cysteine. The problem with this method, although the best at this point in time for concentration of sputum, destroys more than 80% of the viable mycobacteria due to use of NaOH.”
In addition to the background information obtained for this patent application, VerticalNews journalists also obtained the inventors’ summary information for this patent: “The present invention provides a method for decontamination, digestion and concentration of clinical specimens (samples) from a patient including, but not limited to, sputum, bronchial lavage sample (Bronchoalveolar lavage: BAL), induced sputum, gastric washings, urine, fecal material in suspension, ground tissue (including ground skin), peritoneal fluid and pleural fluid for detection of mycobacteria using a combination of a mucolytic reagent such as an acetyl-cysteine or chitin and sodium or calcium hypochlorite (commonly known as bleach). This combination of reagents protects nucleic acids (DNA and RNA) and at the same time selectively kills non-mycobacterial pathogens that interfere with growth of mycobacterial cultures. The processed concentrated pellet can be tested for mycobacteria directly by Fluorescent in Situ Hybridization (FISH), PCR, RT-PCR or by culture confirmation methods. The method is comprised of several steps which are performed in the listed order in the Exemplification Section, below.

“The two most commonly used methods for decontamination and concentration of clinical samples including sputum, BAL, gastric washings, fecal material, urine, include N-acetyl cysteine and sodium hydroxide (NaOH) or sodium hydroxide only, prior to culturing of Mycobacteria. The problem with these methods is that sodium hydroxide destroys RNA. Therefore, the viability of the cells varies and the ability to detect target sequences varies depending on, for example, how well the pellet is washed and the final pH of the pellet. It can be seen then how this procedure often can result in substandard results. When samples were tested by Mycobacteria Genus specific Fluorescent in Situ hybridization (FISH) assays, it was observed that the sensitivity of the NaOH/Nalc processed pellet was always lower than the acid-fast (Ziehl-Neelsen) staining.

“Another method that has been used to detect mycobacteria in sputum includes processing sputum with sodium hypochlorite (bleach) solution (between 2% to 10%). Unfortunately, the cells are not viable after bleach treatment.

“Therefore we have developed a new method using a combination of N-acetyl-cysteine and bleach. In this method an equal volume (or approximately 1-3 volumes) of a solution containing a hypochlorite salt (approximately 0.5% to approximately 2%) including but not limited to sodium hypochlorite (bleach) or calcium hypochlorite and (approximately 0.5 to approximately 2%) N-acetyl cysteine is added to sputum, BAL or other suitable sample, mixed by vortexing and incubated at
room temperature for 15-40 minutes, preferably 30 minutes. In a preferred embodiment of the present invention, processing solution contains 1% sodium hypochlorite and 1% N-acetyl cysteine. Ratio of sputum to processing solution is approximately 1:1 by volume.

“More than one type of hypochlorite salt (i.e., that is, a mixture of two or more) may be used at the same time providing the total concentration does not exceed the concentration range given above. After incubation the solution is then centrifuged at approximately 3000 g for approximately 15 minutes. One of skill in the art will understand that centrifuge speed and centrifuge time are inversely related and that faster centrifuge speeds will allow for shorter centrifuge times. The supernatant is decanted and the pellet is, optionally, washed once with water. The washed pellet is resuspended in approximately 1/10 the volume of water (or physiological saline solution) of the starting sample volume and mixed by vortexing. The resuspended pellet is then tested directly by PCR RT-PCR, FISH or other suitable assay known to those of skill in the art or the mycobacteria can be cultured.”

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