

TB IN 2022: What's New in Research?

CONVENED VIRTUALLY FEBRUARY 28 – MARCH 2, 2022

# **Participating Institutions**

- Bhagwan Mahavir Medical Research Center (BMMRC)
- Byramjee Jeejeebhoy Government Medical College (BJGMC)
- Byramjee Jeejeebhoy Government Medical College (BJGMC)-Johns Hopkins University (JHU) Clinical Research Site (BJGMC-JHU CRS)
- Boston University/Boston Medical Center (BU/BMC)
- Christian Medical College, Vellore (CMC)
- Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER)
- Johns Hopkins University (JHU)
- M. Viswanathan Diabetes Research Center (MVDRC)

- National Institute for Research In Tuberculosis (NIRT)
- National Institute for Research In Tuberculosis (NIRT) – International Centers for Excellence in Research (ICER)
- North Eastern Indira Gandhi Regional Institute of Health & Medical Sciences (NEIGRIHMS)
- P.D. Hinduja National Hospital and Medical Research Centre (Hinduja)
- Postgraduate Institute of Medical Education and Research (PGI), Chandigarh
- Rutgers University
- University of California—San Francisco (UCSF)
- University of Massachusetts (UMass)
- University of Texas Health Science Center at Tyler (UTT)

# **Specialized Labs & Collaborators**

- All Indian Institute of Medical Sciences (AIIMS), New Delhi, India
- Cornell University, New York, USA
- Emory University, Georgia, USA
- Fundação Oswaldo Cruz (FIOCRUZ), Bahia, Brazil
- Indian Institute of Science (IISc), Bengaluru, India
- Indian Institute of Technology Bombay (IIT-B)
  - Proteomics Core, Mumbai, India

- Medgenome, Bengaluru, India
- National Center for Functional Glycomics, Massachusetts, USA
- Office of Cyber Infrastructure and Computational Biology (NIAID), Maryland, USA
- South African TB Vaccine Initiative (SATVI), Cape Town, South Africa
- theraCUES Innovation Pvt Ltd, Bengaluru, India
- Translational Health Science and Technology Institute (THSTI), Faridabad, India

# **Supporting Organizations**

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# **Sponsors**





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RePORT India 2020 Annual Meeting in Mumbai





# CMC-Vellore



BMMRC

## Background

RePORT (Regional Prospective Observational Research for Tuberculosis) India is a bilateral, multi-organizational, collaborative research effort established in 2013 under the Indo-US Vaccine Action Program (VAP). RePORT India is now the largest of six regional consortia—China, Brazil, Indonesia, Philippines, and South Africa are also undertaking multi-organizational tuberculosis (TB) research efforts. Each RePORT consortium is designed to support local, in-country, TB-specific data and specimen biorepositories and associated research. Taken together, the anticipated results include greater global clinical research capacity in high-burden settings and increased local access to quality data and specimens for members of each consortia and their domestic and international collaborators. Leveraging the data, specimens, infrastructure, and scientific partnerships established by RePORT India in Phase 1, the consortium has now launched Phase II.

## **Mission**

RePORT India is charged with:

- 1. Advancing regional TB science in India, towards fulfilling the TB strategic goals of the country;
- 2. Strengthening TB research capacity and infrastructure; and
- 3. Fostering research collaboration within India and with other countries focused on research that can lead to clinically important biomarkers, vaccines, drugs, and diagnostics.

## Phase I - Parent Protocols

Phase I (2013–18) commenced with six Clinical Research Sites (CRSs) in Western and Southern India that were partnered with five U.S. academic institutions. P.D. Hinduja National Hospital and Medical Research Centre was subsequently added as the seventh Indian site. Initially, each site had its own "Parent Protocol" with distinct research topics. Clinical, behavioral, radiological and biological samples were collected from the enrollees, including sputum, blood, urine etc. The specimens were stored at the ICMR-NIRT biobank for scientific analysis. TB patients and their household contacts were followed for a period of two years.

**Cohort A**: Participants who have active TB disease. Studies involving this cohort of patients focused on TB diagnosis and treatment outcomes.

- 2455 patients enrolled with TB inside the lungs (including 133 with drug-resistant TB)
- 588 patients enrolled with TB outside the lungs
- 207 children enrolled with TB

**Cohort B**: Participants who are household contacts (HHCs) of an active case of TB. Studies involving this cohort of participants focused on risk of infection and progression to TB disease after exposure.

3766 HHCs of coughing adult patients with TB inside the lungs enrolled

## Phase I - Parent Protocol Achievements

- 106 scientific publications to advance TB science and public health
- 64 new projects utilizing the collected and stored samples for new biomarkers
- 245 presentations to showcase the work done in the RePORT Consortium
- New child TB diagnosis and treatment response gene-signatures unique for India
- New Transcriptomic, Lipidomic and Metabolomic signatures as blood biomarkers
- New vaccine trials to prevent TB relapse, Clinical biomarkers of TB death and relapse
- Key public health finding that informed the country's National TB Elimination Program guideline policies and more public health findings in the list with potential to guide further.

## Phase I - Common Protocol

Based on the tremendous productivity of RePORT India's Phase I identifying new blood-based, sputum-based and urine-based biomarkers that can diagnose TB, or predict TB patients treatment success or failure or death, and for assessing new vaccines to prevent getting TB again (relapse) for those starting TB treatment, the governments of India and the US bilaterally funded the extension of Phase I in to a "Common Protocol" in 2017. The Common Protocol allowed for standardized data elements and harmonized procedures for enrollment across all sites to 1) identify newer, more accurate biomarkers and 2) confirm the utility of previously discovered biomarkers by validating them on samples stored in the ICMR-NIRT sample bank. The Common Protocol enrolled and followed TB patients and their HHCs for a period of two years.

Cohort A: Participants who have active TB disease.

724 adult patients enrolled with TB inside the lungs

Cohort B: Participants who are household contacts (HHCs) of an active case of TB.

898 household contacts of coughing adult patients with TB inside the lungs enrolled

## Phase II - Common Protocol

Both Indo-US governments have further supported the scientific research goals of RePORT India by expanding the number of sites represented across the country, especially by involving scientists and participants from the Northern and North-eastern parts of the country. In addition to the existing group of TB patients and their household contacts across nine Indian sites in the RePORT India Phase II Common Protocol, the consortium plans to support the enrollment of 1500 adult and child patients who are suspected of having TB inside of outside their lungs, 588 adult patients with TB inside the lungs, and 794 household contacts of adult patients with TB inside the lungs. On the following pages, the Phase II CRSs and their study focus areas are outlined.

#### **BMMRC & UTT**

- Topic of Study: Immunologic Markers of Persons at Highest Risk of Progression of Latent TB Infection to TB
- India PI: Dr. Vijaya Valluri, Bhagawan Mahavir Medical Research Centre (BMMRC), Hyderabad, India
- **U.S. PI**: Dr. Krishna Vankayalapati, University of Texas Health Science Center, Tyler (UTHCT), TX, USA
- Participating Patient Cohort: Cohort B

#### BJGMC, NIRT, & JHU

- **Topic of Study**: Host and Microbial Factors Associated with Poor Treatment Response and Progression to Active TB (C-TRIUMPH)
- India PIs: Drs. Sanjay Gaikwad, Aarti Kinikar and Shashikala Sangle, Byramjee Jeejeebhoy Government Medical College (BJGMC), Pune, India; Dr. Vidya Mave, BJGMC-JHU CRS, Pune, India; Drs. Padma Chandrasekaran and Bhavani PK, National Institute for Research in TB (NIRT), Chennai, India
- U.S. PI: Dr. Amita Gupta, Johns Hopkins University, Baltimore, MD, USA
- Participating Patient Cohorts: Cohort A (Adult Pulmonary TB, Pediatric TB, and Extrapulmonary TB) and Cohort B

#### CMC Vellore & U of Wash/U of Cambridge

- **Topic of Study**: Host Determinants in the Eicosanoid Pathway that Modulate the Inflammatory Response, Disease Outcome, and Treatment Responsiveness in TB
- India PI: Drs. DJ Christopher and Balamugesh Thangakunam, Christian Medical College (CMC), Vellore, India
- U.S. PI: Dr. Lalitha Ramakrishnan, University of Washington/University of Cambridge, UK
- Participating Patient Cohort: Cohort A (Adult Pulmonary TB and TB Meningitis)

### Hinduja & JHU

- Topic of Study: MDR-TB Treatment Outcomes, Adverse Effects, Mtb Genotyping, and Pharmacokinetic Testing
- India PIs: Drs. Zarir F. Udwadia, Tester F. Ashavaid, and Camilla Rodrigues; P.D. Hinduja National Hospital and Medical Research Centre, Mumbai, India
- U.S. Pls: Drs. Amita Gupta and Jeffrey Tornheim, Johns Hopkins University (JHU), Baltimore, MD, USA
- Participating Patient Cohorts: Cohort A (Adult/Adolescent MDR-TB) and Cohort B

#### JIPMER, BU/BMC, & Rutgers

- Topic of Study: Biomarkers for Risk of TB and for TB Treatment Failure and Relapse
- India PIs: Drs. Gautam Roy and Sonali Sarkar, Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Puducherry, India
- **U.S. Pls**: Drs. Jerrold Ellner and Padmini Salgame, Rutgers University, Newark, NJ, USA; Dr. Robert Horsburgh, Boston University (BU), Boston, MA, USA; Dr. Natasha Hochberg, Boston Medical College (BMC), Boston, MA, USA
- Participating Patient Cohorts: Cohort A (Adult Pulmonary TB and Pediatric TB) and Cohort B

#### MVDRC, NIRT-ICER, & UMass

- Topic of Study: Effects of Diabetes and Prediabetes on TB Severity
- India PIs: Dr. Vijay Viswanathan, MV Diabetes Research Centre (MVDRC), Chennai, India; Dr. Subash Babu, National Institute for Research In Tuberculosis (NIRT) International Centers for Excellence in Research (ICER), Chennai, India
- U.S. PI: Dr. Hardy Kornfeld, University of Massachusetts (UMass) Medical School, Boston, USA
- Participating Patient Cohort: Cohort A (Adult Pulmonary TB)

#### **MVDRC**

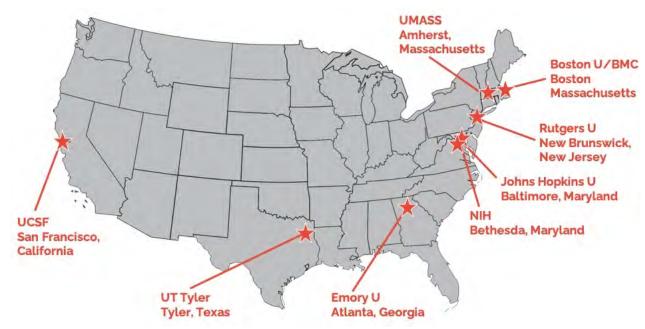




## RePORT India Phase II



Under a Phase II Common Protocol, we are pursuing five specific scientific aims including the following cohorts: Diagnostic (New TB suspects), Cohort A (Active TB disease), and Cohort B (HHCs). Samples collected under this protocol will be curated, stored, and managed at the RePORT India Central Biorepository at NIRT where Phase I Common Protocol samples are currently stored. A data management center is being established at JIPMER in Puducherry and PPD will continue to provide technical support. The Phase II Common Protocol Co-Chairs are: Drs. Kamakshi Prudhula Devalraju (BMMRC) and Robert Bollinger (JHU). The consortium has now been expanded to include two new CRSs in Northern India.



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### Phase II Scientific Aims

#### **AIM 1. DIAGNOSTICS**

Evaluate Novel Diagnostics & Biomarkers of Diverse States of Mtb Infection

Participating Patient Cohort: Diagnostic (New TB suspects) Leads: Dr. Sonali Sarkar (JIPMER) and Dr. Jerry Ellner (Rutgers)

Participating Patient Cohort: Cohort B (XDR HHCs)

Leads: Dr. Tester Ashavaid (Hinduja) and Dr. Jeff Tornheim (JHU)

#### AIM 2. MARKERS OF TREATMENT RESPONSE

Participating Patient Cohort: Cohort A (Active TB disease)

2.A: Identify TB Treatment Response Biomarkers

Leads: Dr. Vijay Viswanathan (MVDRC) and Dr. Hardy Kornfeld (UMass)

2.B: Investigate Host-Related Mechanisms of Treatment Failure

Leads: Dr. Vidya Mave (BJGMC-JHU CRS) and Dr. Natasha Hochberg (BMC)

2.C: Investigate Pathogen-related Mechanisms & Predictors of Recurrence Lead: Dr. David Alland (Rutgers)

#### AIM 3. LUNG INJURY & IMPAIRMENT

Identify Markers of Lung Injury Associated with Unfavorable TB Treatment Outcomes.

Participating Patient Cohort: Cohort A (Active TB disease)

Leads: Dr. DJ Christopher (CMC Vellore), Dr. Ashutosh Aggarwal (PGI Chandigarh), and Dr. Akshay Gupte (JHU)

#### AIM 4. RESISTANCE TO INFECTION

Mechanisms of Protection against TB in Exposed Persons

Participating Patient Cohort: Cohort B (Phase I HHCs)

4.A: Examine Host Antimicrobial Pathways in Inducing their infection resistant (IR) Phenotype in HHC

4.B: Test if IR & Plasma Differ in Modulating Macrophage-Mediated Restriction of Mtb Growth & Evaluate AB Repertoires of Plasma from the IR and infection susceptible (IS) Cohorts

Leads: Dr. Padmini Salgame (Rutgers), Dr. Subash Babu (NIRT-ICER), and Dr. Kamakshi Prudhula Devalraju (BMMRC)

#### AIM 5. PROGRESSION TO DISEASE

Identify Immunologic Markers of Persons at Highest Risk of Progress of Latent TB Infection to TB.

5.A: Stored Samples: Validation of PREDICT29 in Progressors & Nonprogressors from RePORT Sites Participating Patient Cohort: Cohort B (Phase I HHCs)

Leads: Dr. Padmini Salgame (Rutgers) and Dr. Luke Elizabeth Hanna (NIRT)

5.B: Immune & Hormone Studies in Freshly Collected Samples

Participating Patient Cohort: Cohort B (Phase II HHCs)

Leads: Dr. Vijaya Valluri (BMMRC) and Dr. Ramakrishna Vankayalapati (UTT)

In addition to these five aims, we will assess cross-cutting epidemiologic and COVID-19 related aims.

### **Administration**

RePORT India has established a collaborative governance structure composed of: 1) an Executive Committee led by two Chairs and two Co-chairs from India and the U.S.; 2) an Indo-U.S. Coordinating Hub; 3) three Scientific Working Groups (Basic Science, Clinical Epidemiology, Behavioral Science); 4) five Operational Working Groups (Common Protocol Leadership, Study Coordination, Publications Committee, Laboratory Management, and Data Management); and 5) a Data Coordinating Hub (JIPMER). The EC's mission is to set research priorities, guide scientific activities, and offer administration and logistics in support of research priorities.

The consortium is currently led by:

- Chairs: Dr. Sonali Sarkar (JIPMER, Clinical Epi) and Dr. Amita Gupta (JHU, Clinical Epi)
- Co-Chairs: Dr. Vijaya Valluri (BMMRC, Basic Science) and Dr. Padmini Salgame (Rutgers, Basic Science)

## **Funding**

The RePORT India Consortium is supported with bilateral funding from the Government of India's (GOI) Department of Biotechnology (DBT) and the U.S. National Institutes of Health's (NIH) National Institute of Allergy and Infectious Diseases (NIAID), Division of AIDS (DAIDS), and Office of AIDS Research (OAR). CRDF Global administers and oversees the funding from the U.S. government.







## BJGMC



## NIRT

# Hinduja



PRESENTED			
TITLE	INVESTIGATORS		
Histone Deacetylase-1 Is Required for the Protective Immunity against Mycobacterium tuberculosis Infection through the Regulation of STAT1 Activation	Jôsimar Dornelas Moreira, RamaKrishna Vankayalapati, <b>Buka Samten</b>		
Evaluation of Cepheid Xpert TB Host Response for Triage of Pulmonary Tuberculosis	<b>Shah KM</b> , Shankar D, Jaganath D, Denkinger C, Nahid P, Cattamanchi A, Christopher DJ, Andama A, Theron G, Nguyen VN, Yu C		
Comprehensive Phentoyping and Targeting of Myeloid-Derived Suppressor Cells (MDSC) as a TB Host- directed Therapy	Hedwin Kitdorlang Dkhar, Chris Ibegbu, Casey Vatucci, Shivani Vyas, Nicole Alexis Woods, Krishnendu Roy, Jyothi Rengarajan		
Metabolites Enhance Innate Resistance to Human Mycobacterium tuberculosis Infection	Deepak Tripathi, Kamakshi Prudhula Devalraju, Venkata Sanjeev Kumar Neela, Tanmoy Mukherjee, Padmaja Paidipally, Rajesh Kumar Radhakrishnan, Igor Dozmorov Mohammad Soheb Ansari, Varalakshmi Mallidi, Anvesh Kumar Bogam, Karan P. Singh, Vijaya Lakshmi Valluri, Ramakrishna Vankayalapati		

# Young Investigator Abstracts PRESENTED

Histone Deacetylase-1 Is Required for the Protective Immunity against Mycobacterium tuberculosis Infection through the Regulation of STAT1 Activation

Submitting Author: Buka Samten

Co-authors: Jôsimar Dornelas Moreira, RamaKrishna Vankayalapati

**Background:** Histone deacetylases (HDACs), the members of the epigenetic effector molecules of eukaryotic cells, play critical roles in tumorigenesis and immune regulation by removal of acetyl group from the lysine residues of histones and non-histone proteins. However, their roles in Mycobacterium tuberculosis (Mtb) infection remain unexplored.

**Methods:** To study the significance of HDACs in tuberculosis infection, we have screened 11 zinc-dependent HDAC variants with their chemical inhibitors and identified that HDAC-1 has the dramatic effect on cytokine production by Mtb infected macrophages and dendritic cells (DC). To further investigate whether HDAC-1 affects the capacities of innate immune cells to control intracellular bacilli growth, we followed the growth of Mtb in both mouse and human monocyte derived macrophages and DCs in the absence or presence of the HDAC-1 inhibitor. Compared to the cells with vehicle control the cells treated with HDAC-1 inhibitor failed to control the growth of H37Rv with significantly elevated intracellular bacilli growth at 2-, 4- and 6-days post infection.

**Results:** The HDAC-1 inhibitor had no effects on the growth of Mtb in broth culture, indicating that the HDAC-1 inhibitor acts indirectly by interfering with the pathways of innate immune cells mediated Mtb growth control increased lysine acetylation of STAT1 in Mtb infected BMDM treated with IFN-γ, a molecular switch identified

### **PRESENTED: Continued**

increased lysine acetylation of STAT1 in Mtb infected BMDM treated with IFN- $\gamma$ , a molecular switch identified to be critical for the regulation of STAT1 phosphorylation and activation. Consistent with this, the expression of phosphorylated STAT1 in the mouse lung treated with HDAC-1 inhibitor was lower than the vehicle control mice infected with Mtb. The same results were obtained with CRISPR/CAS9 modified HDAC-1 knockout (KO) THP-1 derived macrophages infected with H37Rv, with increased growth of Mtb and reduced phosphorylation of STAT1 in the presence of IFN- $\gamma$  further confirming the findings from the chemical inhibitor of HDAC-1, suggesting a functional significance and requirement of HDAC-1 in active IFN- $\gamma$  signaling for the efficient control of Mtb growth both in cells and mice through removing acetyl groups from the lysine residues of STAT1, a critical signaling molecule downstream of IFN- $\gamma$  stimulation in innate immune cells.

**Conclusion:** Thus, our data indicate that HDAC-1 activity is required for the protective immunity against Mtb infection.

#### **Evaluation of Cepheid Xpert TB Host Response for Triage of Pulmonary Tuberculosis**

Submitting Author: Kinari Shah

**Co-authors:** Shankar D, Jaganath D, Denkinger C, Nahid P, Cattamanchi A, Christopher DJ, Andama A, Theron G, Nguyen VN, Yu C

**Background:** Novel triage tests for tuberculosis (TB) are needed to increase case detection. Gene expression signatures have the potential to improve accuracy, and Cepheid (Sunnyvale, USA) has developed a blood-based PCR assay for a three-gene host mRNA signature that can be measured close to the point-of-care.

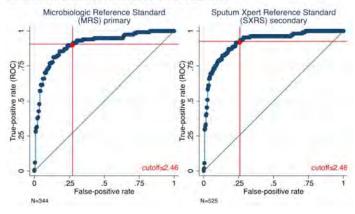
Methods: We screened adults presenting to health centers in Uganda, South Africa, Vietnam, the Philippines and India (Christian Medical College, Vellore) and enrolled those with unexplained cough 2 weeks' duration. All patients received standard sputum-based testing for pulmonary TB (Xpert Ultra x 1 and liquid culture x 2) and had venous or capillary blood collected. Blood was placed in the Xpert TB Host Response (HR) cartridge and tested in standard GeneXpert machines at the local health centers. We calculated the gene expression score per manufacturer recommendations and evaluated the accuracy of the score in comparison to sputum Xpert and liquid culture results (microbiological reference standard, MRS), as well as sputum Xpert results alone (XRS).

**Results:** Of 525 adults enrolled to date (including 51 in India), 232 (44%) were female, median age was 40 years (interquartile range 28-53). 90 (17%) were living with HIV, 61 (12) had diabetes and 117 (22.3%) had microbiologically confirmed TB. The Xpert HR assay had high accuracy (area under the curve 0.89, 95% CI 0.86-0.93). At a gene expression score cut-off that achieved a sensitivity of at least 90% (cut-off = 2.46), specificity was 72.7% (95% CI 66.4-78.4). When using the same cut-off, in comparison to the XRS, sensitivity was 92.6% (95% CI 85.9-96.7) and specificity was 74.1% (95% CI 69.6-78.2). Across countries and key subgroups (women, HIV+, diabetic patients), sensitivity and specificity were in similar ranges.

	Sensitivity (%, 95%CI)	Specificity (%, 95%CI)	
Overall	90.6 (83.8-95.2)	72.7 (66.4-78.4)	
¹Country			
Uganda	90.0 (80.7-95.1)	75.2 (66.4-82.4)	
Philippines	80.0 (54.8-92.9)	69.1 (58.4-78.1)	
Vietnam	95.0 (76.4-99.1)	100 (80.6-100)	
India	100 (49.0-100)	52.4 (32.3-71.7)	
South Africa	100 (70.0-100)		
Female	90.2 (77.2-96.2)	73.5 (64.8-80.6)	
HIV-positive	94.1 (73.0-99.0)	66 (52.6-77.3)	
Diabetic adults	94.1 (73.0-99.0)	72.5 (66.1-78.2)	
Blood collection method			
Venous	90.2 (83.2-94.4)	74.8 (68.6-80.3)	
Capillary <sup>3</sup>	100 (0.61-100)	57.9 (36.3-71.7)	

<sup>&</sup>lt;sup>1</sup> Vietnam, India, South Africa sample sizes are all less than 50.

Figure 1. Receiver operating characteristic curves for Xpert TB HR assay. The curves show sensitivity (y-axis) and specificity (x-axis) of the Xpert TB HR assay and different cut-offs for the gene expression score. The red dot reflects a gene expression score cut-off that achieves the minimum 90% sensitivity recommended for a TB triage test.



<sup>&</sup>lt;sup>2</sup> Microbiological reference standard pending culture results in India.

<sup>&</sup>lt;sup>3</sup> Capillary blood sample size is less than 50.

**PRESENTED: Continued** 

**Conclusions:** In preliminary analyses, the Xpert TB HR assay achieved the target accuracy thresholds for a TB triage test and should be further explored as a novel point-of-care tool to improve TB case detection across different regions of India.

# Comprehensive Phentoyping and Targeting of Myeloid-Derived Suppressor Cells (MDSC) as a TB Host-directed Therapy

Submitting Author: Hedwin Kitdorlang Dkhar

**Co-authors:** Chris Ibegbu, Casey Vatucci, Shivani Vyas, Nicole Alexis Woods, Krishnendu Roy, Jyothi

Rengarajan

**Background:** *Mycobacterium tuberculosis* (Mtb) successfully modulates the function of host cells by regulating the transcriptome and metabolome for its survival. In Tuberculosis (TB), great emphasis was given to understand the presence of an immune-suppressive environment that might be contributed by myeloid suppressor cells. Initially identified in cancer, Myeloid-Derived Suppressor Cells (MDSCs) are heterogenous population of innate myeloid cells with immunoregulatory function. In humans, they are identified by the presence of HLA-DRlow/-ve; CD11b+; CD33+ antigens. Two subgroups of MDSCs exists, monocytic-MDSC bearing CD14+ (M-MDSC) or the granulocytic-MDSC expressing CD15+/CD66+ (G-MDSC). Only few studies have reported the presence of MDSC in human TB patients, Mtb-infected animals and there are scares reports on reduced MDSC post antibiotic treatment which outcome to an improved clinical condition. Therefore, currently MDSCs have become a potential target for TB host-directed therapy where different strategies are being tested to deplete them during Mtb infection.

**Methods:** In this study, we developed a comprehensive multi-color flow cytometry panel which enables us to discretely identify MDSCs with their functional signatures like iNOS and IDO. Using an *in vitro* model of human PBMCs derived MDSCs expansion, we found high frequencies of M-MDSCs. Upon co-culture with Cell trace labelled T cells, we observe the suppression of T cells proliferation. We attempted to deplete these MDSCs ex vivo using our recently developed novel Synthetic Nanoparticle Antibodies (SNAbs) which specifically targets MDSCs.

**Results:** We found that the nanoparticles efficiently deplete the expanded MDSCs. In parallel, we are evaluating the efficiency of the host-directed SNAb nanoparticles in the lung of Mtb-infected mice.

**Conclusions:** Our future goal is to measure and target the MDSCs in TB and HIV patients using our flow cytometry design. We will extend our understanding on the transcriptomics, metabolomics and epigenetics of the sorted MDSCs using scRNAseq to discover novel signatures and pathways.

#### Metabolites Enhance Innate Resistance to Human Mycobacterium tuberculosis Infection

**Submitting Author:** Deepak Tripathi

**Co-authors:** Kamakshi Prudhula Devalraju, Venkata Sanjeev Kumar Neela, Tanmoy Mukherjee, Padmaja Paidipally, Rajesh Kumar Radhakrishnan, Igor Dozmorov, Mohammad Soheb Ansari, Varalakshmi Mallidi, Anvesh Kumar Bogam, Karan P. Singh, Vijaya Lakshmi Valluri, Ramakrishna Vankayalapati

**Background:** Limited information is available on the protective immune responses of household contacts of TB patients who never develop LTBI or TB. We investigated the mechanisms that mediate resistance to Mtb infection in exposed household contacts (HHCs) of tuberculosis (TB) patients.

### **PRESENTED: Continued**

**Methods:** We followed 452 latent tuberculosis infection (LTBI) negative HHCs for two years and who remained LTBI negative throughout the study identified as non-converters. We performed multicolor flow cytometry, multiplex ELISA, whole transcriptomic and metabolomic analysis to investigate responsible factor for resistance to Mtb infection.

**Results**: At baseline, nonconverters had a higher percentage of CD14+, CD14+CD16+ and CD3-CD56+CD27+CCR7+ memory-like natural killer (NK) cells. Using a whole transcriptome and metabolomic approach, we identified a metabolite in the plasma of non-converters deoxycorticosterone acetate that enhanced glycolytic ATP flux in macrophages and restricted Mtb growth by enhancing antimicrobial peptide production through the expression of surface receptor sialic acid binding ig-like lectin (Siglec)-14. Another metabolite 4-hydroxypyridine, from the plasma of non-converters significantly enhanced the expansion of memory-like NK cells.

**Conclusions:** Our findings demonstrate that increased levels of specific metabolites can regulate innate resistance against Mtb infection in HHCs of TB patients who never develop LTBI or active TB.



## Hinduja

SUBMITTED			
TITLE	INVESTIGATORS		
Clinical and Laboratory Predictors of Tuberculosis Recurrence	Sonya Krishnan, Nikhil Gupte, Shreyas Desmukh, Padma Priyadarshini, Sanjay Gaikwad, Vijay Vishwanathan, Madhusudan Barthwal, Amita Gupta, Hardy Kornfeld, Jonathan Golub, Vidya Mave		
Characterization of Monocyte Responses in Pulmonary TB Patients With or Without Type 2 Diabetes mellitus	<b>Arul Nancy</b> , Nathella Pavan Kumar, Kadar Moideen, Vijay Viswanathan, Shanmugam Sivakumar, Syed Hissar, Hardy Kornfeld, Subash Babu		
Pharmacokinetics of Linezolid in Indian Multidrug Resistant Tuberculosis Patients	Prerna R. Arora, Bhamini Keny, Alpa J. Dherai, Zarir F. Udwadia, Ashok A. Mahashur, Lancelot Pinto, Mullerpattan Jai, Ayesha Sunavala, Camilla Rodrigues, Amita Gupta, Neil Martinson, Ebrahim Variava, Firdaus Nabeemeeah, Juan Eduardo Resendiz-Galvan, Mahmoud Abdelwahab, Paolo Denti, Jeffrey A. Tornheim, Tester F. Ashavaid		
Impact of Undernutrition on Tuberculosis Treatment Outcomes in India: A Multicenter Prospective Cohort Analysis	Pranay Sinha, Chinnaiyan Ponnuraja, Nikhil Gupte, Senbagavalli Prakash Babu, Samyra R. Cox, Sonali Sarkar, Vidya Mave, Mandar Paradkar, S.Govindrajan, Aarti Kinikar, N. Priya, Sanjay Gaikwad, Balamugesh Thangakunam, Arutselvi Devarajan, Mythili Dhanasekaran, Jeffrey A. Tornheim, Amita Gupta, Padmini Salgame <sup>1</sup> , Devashyam Jesudas Christopher, Hardy Kornfeld, Vijay Viswanathan, Jerrold J. Ellner, C. Robert Horsburgh, Jr., Akshay Gupte, Chandrasekaran Padmapriyadarsini, Natasha S. Hochberg		
Predictors of Weight Loss During the Intensive Phase of Tuberculosis Treatment in Patients with Drug Susceptible Pulmonary Tuberculosis in South India	Jayashree Kalva, Senbagavalli Prakash Babu, Prakash Babu Narasimhan, Kalaivani Raghupathy, Komala Ezhumalai, Selby Knudsen, Charles Robert Horsburgh, Natasha Hochberg, Padmini Salgame, Gautam Roy, Jerrold Ellner, Sonali Sarkar		
Sputum Conversion Rates after Intensive Phase of Tuberculosis Treatment	Prabavathy Gopalakrishnan, Kalaivani Raghupathy, Komala Ezhumalai, Prakash Babu Narasimhan, Senbagavalli Prakash Babu, Selby Knudsen, Charles Robert Horsburgh, Natasha Hochberg, Padmini Salgame, Gautam Roy, Jerrold Ellner, Sonali Sarkar		

SUBMITTED (Continued)			
TITLE	INVESTIGATORS		
Effect of Smoking on Hematological Parameters in Pulmonary Tuberculosis Patients	Komal M Jain, Komala Ezhumalai, Kalaivani Raghupathy, Prakash Babu Narsimhan,Senbagavalli Prakash Babu, Selby Knudsen, Charles Robert Horsburgh, Natasha Hochberg, Padmini Salgame, Gautam Roy, Jerrold Ellner, Sonali Sarkar		
Association between Baseline Anemia and TB Treatment Outcome among Pulmonary Tuberculosis Patients of Puducherry: Evidence from a Cohort Study	Suganya Jayaram, Senbagavalli Prakash Babu, Komala Ezhumalai, Kalaivani Raghupathy, Prakash Babu Narasimhan, Selby Knudsen, Charles Robert Horsburgh, Natasha Hochberg, Padmini Salgame, Gautam Roy, Jerrold Ellner, Sonali Sarkar		
Impact of Clofazimine on Self-image and Psychology among Patients Treated for Multidrug-resistant Tuberculosis in the Private Sector in Mumbai	Reema Raviraj, Namrata Sawant, Ishita Gajjar, Prerna R. Arora, Yohaan Shirali, Megha Karane, Amita Gupta, Jeffrey A Tornheim, Ashok Mahashur, Jai Mullerpattan, Lancelot Pinto, Ayesha Sunavala, Camilla Rodrigues, Zarir Udwadia, Tester Ashavaid		
A Case Report on Drug Induced Hypersensitivity Reactions Caused by Multiple Drugs in an Adult with Drug Resistant TB and the Drug Reintroduction Tests Performed to Determine the Offending Agents	Yohaan Shirali, Prerna R. Arora, Jigneshkumar Patel, Ishita Gajjar, Smruti Kharat, Reema Shetty, Tejeshwi Patil, Megha Karane, Namrata Sawant, Nikita Dawal, Amita Gupta, Jeffrey A Tornheim, Camilla Rodrigues, Tester F. Ashavaid, Zarir F. Udwadia		
Sputum Mycobacterial Culture Conversion in Indian Multidrug Resistant Tuberculosis (MDR-TB) Patients	Heeral U.B. Pandya, Utkarsha Surve, Prerna R. Arora, Sanjana Valecha, Priti Dubey, Ishita Gajjar, Zarir F. Udwadia, Ashok Mahashur, Jai Mullerpattan, Lancelot Pinto, Ayesha Sunawala, Amita Gupta, Tester F. Ashavaid, Jeffrey A. Tornheim, Camilla Rodrigues		
Monitoring the Reaction of Clofazimine on Multidrug Resistant Tuberculosis Patients	<b>Tejeshwi Patil,</b> Prerna R. Arora, Smruti Kharat, Namrata Sawant, Jigneshkumar Patel, Yohaan Shirali, Ishita Gajjar, Reema Raviraj, Ashok Mahashur, Jai Mullerpattan, Lancelot Pinto, Ayesha Sunavala, Amita Gupta, Jeffrey A Tornheim, Camilla Rodrigues, Zarir Udwadia, Tester Ashavaid		
The Prevalence of Latent Tuberculosis Infection among Spouse and First- degree Relative Household Contacts of Pulmonary Tuberculosis Patients	Komala Ezhumalai, Prakash Babu Narasimhan , Kalaivani Raghupathy, Senbagavalli Prakash Babu, Selby Knudsen, Charles Robert Horsburgh, Natasha Hochberg, Padmini Salgame, Gautam Roy, Jerrold Ellner, Sonali Sarkar		

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TITLE	INVESTIGATORS		
Phenotypic DST Testing for MTB Including MIC and Critical Concentration by MGIT under the MDR- TB Free: Monitoring Adverse Effects, Utilizing Resources Optimally, Knowing Resistance Patterns, and Treatment Strategy Study (MUKT)	Utkarsha Surve, Prerna R. Arora, Heeral U.B. Pandya, Sanjana Valecha, Priti Dubey, Ishita Gajjar, Zarir F. Udwadia, Ashok Mahashur, Jai Mullerpattan, Lancelot Pinto, Ayesha Sunawala, Amita Gupta, Tester F. Ashavaid, Jeffrey A. Tornheim, Camilla Rodrigues		
Baseline Biochemical and Haematological Profile of People with TB at Different Levels of Glucose Intolerance	<b>Arutselvi Devarajan</b> , Mythili Dhanasekaran, Satyavani Kumpatla, Hardy Kornfeld, Vijay Viswanathan		
Performance of QuantiFERON Assay across Different Age Groups	<b>Brindha B</b> , Murugesan S, Sathyamurthi P, Kannan T, Evangeline Ann Daniel, Madeshwaran A, Sangeetha A, Syed Nissar RK, Amsaveni Sivaprakasam, Hanna LE, Padmapriyadarsini C		
Tuberculosis Risk Signatures and Differential Gene Expression May Identify Individuals Who Fail Treatment	Arthur VanValkenburg, Senbagavalli Prakash Babu, Noyal Mariya Joseph, Sonali Sarkar, C. Robert Horsburgh, Natasha S. Hochberg, Padmini Salgame, W. Evan Johnson, Jerrold J Ellner		

# **Young Investigator Abstracts SUBMITTED**

#### **Clinical and Laboratory Predictors of Tuberculosis Recurrence**

Submitting Author: Sonya Krishnan

**Co-authors:** Nikhil Gupte, Shreyas Desmukh, Padma Priyadarshini, Sanjay Gaikwad, Vijay Vishwanathan, Madhusudan Barthwal, Amita Gupta, Hardy Kornfeld, Jonathan Golub, Vidya Mave

**Background:** Despite successful completion of therapy for drug-susceptible pulmonary tuberculosis (PTB), a subset of individuals experience an unfavorable treatment outcome of tuberculosis (TB) recurrence. India accounts for 26% of the global burden of TB and few data on predictors of TB recurrence exist, especially with a focus on India. A TB recurrence prediction model could enable clinicians to identify patients at risk for recurrence during antituberculosis therapy (ATT) and may be used to alter patient care strategies, such as enhanced monitoring post treatment for high-risk individuals

Methods: We conducted a retrospective analysis leveraging 3 NIH and Indian government funded observational TB cohorts in India (TB-DM, c-TRIUMPh, and eDOTS) designed to assess risk factors associated with unfavorable TB treatment outcomes. Adults newly diagnosed with PTB were enrolled and initiated on ATT, with 18-24 months of follow-up. A priori we selected 8 clinical and laboratory candidate predictors for recurrence based on previously published prediction models and expert opinion. We randomly selected 80% of the dataset and used multivariable logistic regression and bootstrapped backwards selection (repetitions=1000) to identify the best predictors of TB recurrence. We measured model accuracy by receiver operating characteristic (ROC) curve and area under the curve (AUC). We tested model fit by Akaike information criterion (AIC) and reliability by Kappa statistic. We internally validated the model with the remaining 20% of the dataset, generating the model accuracy, sensitivity, and specificity.

**Results:** Among 1164 adults diagnosed with PTB who completed ATT and achieved cure, 95 (8%) subsequently experienced recurrence. The most important predictors of TB recurrence were female sex, low body mass index (BMI), ever smoker history, month 2 (M2) smear positivity, and M2 culture positivity (Table 1). The model exhibited a c-statistic of 0.68 (95% CI 0.52-0.84) and a Kappa statistic of 0.23. Internal validation revealed an accuracy of 90% (95% CI 0.86-0.93), a sensitivity of 0.94 and a specificity of 0.31.

**Conclusions:** Our prediction modeling revealed female sex, low BMI, ever smoker history, M2 smear positivity, and M2 culture positivity as the most important predictors to discriminate TB recurrence from sustained cure.

Table 1. Key clinical and laboratory variables from final model to predict tuberculosis recurrence

Predictor Variable for Tuberculosis Recurrence*	Coefficient	Standard Error
Intercept	-2.10	0.70
Female Sex	-0.56	0.30
Ever smoker history (Yes)	-0.51	0.37
Body mass index	-0.02	0.04
Smear positivity (month 2)	0.64	0.40
Culture positivity (month 2)	0.73	0.35
Age		
Alcohol use		
Chest x-ray cavitation (month 6)		

<sup>\*</sup>Key variables selected using multivariable logistic regression and bootstrapped backwards selection (bootstraps=1000).

## Characterization of Monocyte Responses in Pulmonary TB Patients With or Without Type 2 Diabetes mellitus

**Submitting Author:** Arul Nancy

**Co-authors:** Nathella Pavan Kumar, Kadar Moideen, Vijay Viswanathan, Shanmugam Sivakumar, Syed Hissar, Hardy Kornfeld, Subash Babu

**Background:** Tuberculosis (TB) and diabetes mellitus (DM) are two common diseases that independently have immense public health significance globally. Monocytes are important to the innate immune system and play a crucial role in several inflammatory conditions associated with chronic infection, including TB. However, surface markers of human monocyte subsets and inflammatory or anti-inflammatory functional monocyte phenotypes in TB-DM co-morbidity remain undefined.

**Methods:** We examined the monocyte surface marker expression and monocyte cytokine responses in pulmonary TB patients with diabetes and without diabetes compared with only diabetes and healthy controls. We studied 40 TB patients [with diabetes (TB-DM) (n=20) and without diabetes (TB) (n=20)] and compared them to patients with diabetes mellitus alone (DM) (n=20), and healthy controls (HC) (n=20). TB patients were followed up to 6 months till completion of anti-TB treatment. We performed an in-vitro cell culture by stimulating with PPD, Mtb whole cell lysate (WCL), and LPS (TLR4)/ Pam2 (TLR2).

**Results:** The frequencies of monocyte surface markers, CD163, CD80 and CD86 were elevated at baseline and the frequencies of PDL-2, CD163, CD206 were elevated upon PPD and WCL stimulation in TB-DM in comparison to TB, DM and HC. Monocyte associated cytokines such as IL-6, IL-12, IL-1b, TNFa and IL-10 were elevated at baseline and upon PPD and WCL stimulation in TB-DM in comparison to TB, DM and HC. Finally, after successful completion of anti-TB treatment, frequencies of monocyte surface markers and cytokines were significantly diminished in both in TB-DM and TB group.

**Conclusions:** Our data demonstrate that TB antigen specific monocyte surface marker expression and cytokine responses potentially are significantly augmented in tuberculosis-diabetes co-morbidity. Thus, TB-DM is mainly characterized by enhanced monocyte activation and function.

#### Pharmacokinetics of Linezolid in Indian Multidrug Resistant Tuberculosis Patients

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**Co-authors:** Bhamini Keny, Alpa J. Dherai, Zarir F. Udwadia, Ashok A. Mahashur, Lancelot Pinto, Mullerpattan Jai, Ayesha Sunavala, Camilla Rodrigues, Amita Gupta, Neil Martinson, Ebrahim Variava, Firdaus Nabeemeeah, Juan Eduardo Resendiz-Galvan, Mahmoud Abdelwahab, Paolo Denti, Jeffrey A. Tornheim, Tester F. Ashavaid

**Background:** Linezolid is widely used as a second line drug for anti-tuberculosis treatment. It is well absorbed orally but its pharmacokinetics (PK) is known to exhibit wide inter-individual variability warranting the need for therapeutic drug monitoring. The present study aimed to model the pharmacokinetics of linezolid among Indian adults and adolescents on ongoing therapy.

**Methods:** The study was a part of the RePORT India Parent Protocol which included treatment naïve multidrug resistant tuberculosis (MDR-TB) patients on daily linezolid dosage of 300 or 600 mg. Blood samples were collected at 0,1,2,4,6 and 8 hours after linezolid dose for intensive PK and 0 and 2 hours post-dose for sparse PK and analysed using a homogenous enzyme-immunoassay. Two pharmacokinetic models were selected from the literature to assess their ability to predict concentrations. Analysis was performed using NONMEM, and model fit was evaluated using the visual predictive check plots.

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**Results:** The frequencies of monocyte surface markers, CD163, CD80 and CD86 were elevated at baseline and the frequencies of PDL-2, CD163, CD206 were elevated upon PPD and WCL stimulation in TB-DM in comparison to TB, DM and HC. Monocyte associated cytokines such as IL-6, IL-12, IL-1b, TNFa and IL-10 were elevated at baseline and upon PPD and WCL stimulation in TB-DM in comparison to TB, DM and HC. Finally, after successful completion of anti-TB treatment, frequencies of monocyte surface markers and cytokines were significantly diminished in both in TB-DM and TB group.

**Conclusions:** Our data demonstrate that TB antigen specific monocyte surface marker expression and cytokine responses potentially are significantly augmented in tuberculosis-diabetes co-morbidity. Thus, TB-DM is mainly characterized by enhanced monocyte activation and function.

# Impact of Undernutrition on Tuberculosis Treatment Outcomes in India: A Multicenter Prospective Cohort Analysis

**Submitting Author:** Pranay Sinha

**Co-authors:** Chinnaiyan Ponnuraja, Nikhil Gupte, Senbagavalli Prakash Babu, Samyra R. Cox, Sonali Sarkar, Vidya Mave, Mandar Paradkar, S.Govindrajan, Aarti Kinikar, N. Priya, Sanjay Gaikwad, Balamugesh Thangakunam, Arutselvi Devarajan, Mythili Dhanasekaran, Jeffrey A. Tornheim, Amita Gupta, Padmini Salgame<sup>1</sup>, Devashyam Jesudas Christopher, Hardy Kornfeld, Vijay Viswanathan, Jerrold J. Ellner, C. Robert Horsburgh, Jr., Akshay Gupte, Chandrasekaran Padmapriyadarsini, Natasha S. Hochberg

**Background:** Undernutrition is the leading risk factor for tuberculosis (TB) disease worldwide, but its impact on treatment outcomes is poorly defined. We assessed how acute and chronic undernutrition affect TB treatment outcomes.

**Methods:** We analyzed prospectively collected data (2015-2019) for adults with newly-diagnosed drugsensitive pulmonary TB enrolled at five sites in the Regional Prospective Observational Research on Tuberculosis (RePORT) India consortium. We used multivariable Poisson regression to assess the independent associations between nutritional status and unfavorable treatment outcomes. Nutritional status was defined as severe, moderate or mild undernutrition (body mass index [BMI] <16 kg/m2, 16-16.99, and 17-18.5 respectively), normal BMI (18.5-23 kg/m2), or overweight (BMI>23kg/m2). We also analyzed the impact of percent change in BMI after two months of therapy and stunting (height-for-age Z-score < -2). Unfavorable treatment outcome was a composite variable comprising clinical or bacteriological failure, death, or recurrence. Multivariable models included potential confounders.

**Results:** Of 2931 persons with TB, 1783 (60.8%) were undernourished and 1071 (36.5%) were stunted at baseline. After two months, 713 (24.3%) participants had BMI change ≤0%. In multivariable analyses, severe and moderate undernutrition were associated with unfavorable outcomes (adjusted incidence rate ratio[alRR]:2.05; 95% confidence interval [CI]: 1.38-3.06 and alRR; 1.62; 95% CI: 1.03-2.53, respectively). BMI change ≤0% after two months was associated with increased risk of unfavorable outcomes (alRR: 1.81; 95% CI: 1.25-2.63). Stunting was not significantly associated with unfavorable outcomes (alRR 1.24, 95% CI: 0.94-1.64). We did not find evidence for interaction between nutritional status and diabetes, symptom duration, alcohol use, or smoking status.

**Conclusions:** Baseline undernutrition and lack of BMI change during treatment are independently associated with increased unfavorable outcomes. Systematic nutritional assessment at baseline and during therapy treatment should be integrated into standard of care. Future studies should evaluate whether nutritional support improves TB treatment outcomes.

Predictors of Weight Loss During the Intensive Phase of Tuberculosis Treatment in Patients with Drug Susceptible Pulmonary Tuberculosis in South India

Submitting Author: Jayashree Kalva

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**Background:** Tuberculosis is well-known for causing wasting. Patients on treatment gain weight, of which majority happens during the intensive phase. Body weight change is an important marker for treatment outcome, weight loss being associated with unfavorable outcomes like clinical relapse, treatment failure and death. But there is limited description of weight loss during treatment and understanding of its predictors.

**Objectives:** Primary objective was to assess the predictors of weight loss during the intensive phase of TB treatment among new sputum positive pulmonary TB patients. The secondary objective was to understand whether weight loss is associated with other indicators of poor response to treatment such as sputum conversion at the end of intensive phase of treatment.

**Methods:** Data collected as a part of the prospective TB cohort of RePORT India Phase 1 was used for this study. The study was conducted in Pondicherry, and Cuddalore and Viluppuram districts of Tamil Nadu. Sputum smear and body weight comparison were made in the baseline and at the end of second month of treatment (intensive phase).

**Results:** Total of 726 participants had the weight measurements at the two time points. About 18.7% (n = 136) patients had weight loss at the end of intensive phase ranging from 0.1 to 22.2 kgs, the mean (SD) weight lost being 2.3 (3.05) Kgs from the pre-treatment weight (t = -15.784, p<0.001). Mean weight loss was more among males (2.4kg), diabetics (2.8 kg) and alcoholics (2.1 kg). Alcohol consumption was the only predictor of weight loss after adjusting for age, diabetes, marital status and BMI (aRR 1.52, p 0.02). Weight loss was not associated with sputum conversion at the end of second month, however it was strongly associated with adverse treatment outcome (p<0.001)

**Conclusion**: Of the multiple factors associated with adverse TB treatment outcomes, alcohol use emerged as the predictor for weight loss during the intensive phase.

#### Sputum Conversion Rates after Intensive Phase of Tuberculosis Treatment

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**Background and Objectives:** In pulmonary tuberculosis (PTB) patients, bacteriological status at the end of Intensive Phase (IP) of treatment affects prognosis and those failing to achieve sputum conversion are more likely to have poor treatment outcomes. The study aimed to identify the factors associated with sputum nonconversion at the end of IP among PTB patients.

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**Methods:** A total of 893 newly diagnosed sputum smear-positive TB patients were included in the study. Data was collected as part of RePORT India Phase I conducted during 2014 to 2018 at JIPMER site in collaboration with Boston University Medical Campus and Rutgers University. Data were analysed in STATA version 14.0 using Chi square test for univariate analysis. Variables with p<0.2 were included in the multivariable model using binary logistic regression.

**Results:** Sputum smear conversion was observed in 759 (85%) patients [male (83%), female (90%), smear grade 1+ (92%), 2+ (84%) and 3+ (80%)] at the end of IP. In univariate analysis, sputum conversion was lower among male, employed, alcohol users, smokers, high sputum smear grading (2+/3+), those having leukocytosis, thrombocytopenia and lymphopenia, whereas age, BMI (Body Mass Index), WBC, lymphocytes and monocyte counts were not significant. Thrombocytopenia (RR: 2.80, CI 1.40 - 5.61), erythrocytosis (RR:2.18, CI 1.09 - 4.34), high hematocrit (RR:2.30, CI 1.15 - 4.58) and high sputum smear grading 2+(RR:1.83, CI 1.15 - 2.92), 3+(RR: 2.45, CI 1.59 - 3.79) were significantly associated with sputum non-conversion in the multivariable analysis which included the variables found to be significant in univariate analysis with p<0.2, namely alcohol, smoking, gender and employment status.

**Conclusion:** As expected, the study shows that patients with baseline high bacillary load (2+/3+) are at higher risk of sputum non-conversion. However, the role of erythrocytosis, high hematocrit and thrombocytopenia on Mycobacterium tuberculosis in patients on treatment need further exploration.

#### Effect of Smoking on Hematological Parameters in Pulmonary Tuberculosis Patients

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**Co-authors:** Komala Ezhumalai, Kalaivani Raghupathy, Prakash Babu Narsimhan, Senbagavalli Prakash Babu, Selby Knudsen, Charles Robert Horsburgh, Natasha Hochberg, Padmini Salgame, Gautam Roy, Jerrold Ellner, Sonali Sarkar

**Background:** The use of tobacco affects the hematological parameters. Several studies have reported that smokers have increased white blood cells, red blood cells, haemoglobin, hematocrit, platelets, neutrophils and lymphocytes. The hematological parameters in patients with tuberculosis show variability with decrease in hemoglobin and RBCs but increase in WBC, neutrophils and platelets. There is discordance observed between different studies. The effect smoking has on hematological parameters of pulmonary tuberculosis patients are not yet clear. In this study we evaluated the hematological parameters between smokers and non-smokers in pulmonary tuberculosis patients to understand the effects of smoking. A higher number of neutrophils and WBC have been linked to disease severity in TB patients and therefore have considerable impact on mortality.

**Methods:** This is a retrospective study with hematological data obtained from of 1246 new culture confirmed pulmonary tuberculosis patients between the age group of 13 – 82 years enrolled at the JIPMER site under RePORT India from 2014-18. The participants that did not smoke for the past one month were classified as non-smokers and rest were considered as smokers. The factors analyzed were WBC, RBC, hemoglobin, hematocrit, platelets, neutrophils and lymphocytes. Two-proportion test was used to analyze the data.

**Results:** Among the 1246 participants, 48.3% were smokers. WBC and neutrophils were significantly higher in smokers in comparison to non-smokers. The p-value for WBC and neutrophils was significant with 0.004 and 0.0187 respectively. The p-value for platelets was 0.0763. There was no significant difference in red blood cells, hemoglobin, hematocrit and lymphocytes between smokers and non-smokers.

**Conclusions:** This study shows that RBC, hemoglobin, hemocrit and lymphocytes are not higher in tuberculosis patients with smoking in comparison to other studies conducted on smokers in healthy population. There is no difference observed in RBC, hemoglobin, hemocrit and lymphocytes between smoker and non-smokers with pulmonary tuberculosis. However, greater proportion of smokers had higher WBC and neutrophils as compared to non-smokers among the pulmonary tuberculosis patients.

Importantly, the treatment of low dose aerosol H37Rv-infected mice with HDAC-1 inhibitor also induced a significantly increased bacterial burden in lungs at 14 days and in the lungs, spleens and mediastinal lymph nodes at 28 days post-infection despite elevated production of IFN- $\gamma$ , an essential cytokine in the protective immunity against TB infection, as compared with that in the vehicle control mice, supporting the in vivo significance of HDAC-1 in control of Mtb growth by the regulation of IFN- $\gamma$  signaling in innate immune cells. Consistent with this, HDAC-1 inhibitor rendered IFN- $\gamma$  mediated control of Mtb growth blunted in bone marrow derived macrophages (BMDM) with significantly increased bacilli growth compared to that in BMDM with IFN- $\gamma$  and vehicle control, and further determination of IFN- $\gamma$  downstream signaling molecule, STAT1, showed reduced phosphorylation of STAT1 in Mtb infected BMDM and human primary macrophages treated with HDAC-1 inhibitor. Consistent with reduced phosphorylation of STAT1, the presence of HDAC-1 inhibitor.

# Association between Baseline Anemia and TB Treatment Outcome among Pulmonary Tuberculosis Patients of Puducherry: Evidence from a Cohort Study

Submitting Author: Suganya Jayaram

**Co-authors:** Senbagavalli Prakash Babu, Komala Ezhumalai, Kalaivani Raghupathy, Prakash Babu Narasimhan, Selby Knudsen, Charles Robert Horsburgh, Natasha Hochberg, Padmini Salgame, Gautam Roy, Jerrold Ellner, Sonali Sarkar

**Background:** Anemia is the most common hematological problem among TB patients. There is paucity of data on the association between anemia and TB Treatment outcome in India. This study aims to estimate the independent risk of unfavorable TB treatment outcome among pulmonary tuberculosis patients (PTB) with anaemia at baseline..

**Methods:** This was a Cohort study done among new PTB, enrolled at the JIPMER site of RePORT India from 2014-18. Patients were evaluated for their details on demography, clinical history, serum biochemistry and sputum microscopy. The data was analyzed using Stata software version 14.0. Descriptive and Log-binomial regression analysis was carried out to find the association between anemia and TB treatment outcome.

**Results:** Of the 1,015 TB patients, 706 (69.56%) were anemic. Among the anemic, 43.34%, 48.30% and 8.35% had mild (Male: 11.1 – 12.9, Female: 11.1-11.9 gm/dl), moderate (8-11 gm/dl) and severe (<8 gm/dl) anemia respectively. Anemic patients were 1.2 times more likely to have unfavorable treatment outcome as compared to non-anemic patients (RR 1.2, Cl 0.75- 2.0 p= 0.38). Risk in those having mild and moderate anemia was higher, but not statistically significant. Severe anemia was significantly associated with unfavorable TB treatment outcome (RR=2.1, 95% Cl 1.4-3.1 p= <0.001) in bivariate analysis, but not in the multivariable model (RR 1.6 Cl 0.9 – 2.6 P=0.50). Other variables like, male gender, tobacco smoking (former and present smoker), alcohol use, thrombocytosis and thrombocytopenia was significantly associated with unfavorable treatment outcome in bivariate analysis, were not significant after adjustment with possible confounders.

**Conclusion:** More than two third of the PTB patients in our setting were anemic (69.56%), but anaemia was not an independent predictor of adverse treatment outcomes after adjusting for BMI (Body Mass Index) and other demographic, microbiologic and haematological parameters. The role of anaemia in TB needs further investigation.

Impact of Clofazimine on Self-image and Psychology among Patients Treated for Multidrugresistant Tuberculosis in the Private Sector in Mumbai

Submitting Author: Reema Raviraj

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**Background:** Clofazimine is very effective drug used in treatment of multidrug resistant tuberculosis (MDR-TB). However, it leads to visible discoloration, redness and drying of skin and is likely to have an impact on self-image. We assessed the impact of clofazimine on self-image among Indian MDR-TB patients.

**Methods:** Newly diagnosed adult and adolescents with MDR-TB were enrolled in an ongoing RePORT India Parent Protocol study in Mumbai. Quality of life assessed by the WHOQOL-BREF was recorded for each participant at baseline, months 6,12,18 and 24 of treatment. Six questions from the psychological domain were assessed to evaluate the impact of clofazimine on psychological wellbeing. The analysis was performed using chi-square test and variables with p<0.05 were considered statistically significant.

**Results:** In total, 143 participants (65.7% females) average aged 26 years on a daily 100mg clofazimine dose were evaluated. We observed a significant improvement across several domains. Positive feelings improved between baseline and M6 (p=0.019), M12 (p=0.003), M18 (p<0.001), and M24 (p<0.001) of treatment. Personal belief and wellbeing and concentration did not change significantly over the first year, but was significantly better from baseline to M18 (p<0.001 and p=0.003 respectively) and M24 (p=0.035 and p=0.023 respectively) of treatment. Appearance and self-esteem both improved during the first 6 months of treatment (p=0.040 and p=0.048, respectively), with self-esteem further improving at M18 and M24 (p=0.005, and p<0.001, respectively). Negative feelings improved from baseline to M12 (p=0.014), M18 (p=0.002), and M24 (p<0.001).

**Conclusions and Recommendations:** In this ongoing study, we identified significant improvement among study participants' self-esteem and positive feelings over the first 6 months, with progressive improvement during the second year of MDR-TB treatment. These coincide with the known timeline of dermatologic side effects from clofazimine treatment. Our findings underscore the importance of counselling and psychosocial support for MDR-TB patients during clofazimine.

A Case Report on Drug Induced Hypersensitivity Reactions Caused by Multiple Drugs in an Adult with Drug Resistant TB and the Drug Reintroduction Tests Performed to Determine the Offending Agents

Submitting Author: Yohaan Shirali

**Co-authors:** Prerna R. Arora, Jigneshkumar Patel, Ishita Gajjar, Smruti Kharat, Reema Shetty, Tejeshwi Patil, Megha Karane, Namrata Sawant, Nikita Dawal, Amita Gupta, Jeffrey A Tornheim, Camilla Rodrigues, Tester F. Ashavaid, Zarir F. Udwadia

**Background:** Drug hypersensitivity reaction (DHR) is an adverse drug reaction (ADR) defined as "Objectively reproducible symptoms or signs initiated by exposure to a defined stimulus at a dose tolerated by normal persons".

**Method:** A case report of a 29 year-old female patient diagnosed with DR tuberculosis, affecting her pleura and spine.

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**Results:** Patient was admitted presenting with fever, dry cough, breathlessness, palpitations, headaches for 2 weeks, with increasing intensity. She was diagnosed with drug resistant TB and second-line treatment was started. She was discharged about a week later. Her initial treatment consisted of:

- Pyrazinamide
- Ethambutol
- · Cycloserine
- Clofazimine
- Moxifloxacin
- Linezolid
- Amikacin
- Bedaquiline

After three weeks of treatment, she presented with pruritus, breathlessness, fever and generalized rash. She was then instructed to keep the drugs on hold for a week. Pyrazinamide was not restarted due to resistance.

With the first reintroduction test she took one drug every fourth day. After the second week, she reported generalized rash, pruritus and fever immediately with cycloserine. Bedaquiline, amikacin and clofazimine triggered no reaction.

After holding drugs for a week, during the second reintroduction test, she took one drug every week, with progressively increasing doses. After no reaction with bedaquiline, amikacin, clofazimine, linezolid and ethambutol, one dose of cycloserine again triggered pruritus, rash and fever immediately. Two weeks later, low dose moxifloxacin produced the aforementioned symptoms. A month after that, levofloxacin triggered only pruritus.

**Conclusions:** An unusual case of drug allergies, with delayed DHR seen after three weeks of treatment but immediate hypersensitivity reactions with reintroduction tests of varying intervals, doses. The likelihood of drug interactions being responsible seems unlikely since the allergic drugs caused a reaction when given individually as well. There also appears to be some degree of cross-reactivity between the two aforementioned fluoroquinolones, considering they triggered varying degrees of allergic responses.

## Sputum Mycobacterial Culture Conversion in Indian Multidrug Resistant Tuberculosis (MDR-TB) Patients

Submitting Author: Heeral U.B. Pandya

**Co-authors:** Utkarsha Surve, Prerna R. Arora, Sanjana Valecha, Priti Dubey, Ishita Gajjar, Zarir F. Udwadia, Ashok Mahashur, Jai Mullerpattan, Lancelot Pinto, Ayesha Sunawala, Amita Gupta, Tester F. Ashavaid, Jeffrey A. Tornheim, Camilla Rodrigues

**Background:** The spread of multidrug resistant (MDR-TB) is of a great concern and early treatment of patients is of utmost importance. Mycobacterial culture conversion of sputum from positive to negative is said to be an early indicator of successful TB treatment, but may take longer for drug-resistant TB strains than drug susceptible strains. We calculated time to culture conversion among participants in MDR-TB MUKT.

**Methods:** Adults and adolescents with confirmed MDR-TB and <2 weeks of treatment were enrolled in the RePORT India parent protocol. Participants with pulmonary TB submitted serial sputum samples with time to culture conversion defined as time in months from treatment initiation until the first negative sputum test was collected. Drug susceptibility test (DST) results at the start and end to culture positivity were compared to identify any changes.

**SUBMITTED: Continued** 

**Results:** Of 200 study participants 71 had baseline culture-positive sputum. Majority of participants were females (61.97%) with the median age of 25 years (IQR 18-36). Typical TB symptoms including cough, fever, sweat, or weight loss were noted by 36/71 participants (50.70%). Out of the 71 patients who had a positive baseline sputum culture, 51 had more than one culture available for analysis of time to conversion. Of these, 21 converted their cultures by month 1 (41.18%), 16 by month 2 (31.37%), 13 by month 3 (25.49%), and 1 by month 5 (1.96%). Among the patients with consecutive sputum cultures, median time to sputum culture conversion was 60 days (IQR 36.5-73.5). There were no significant changes in the DST pattern of the patients who had consecutive positive cultures.

**Conclusion and Recommendations:** Most study participants with treatment-naïve MDR-TB on DST-guided therapy had culture conversions within 12 weeks of treatment initiation. These data support repeat DST for those with positive cultures persisting longer than 3 months to identify emergence of resistance

#### Monitoring the Reaction of Clofazimine on Multidrug Resistant Tuberculosis Patients

Submitting Author: Tejeshwi Patil

**Co-authors:** Prerna R. Arora, Smruti Kharat, Namrata Sawant, Jigneshkumar Patel, Yohaan Shirali, Ishita Gajjar, Reema Raviraj, Ashok Mahashur, Jai Mullerpattan, Lancelot Pinto, Ayesha Sunavala, Amita Gupta, Jeffrey A Tornheim, Camilla Rodrigues, Zarir Udwadia, Tester Ashavaid

**Background and Rationale:** Clofazimine has shown activity against tuberculosis and is a WHO recommended drug to treat multidrug resistant tuberculosis (MDR-TB) as a medicine with "Unclear Efficacy". However, the side effects include skin discolouration, ichythyosis and gastro intestinal events. The present study aimed to assess the impact of clofazimine on skin discolouration MDR-TB patients enrolled in Cohort-A of the RePORT India Parent Protocol in Mumbai.

**Methods:** We evaluated the skin discoloration by taking pictures of the shoulder or back in 38 patients on Clofazimine regimen at baseline, Months 1, 6 and 12. Assessment of skin discoloration were done using the Munsell colour chart scale HY10R to match the skin tones. A grading of mild, moderate or severe was done to evaluate the severity of skin discoloration.

**Result:** The present study represents data for 38 patients on ongoing treatment. Most patients (n=16, 42.1%) were on clofazimine for 180-398 days (6M-12M), 10 patients (26.3%) for 40-187 days (1M-6M) and 12 patients (31.6%) for 24-37 days (baseline-1M). Using the Munsell color charts, skin discoloration was graded as severe for 16 patients (42.1%) and all of these were on >180 days of clofazimine treatment (range 180-398 days). Moderate discoloration was seen in 10 patients (26.3%) who were on treatment for 1M-6M (40-187 days) while 12 patients (31.6%) had mild discoloration who were just started on treatment (24-37 days). This represented a perfect correlation between exposure and extent of discoloration. Data collection is ongoing to evaluate the impact of clofazimine on colour change over longer durations of therapy.

**Conclusion:** The study concluded that the patients who were on clofazimine regimen for a longer duration majorly experienced side effect of skin discoloration. Since clofazimine has a long half-life, the severity of skin discoloration increases as the duration of treatment increases.

# The Prevalence of Latent Tuberculosis Infection among Spouse and First-degree Relative Household Contacts of Pulmonary Tuberculosis Patients

Submitting Author: Komala Ezhumalai

**Co-authors:** Prakash Babu Narasimhan , Kalaivani Raghupathy, Senbagavalli Prakash Babu, Selby Knudsen, Charles Robert Horsburgh, Natasha Hochberg, Padmini Salgame, Gautam Roy, Jerrold Ellner, Sonali Sarkar

**Background and Rationale:** Household contacts (HHC) of TB patients have higher prevalence of LTBI as compared to the general population with a higher risk of progression to active TB. However, it is not known whether the prevalence differs based on their relationship to the IC.

**Methods:** The cohort study was conducted at JIPMER site under RePORT India among HHC of new culture confirmed pulmonary TB patients. The patient's relatives included parents, siblings and children, considered as first-degree relative (FDR) and spouses. All the participants underwent TST and/or IGRA to determine the LTBI status. Prevalence Ratios (PR) with 95% CI was used to assess the risk factors associated with the LTBI. Multivariable mixed effects generalized linear modelling was performed.

**Results:** The mean (SD) age of male and female of 1318 HHC were 25.4 (14.8) and 33.0 (16.3) years respectively. Of 1318 HHCs, 766 (58.1%; 95%CI: 55.4%-60.8%) had LTBI and 6 (0.5%; 95%CI: 0.2%-0.9%) developed active TB disease. The prevalence of the LTBI among spouses was 64.2% (95%CI: 59% - 69.2%) and FDR was 55.8% (95%CI: 52.6% - 59.0%). LTBI positivity was significantly higher among spouses (PRR 1.42 (95% CI:1.11-1.83)) compared to FDR. As compared to ≤40 years, 40-59 years (aPR 2.2, 95% CI: 1.6 - 2.9, p<0.001) and ≥60 years (aPR 1.5, 95% CI: 0.8 - 2.7, p=0.17) had higher prevalence of LTBI. Those sharing bed had higher prevalence of LTBI (aPR 1.98, 95% CI: 1.4 - 2.7, p<0.001). Similarly, female gender, time spent with index cases, undernutrition, overweight/obese and alcohol use were significantly associated with LTBI in the multivariable model. Time spent in providing care for IC was significantly higher among LTBI positive female spouses compared to male spouses.

**Conclusion**: Among the HHC, screening program should focus on female spouse, undernourished, overweight/obese and alcohol users.

Phenotypic DST Testing for MTB Including MIC and Critical Concentration by MGIT under the MDR-TB Free: Monitoring Adverse Effects, Utilizing Resources Optimally, Knowing Resistance Patterns, and Treatment Strategy Study (MUKT)

Submitting Author: Utkarsha Surve

**Co-authors:** Prerna R. Arora, Heeral U.B. Pandya, Sanjana Valecha, Priti Dubey, Ishita Gajjar, Zarir F. Udwadia, Ashok Mahashur, Jai Mullerpattan, Lancelot Pinto, Ayesha Sunawala, Amita Gupta, Tester F. Ashavaid, Jeffrey A. Tornheim, Camilla Rodrigues

**Background:** Traditional drug susceptibility testing (DST) in liquid culture (MGIT960) can only test a single drug concentration at a time. Minimum inhibitory concentration (MIC) testing by microtitre plates offer a way to simultaneously test several anti-tuberculosis drugs over a wide range of concentrations.

**Methods:** We evaluated 135 isolates of MDR-TB collected from participants in MDR-TB MUKT. Each was tested by MGIT susceptibility as well as MIC testing for multiple MDR-TB active drugs, including two new (bedaquiline (BDQ) and delamanid (DLM)) and two repurposed drugs (clofazimine (CFX) and linezolid (LZD)) from a single inoculum suspension using the semi-automated auto-inoculator. MIC values were recorded on Day 7, 10, 14, and 21 using the Vizion: Digital Viewing System. MIC distributions were compared with those of a susceptible laboratory strain (H37Rv) and MIC results were assessed for accuracy compared MGIT DST.

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### **SUBMITTED: Continued**

**Results:** Mean time-to-result was 13 days by MGIT and 14.22 days by MIC assay. MIC values were significantly higher among resistant isolates than susceptible isolates for all drugs tested with the exception of capreomycin (p=0.07). The accuracy of MIC testing was found to be >90% for majority of the drugs as compared to that with MGIT 960. It was also found that the sensitivity with the sensititre plate was > 90% for isoniazid, rifampicin, ethionamide, moxifloxacin 1, moxifloxacin 0.25 and linezolid whereas the specificity was found to be >90% for kanamycin, moxifloxacin 0.25, amikacin, capreomycin and linezolid respectively.

**Conclusions:** MIC testing is a practical, quantitative method that requires only basic infrastructure, provides accurate results compared to current MGIT DST, and provides nuanced resistance results that could facilitate individualized drug therapy for each patient.

## Baseline Biochemical and Haematological Profile of People with TB at Different Levels of Glucose Intolerance

Submitting Author: Arutselvi Devarajan

Co-authors: Mythili Dhanasekaran, Satyavani Kumpatla, Hardy Kornfeld, Vijay Viswanathan

**Background:** There are few studies which looked into the biochemical and haematological profile of people with TB and DM. Hence the main aim of the study was to assess and compare the bio-chemical and selected haematological parameters among persons with TB at different levels of glucose intolerance.

**Methods:** We used data from EDOTS cohort conducted as part of RePORT Phase I from 2014 to 2018. We included age, BMI, biochemical and selected baseline haematological parameters such as WBC, Neutrophil, Lymphocyte, Platelets, RBC and Haemoglobin. The study groups included TBnonDM (n=139), TB with known diabetes(TBDM) (n=166), TB with new diabetes(TB new DM) (n=97) and TB with pre-diabetes(TB pre-DM (n=34). The proportions and median(range) are reported accordingly. Chi square test and Kruskall Wallis tests were used for data analysis.

**Results:** The participants in TBnonDM group were found to be younger than all the other groups. BMI was significantly lesser in TBnonDM (16.5 median years) group compared to TBDM(20.6) and TB New DM groups(18.7)(p<0.001). Levels of fasting glucose, HbA1c, Triglycerides were higher in TBDM and TB New DM compared to TBnonDM group. Total cholesterol and LDL cholesterol were also significantly higher in TBDM group. The proportion of leucocytosis, Neutrophilia were higher in TBDM compared to TBnonDM group. Vitamin D deficiency was high among TBDM (72.9%) compared to TBnonDM group(50.4%) (p<0.001). But higher proportion of thrombocytosis (48.2%) was found in TBnonDM compared to TB New DM group (33%)(p<0.05). Erythrocytopenia (41.7%) was also significantly high in TBnonDM than TBDM (20.5%)(p<0.001) and TB New DM groups(34%)(p<0.05). Bilirubin was high among TBDM group.

**Conclusion:** Leucocytosis, Neutrophilia and VitaminD deficiency were found to be high among TBDM group. Thrombocytosis was found to be high among TBnonDM group. Further analysis is required to see the impact of these parameters on TB treatment outcomes.

#### Performance of QuantiFERON Assay across Different Age Groups

Submitting Author: Brinda B

**Co-authors:** Murugesan S, Sathyamurthi P, Kannan T, Evangeline Ann Daniel, Madeshwaran A, Sangeetha A, Syed Nissar RK, Amsaveni Sivaprakasam, Hanna LE, Padmapriyadarsini C

**Background:** Interferon-γ release assays (IGRAs) have emerged as attractive alternatives for the tuberculin skin test (TST) and are now being widely employed for the diagnosis of latent TB infection (LTBI). While the T-spot TB test uses an even number of cells for the test, the QuantiFERON (QFT) assay does not. There is some evidence to suggest that defining infection across all age-groups using a single cut-off recommended by the manufacturers of the QFT assay may not be precise, given age-related differences in immune function.

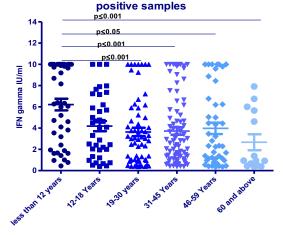
**Aim:** To assess the performance of the QuantiFERON Gold In-Tube (QFT-GIT) test across all age groups and to assess the suitability of employing a uniform cut-off to interpret the results.

**Methods:** We analyzed QFT-GIT data of 524 household contacts (HHC) of active TB cases aged between 10 months and 70 years, enrolled in a study titled "Cohort for Tuberculosis Research by the Indo-US Medical Partnership (C-TRIUMPH)" at the ICMR-National Institute for Research in Tuberculosis, Chennai, India. The study population was categorized into 6 groups as <12 years (children, n=79), 13-18 years (adolescents, n=73), 19-30, 31-45 and 46-60 years (adults, n=136, 141 and 75 respectively) and 61-70 years (elderly, n=20). TB-antigen induced IFN- $\gamma$  (TB-antigen minus Nil) production was measured in all groups and expressed as median values. Spearman correlation analysis was performed to analyze the correlation between IFN- $\gamma$  levels and age.

**Results:** Among the 524 HHC, 278 tested positive on QFT-GIT (cut-off >0.35 IU/ml as per manufacturer's guidelines). Children <12 years had the highest TB-specific IFN-γ response (6.340 IU/ml), and older adults aged >60 years had the lowest response (0.94 IU/ml). IFN-γ levels in the adult groups were more or less similar. Spearman correlation analysis revealed a significant inverse correlation between TB-specific IFN-γ response and age (r= -0.2238; p=0.002). This could possibly be attributed to decline in the number of lymphocytes that are believed to be the major producers of IFN-γ during TB infection with age.

**Conclusion:** Our analysis provides evidence to indicate that a uniform cut-off may not be most accurate in detecting LTBI across all age groups, and suggests the need for redefining QFT cut-offs, particularly for children and older adults.

#### Concentration of IFN gamma in nil corrected TB antigen tube for IGRA



Median value of IFN-g gamma concentration in nil corrected TB tubes in QFT-GIT positive samples						
Age group	less than 12 years	12-18 years	19-30 years	31-45 years	46-59 years	60 and above
Median	6.305	4.075	3	2.6	2.34	0.94

## Tuberculosis Risk Signatures and Differential Gene Expression May Identify Individuals Who Fail Treatment

**Submitting Author:** Arthur VanValkenburg

**Co-authors:** Senbagavalli Prakash Babu, Noyal Mariya Joseph, Sonali Sarkar, C. Robert Horsburgh, Natasha S. Hochberg, Padmini Salgame, W. Evan Johnson, Jerrold J Ellner

**Background:** Although Tuberculosis (TB) remains the second leading infectious disease killer, it is treatable. However, some cases fail treatment protocols after 5-6 months, and these individuals remain potentially contagious. Identifying early those who fail treatment could help retain the spread of TB and adapt therapy to those individuals. Those who fail treatment may have differentially expressed genes (DEGs) compared to those who respond to treatment. However, only a few studies have searched for a predictive gene signature in these patients. Furthermore, existing signatures designed to predict the risk of TB progression might help differentiate treatment failures from treatment success.

**Methods:** RNA-seq data from individuals with TB at baseline and two months of treatment were analyzed for differences in gene expression between those who benefited from treatment and those who did not. DEGs were analyzed with Qiagen's Ingenuity Pathway Analysis to determine relevant pathways involved in treatment failure. In addition, several TB signatures were scored with ssGSEA using the TBSignatureProfiler.

**Results**: DEGs from the RNAseq data separated treatment failures and controls using dimension reduction and clustering from limma. Several TB signatures were enriched in the treatment failure group at baseline and month two. The DEGs were associated with several immune pathways, including the T and B cell Receptor Signaling pathways, Estrogen Receptor Signaling (upregulated in the treatment failure group), and Oxidative Phosphorylation Signaling (decreased in the treatment failure group). These results were replicated when treatment non-compliant patients were removed from the study, although fewer DEGS at baseline and more DEGs at month two were identified.

**Conclusion:** These results suggest the possibility that future signatures may identify treatment failure at either baseline or month two and suggest potential pathways leading to treatment failure.







JIPMER



BMMRC

NIRT's Biorepository







BJGMC's Data Management Centre



Hinduja's Hematology Lab



PCR at MVDRC

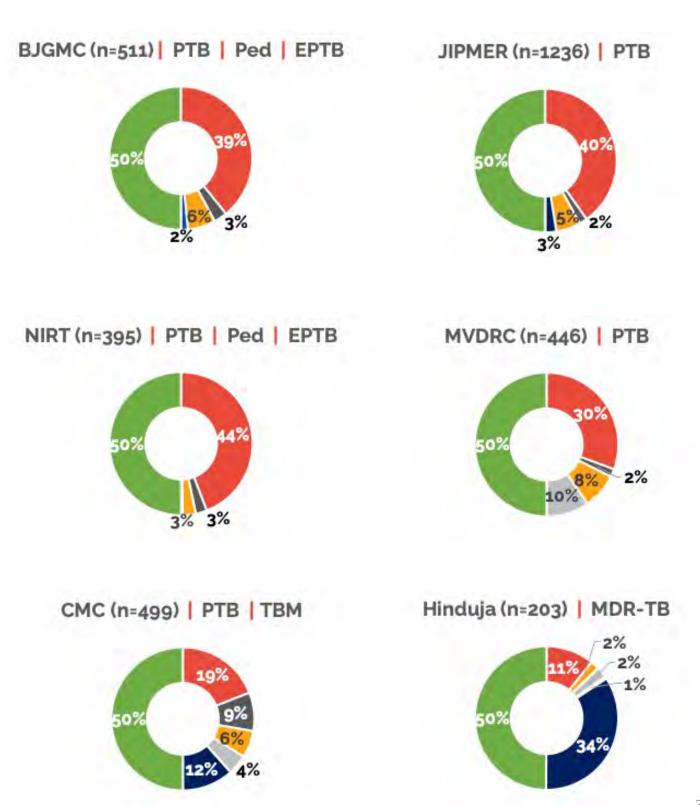


Centrifuge at BMMRC

#### Parent Protocol Cohort A: Accrual Status



PTB=Pulmonary TB; TBM=TB Meningitis; EPTB=Extrapulmonary TB; Ped=Pediatric TB (<15 years); MDR=Multidrug-resistant TB



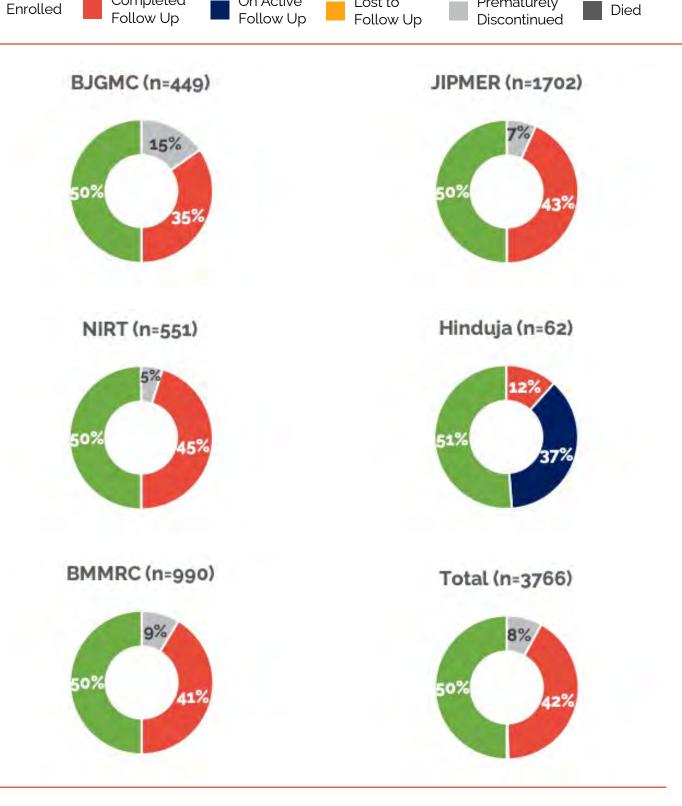
#### Parent Protocol Cohort B: Accrual Status

On Active

Lost to

Prematurely

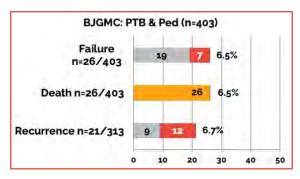
Completed

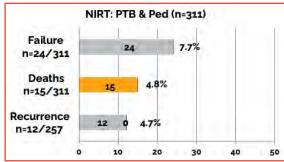


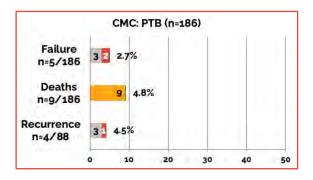
<sup>\*</sup>There were 16 BJGMC participants who were off study because index case diagnosed with MDR-TB.

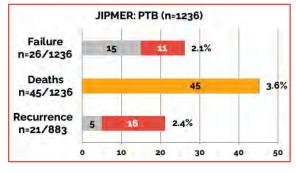
<sup>\*\*</sup>Follow-up terminated for 83 participants due to study period ending at JIPMER.

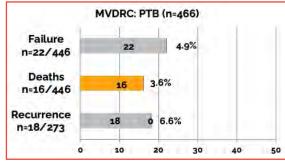
#### Parent Protocol Cohort A: Treatment Outcomes

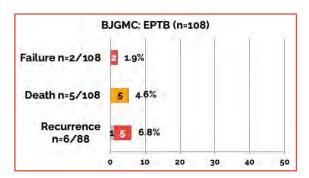


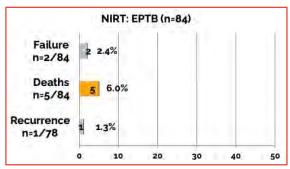


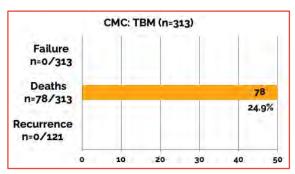


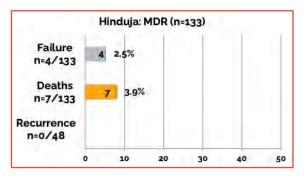














For proportion of participants who failed treatment or died, denominator is total number of participants enrolled. For proportion of participants with TB recurrence, denominator is total number of participants who completed treatment.

As participants at Hinduja remain in active follow-up, final outcomes are not yet available for this cohort.

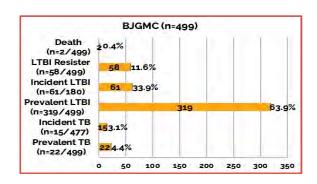
Failure=TB patients enrolled in the parent protocol and declared treatment failure between month five and end of treatment.

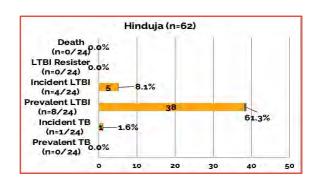
Deaths=All-cause death

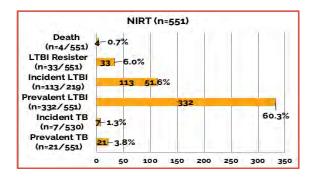
Recurrence=Patients diagnosed with TB after being declared as cured or treatment complete.

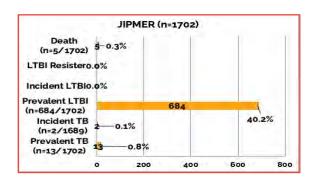
(PTB=Pulmonary TB; Ped=Pediatric; EPTB=Extrapulmonary TB; TBM=TB Meningitis)

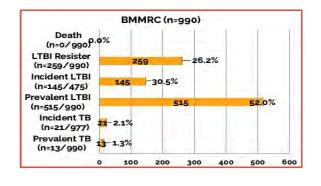
#### Parent Protocol Cohort B: Study Outcomes













#### LTBI=Latent TB Infection

Prevalent TB-TB disease reported at baseline (clinical or bacteriological confirmation).

Incident TB=TB disease diagnosed during follow-up (clinical or bacteriological confirmation). Denominator excludes prevalent TB.

Prevalent LTBI=TST or IGRA positive at baseline.

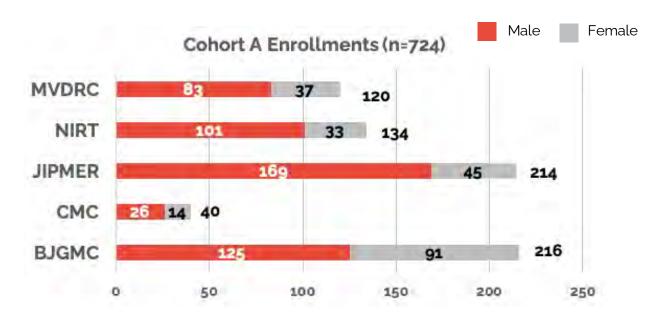
Incident LTB=TST or IGRA conversion during follow-ups. Denominator excludes prevalent LTBI.

LTBI Resister=TST and IGRA negative throughout follow-ups.

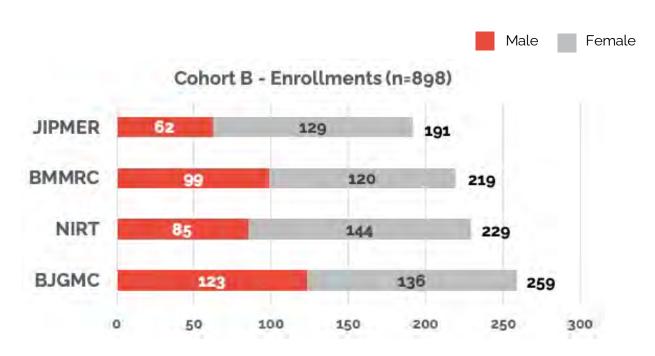
Death=All-cause death

As participants at Hinduja remain in active follow-up, final outcomes are not yet available for this cohort.

#### **Common Protocol Enrollment**



\*Of 216 participants enrolled at BJGMC, 7 (3%) were <15 years. All other sites enrolled adult pulmonary TB patients only.



\*Of 898 total Cohort B participants enrolled, 134 (15%) were <15 years old.

Source: Common Protocol data was provided by individual sites and aggregated by SAS-CHRD. The RePORT India Coordinating Hub prepared graphs. Data cutoff date: Dec 31, 2021.

#### Common Protocol Cohort A: Accrual Status





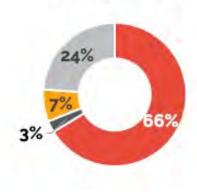




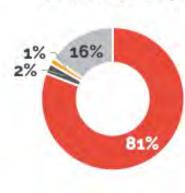




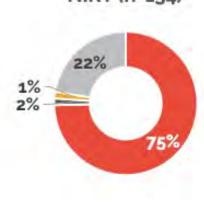




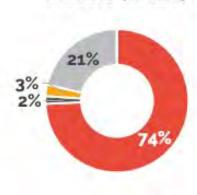




NIRT (n=134)



MVDRC (n=120)



#### CMC (n=40)



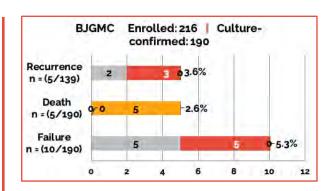
No Cohort A Common Protocol Participants remain in active follow-up.

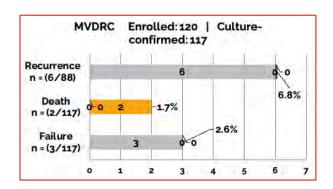
Completed Follow-up=Participants who met confirmatory inclusion criteria and completed the 6-month post-treatment visit.

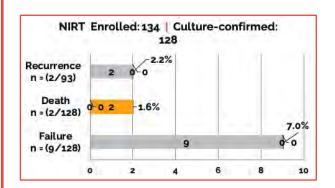
Prematurely Discontinued = Participants who met any protocol-mandated reason for discontinuation, including:

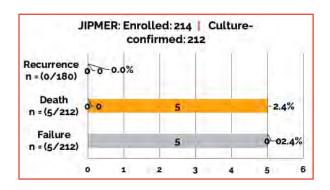
- Provisionally enrolled but culture-negative
- Met an outcome
- Participant withdrawal
- Moved out of area
- Co-enrolled in VPM study

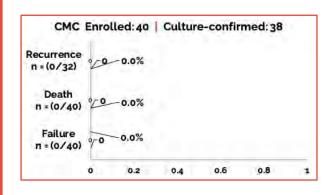
#### Common Protocol Cohort A: Treatment Outcomes













For proportion of participants who failed treatment or died, denominator is total number of participants enrolled and culture-confirmed (i.e. met confirmatory inclusion criteria). For proportion of participants with TB recurrence, denominator is total number of participants who completed treatment.

Failure=TB patients enrolled in the common protocol and declared treatment failure between month five and end of treatment.

Recurrence=Patients diagnosed with TB after being declared as cured or treatment complete.

Death-All-cause death. Only deaths among participants who met confirmatory inclusion criteria are reported.

#### Common Protocol Cohort B: Accrual Status



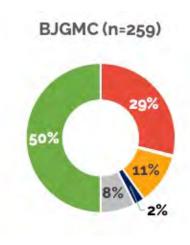




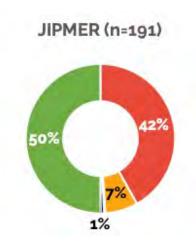




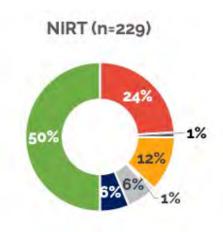




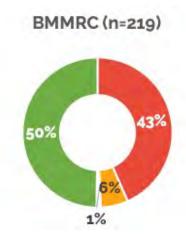
BJGMC: 67 (26%) participants on active follow-up. As part of LOA#2 (started Aug 5 2020), additional follow-up expected for 208 total participants.



JIPMER: As part of LOA#2 (started Nov 20 2020), additional follow-up expected for 160 total participants.



NIRT: 161 (70%) participants on active follow-up. As part of LOA#2 (to be started), additional follow-up expected for 211 total participants.



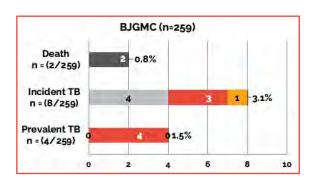
BMMRC: 90 (41%) participants on active follow-up. As part of LOA#2 (to be started), additional follow-up expected for 202 total participants.

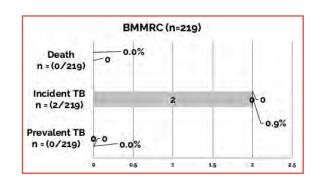
Completed Follow-up = Participants who completed the 24-month visit.

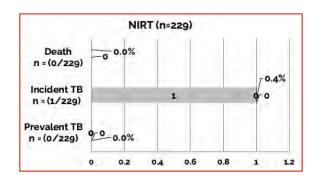
Prematurely Discontinued = Participants who met protocol-mandated reason for discontinuation, including: met an outcome, participant withdrawal, or moved out of area.

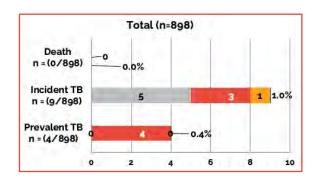


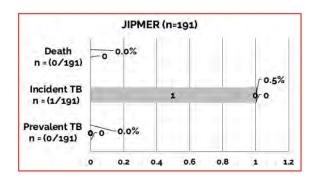
## **Common Protocol Cohort B: Study Outcomes**













Prevalent TB = TB disease reported at baseline (date of outcome ≤30 days from date of HHC enrollment). Total prevalent TB across sites = 4.

Incident TB = TB disease diagnosed during follow-up (date of outcome >30 days from date of HHC enrollment). Denominator excludes Prevalent TB. Total incident TB across sites = 9.

Death=All-cause death

LTBI outcome data is available upon request.



## **Related Grants**



## BJGMC



JIPMER



CMC

# RePORT INTERNATIONAL & CFAR SUPPLEMENTAL FUNDED PROJECTS AWARDED

	TITLE	PARTNERS	CRDF#	START DATE	INVESTIGATORS
1	T Cell Biomarkers and T- Regulatory Responses to Pediatric TB	Emory, JHU, BJGMC, NIRT	65373	2020	Rengarajan J, Kagal A, Kinikar A, Mave V, Padmapriyadarsini C, Hanna L, Paradkar M
2	Pregnancy Associated Immune Responses to TB and HIV in India and South Africa (PARTHISA study)	JHU, BJGMC, Wits Health Consortium, Cornell	65344	2020	Gupta A, Martinson N, Mathad J, Bhosale R, Kagal A, Alexander M, Kulkarni V
3	Pharmacokinetic Assessment of MDR-TB Drugs in the Treatment of TB Meningitis	JHU, PD Hinduja, Beijing Chest Hospital, BJGMC, Wits Health	65351	2020	Tornheim JA, Ashavaid T, Rodrigues C, Udwadia Z, Duan H, Sangle S, Varaiava E, Dooley K, Ignatuius E, Mave V, Gupta A, Shivakumar SVBY, Chawla P, Patil S, Kulkarni V
4	Inflammasome Genetics and TB Treatment Outcomes	UPenn, JHU, UMass, NIRT, MVDRC, BGJMC	65375	2020	Bisson G, Gupte A, Viswanathan V, Gupta A, Kornfeld H, Hanna L, Babu S, Andrade B, Dhanasekaran M
5	Host RNA Expression for Diagnosis and Monitoring of Pediatric TB in Africa and India	NIRT, BGJMC, JHU, Univ. Cape Town, Imperial College, London	64080	2019	Kinikar A, Paradkar M, Hissar S, Workman L, Dawre R, Gupte N, Tornheim JA, Kulkarni V
6	Determination of Efficacy of Xpert PCR Ultra And Transcriptional Signatures In The Diagnosis of Pleural Tuberculosis	CMC, Vellore & University of Cape Town, SA	64074	2018	Christopher DJ, Keertan Dheda
7	Validation of Transcriptional Signature to Predict Active TB Disease among Advanced HIV Patients	RePORT Brazil, BMC, BJGMC, JHU	63158	2017	Mave V, Rolla V, Salgame P, Kadam D, Andrade B, Gupta A, Meshram S, Kulkarni V, Ellner J
8	Molecular Signatures of Tuberculosis-Diabetes Interaction (MSTDI) Study	JHU, UMass, BJGMC, NIRT, MVDRC	63459	2017	Kornfeld H, P Chandrasekaran, Gupte A, Mave V, Bharadwaj R, Golub J, Andrade B, Paradkar M, Luke H, Kulkarni V, Gupte N, Shivakumar SVBY, Gupta A
9	Biomarkers for TB Diagnosis and Treatment Response	BJGMC, NIRT, Emory, JHU	63069	2016	Rengarajan J, Hanna LE, Mave V, Padmapriyadarsini C, Thiruvengadam K, Toidi A, Gupte N, Kulkarni V, Gupta A and CTRIUMPH team
10	Impact of HIV and Diabetes Mellitus on TB Drug Resistance and Recurrence	BJGMC, NIRT, JHU, MVDRC, UMass, Rutgers	63221	2016	Mave V, Devi U, Padmapriyadarsini C, Mathema B, Vishwanathan V, Kornfeld H, Kreiswirth B, Golub J, Gupte N, Shivakumar SVBY, Gupta A
11	MDR-TB and HIV at RePORT Sites India	BJGMC, NIRT, JIPMER, JHU, BMC	63076	2016	Horsburg R, Padmapriyadarsini C, Mave V, Gupta A, Sarkar S
12	Validation and Fine Tuning of the Computer Aided Diagnosis of Pulmonary Tuberculosis Model for the Indian Subcontinent	CMC	62922	2016	Christopher DJ, Thangakunam B, Lal B, Agrawal A
13	Extracranial Involvement as Detected by Positron Emission Tomography Scan in Patients with Tubercular Meningitis	CMC	62906	2016	Thangakunam B, Christopher DJ

## RePORT INTERNATIONAL & CFAR SUPPLEMENTAL FUNDED PROJECTS

#### **AWARDED (Continued)**

	TITLE	PARTNERS	CRDF#	START DATE	INVESTIGATORS
23	Inflammatory Biomarkers as a Triage Test for Screening Symptomatic TB	JIPMER, Rutgers, BMC	63466	2016	Ellner J, Salgame P, Sarkar S, Pleskunas J
24	Characterization of Monocyte Responses in Pulmonary TB Patients with or without Type 2 Diabetes	NIRT-NIH – ICER, MVDRC	62911	2016	Kumar P
25	Effect of Malnutrition on Latent TB	Approved: JIPMER, Rutgers, BMC	23719	2016	Hochberg NS, Negi VS, Mahalakshmy T, Johnson WE, Salgame P, Pleskunas J
26	Determining Barriers to TB Care	JIPMER, BMC/BU	64020	2016	Sabin L, Sarkar S, Hochberg NS, Fernandes P, Pleskunas J, Amsaveni
27	TH17 Cell Subsets as Potential Risk Markers of Latency and Active TB Infection in Household Contacts	BMMRC, UT	62916	2016	Devalraju KP, Neela VSK, Valluri VL, Vankayalapati K
28	Comparison of Available Purified- Protein Derivative (PPD) Tuberculin Skin Test (TST) Antigen Solutions in Detecting Latent Tuberculosis Infection in India	CMC, BJGMC, JIPMER, BMMRC, NIRT, JHU, BMC	61783	2015	Christopher DJ, Shankar D, Roy G, Sarkar S, Prakash Babu S, Gupta A, Deluca A, Cox SR, Hochberg NS, Horsburgh R

#### AWARDED

	TITLE	PARTNERS	GRANT SOURCE	START DATE
1	Impact of latent TB infection and trained immunity on susceptibility to SARS-CoV-2 infection in India and the Philippines	Rutgers, JIPMER (Approved), University of the Philippines-Manila College of Medicine	RICC	2021
2	The Regional Prospective Observational Research for Tuberculosis (RePORT) India Phase II Common Protocol	CMC Vellore	EC Approved-2020	
3	Signature of Profiling and Staging the Progression of TB from Infection to Disease	NIH/NIAID	Ro1	2020
4	Hybrid trial for Alcohol reduction among people with TB and HIV in India (HATHI)	JHU, BJGMC, London School of Hygiene and Medicine, DY Patil	NIH	Submitted 2019 - Pending
5	Microbiome-Associated Effects of Diabetes and BMI on Tuberculosis Severity	MVDRC & UMass	NIH	Submitted 2020 - Pending
6	Rapid Research for Diagnostics Development in TB Network	CMC Vellore, UCSF, NIRT	NIH	Submitted 2020 - Pending
7	Rapid Research in Diagnostics Development for TB Network (R2D2 TB Network) Study	Approved: CMC/UCSF	Not issued yet	2020
8	Innate immune response of LTBI+HIV+ children	BMMRC UT	RO1 A142672-01A1	
9	Thyroxine (T4) hormone inhibits expansion of immunosuppressive CD4CD25+Foxp3+ (Tregs) cells (Administrative Supplement for current R01"IFN-independent inhibition of MTB growth in human macrophages	BMMRC UT	Ro1	2020
10	Understanding Mycobacterium tuberculosis mediated host metabolomics in pulmonary tuberculosis: correlation with dis-ease severity and treatment course.	IISER, Pune	PEER Women in Science SEED Grants 2021, funded by the National Academies of Sciences Engineering and Medicine	September 2021
11	Immune Responses and Effect of Disulfiram on MTB Infected PBMCs as a Potential Host Directed Therapy	BJGMC, NIRT, JHU, THSTI	Funding from Translational Health Sciences and Technology (THSTI)	2019
12	Whole Genome Sequencing of Drug Resistant Tuberculosis in India: Genotype-Phenotype Correlation, Clinical Impact of Resistance, and Sequencing Directly from Sputum	Hinduja, JHU	NIH - 1K23Al135102-01A1	2018
13	Validating a Th17 Switch as a Novel Correlate of Protective Immunity to TB	NIRT, BJMC, IISc, Bangalore, JHU	DBT/ IISc	2018
14	Characterization of Genomics and Metabolomics among Individuals (TB-GWAS)	Emory, JHU, BJGMC, NIRT, PHRU, McGill	NIH Ro1	2018
15	Tuberculosis: Learning the Impact of Nutrition (TB LION)	JIPMER, BMC, Rutgers, Tufts, NIRT	Warren Alpert Foundation	2018-2023
16	Transcriptomic and Metabolomic Analysis of Microbiologically Confirmed Pediatric Tuberculosis Patients and Uninfected Household Contacts	BJGMC, JHU	Ujala Foundation Wyncote Foundation BWI-CTU C-TRIUMPH	2017
17	Multicenter Phase II/III Double-Blind, Randomized, Placebo Controlled Study to Evaluate the Efficacy and Safety of VPM1002 in the Prevention of TB Recurrence in Pulmonary TB Patients after Successful TB Treatment.	RePORT India Sites	Serum Institute	2017-2022
18	Therapeutic Outcomes with Second-Line Drug Exposures in a Cohort of South African and Indian Patients with Drug Resistant TB: A Pharmacokinetic-Pharmacodynamic Assessment	Hinduja, PHRU, JHU	DBT/South Africa MRC	2017

#### **AWARDED**

	TITLE	PARTNERS	GRANT SOURCE	START DATE
19	Association of Lipid Mediators of Inflammation with TB Treatment Outcomes	JHU, NIRT, BJGMC	CTRIUMPH and Gilead Foundation	2017
20	The Role of Innate Immunity in the Acquisition of Sterile Protection Against TB Infection	U Colorado, JHU, BJMC	NIH R21	2017
21	IFN-γ Independent Inhibition of MTB Growth in Human Macrophages	BMMRC, UT	NIH/NIAID: R01Al123310-01A1	2017
22	Predictors of Resistance Emergence Evaluation in MDR-TB Patients on Treatment - (PREEMPT)	JIPMER, NIRT, BJGMC, Brazil, Vanderbilt, Rutgers, CDC, JHU, BMC, Hinduja	NIH/NIAID: Ro1	7/1/2017-6/30/2022
23	MDR-TB Free: Monitoring Adverse Effects, Utilizing Resources Optimally, Knowing Resistance Patterns, and Treatment Strategy (MDR TB – MUKT)	Hinduja, JHU	Hinduja	2017
24	The Role of Monocyte Subpopulation in HIV+LTB+ Individuals and Development of Active TB	BMMRC, UT	NIH: R21Al127178-01 Indo-US Vaccine Program, RePORT India Cohort	2016-2018
25	Studying T cell Memory Responses for Understanding Protective Immune Response in Tuberculosis (TB)	CMC, NIRT, Saint Louis U	American Society of Tropical Medicine and Hygiene/ Burroughs Wellcome Fund)	2016
26	Role of Iron Deficiency in Resistance of Women of Child- Bearing Age to Tuberculosis	JIPMER, BMC	NIH	2016-2017
27	Measuring TB Drugs in Hair as a Tool to Monitor Adherence, Exposure and Response	BJGMC, NIRT, JHU	NIH/NIAID: R21	2016-2018
28	Impact of Immune Changes of HIV and Stages of Pregnancy on TB	BJGMC, NIRT, JHU	NIH/NICHD: R01	2015-2020
29	Residual Respiratory Impairment Following Pulmonary Tuberculosis: The Lung Health Sub-Study	BJGMC, NIRT, JHU	UJALA/ Gilead Foundation/ RePORT India	2015-2017
30	Association of Lipid Mediators of Inflammation with TB Treatment Outcomes	JHU, NIRT, BJGMC	CTRIUMPH and Gilead Foundation	2017
31	The Role of Innate Immunity in the Acquisition of Sterile Protection Against TB Infection	U Colorado, JHU, BJMC	NIH R21	2017
32	IFN-γ Independent Inhibition of MTB Growth in Human Macrophages	BMMRC, UT	NIH/NIAID: R01Al123310-01A1	2017
33	Understanding of Tuberculosis Infection and Preventive Therapy Among Skin-Test Positive Household Contacts of Tuberculosis Cases	BJGMC, NIRT, JHU	NIH CFAR and D43	2015
34	D4GDI-mediated Immune Responses in LTBI+HIV+ Individuals	BMMRC, UT	NIH: R21Al120257-01 Indo-US Vaccine Program, RePORT India	2015-2017
35	T-regs Mediated Immune Responses in LTBI+HIV+ Individuals	BMMRC, UT	UT	2015
36	Impact of Pregnancy on Tuberculosis	JIPMER, BMC	NIH/NIAID Ro1	2015-2018
37	Compare Drug Levels in Newly Diagnosed or Relapsed PTB/ EPTB Following Daily ATT vs DOTS Regimen	CMC	Internal fluid research grant	2015
38	Impact of Personal Exposure to Black Carbon on Pulmonary Tuberculosis Severity	JIPMER BMC	Potts Memorial Foundation	2014-2018
39	Yield of TB using GeneXpert (Xpert MTB-Rif) by Induced Sputum Compared to Standard Sputum Samples	CMC	Internal fluid research grant	2014

#### AWARDED

	TITLE	PARTNERS	GRANT SOURCE	START DATE
40	Dried Plasma Spots as a Simple Sampling Strategy to Measure Rifampicin Concentration to Facilitate this Service In Resource Limited Settings	CMC	Internal fluid research grant	2019
41	Prevalence of Latent Tuberculosis in Rheumatoid Arthritis and Ankylosing Spondylitis	CMC	Internal fluid research grant	2018
42	The Effect of Appropriate Anti Tuberculous Treatment on Recovery of Pulmonary And Pleural Tuberculosis and the Impact of Tuberculosis on Lung Function and Quality of Life in Newly Diagnosed Patients	CMC	Internal fluid research grant	2018
43	Validation of Indigenously Developed Technology (TruNat MTB) for Diagnosis of Extra-pulmonary Tuberculosis: Multi- centric Validation	CMC, Hinduja, NIRT, AIIMS	ICMR	2018
44	Evaluation of diagnostic potential of aptamer-based assays for pulmonary tuberculosis- a pilot study	CMC	THSTI	2019
45	Host and Microbiome Transcriptional Profiling in the Upper Airways for TB Susceptibility	JIPMER	CTSI Pilot Grant, BU, US	
46	Learning about Experience with nutritional Supplementation in Tuberculosis (LENS)- an Exploratory study.	JIPMER	India (Seed Grant)	
47	VITAL TB (Vitamins And Latency in Tuberculosis)	JIPMER	U.S. Department of State's Partnership 2020 educational initiative	
48	Dynamics and immune mechanisms of QFT response in close contacts of TB cases	JIPMER	NIH	
40	Characterization of Genomics and Metabolomics among Individuals Highly-Exposed, but Resistant to Mtb Infection	JIPMER	NIH	

#### NOT AWARDED

	TITLE	PARTNERS & IRB SUBS	GRANT SOURCE	START DATE/ DURATION	INVESTIGATORS
1	VITAL-TB (Vitamins And Latency in Tuberculosis)	JIPMER, BU/BMC, Rutgers	NIH Ro1	2020	Hochberg, NS, Salgame P, Sarkar S, Lakshminarayanan S
2	Immune Mechanisms of Protection against Mycobacterium tuberculosis Center	CMC, UCSF	(IMPAc-TB) NIAID AI	2019	Ernst J, Cattamanchi A, Nahid P, Christopher DJ,
3	Analysis and Consequences of Humoral Responses during Mycobacterium tuberculosis Infection	Rockefeller, JHU, Emory, BJGMC	NIAID Po1	2019	Ravetch J, Ahmed R, Gupta A, Gandhi NR, Chandele A, Amara R
4	Protective Immune Responses and Effective Vaccines to End TB (PREVEN-TB) (IMPAcT-TB)	Emory, JHU, Tulane, RePORT Brazil, RePORT India	NIH	2018	Rengarajan J, Sterling T, Gupta A, Bollinger RC, Gaikwad S
5	Sex and TB Immunity (SATI) (IMPAcT-TB)	Rutgers, JHU, Stanford, Saint Louis, Tulane, Emory	NIH	2018	Gennaro ML, et al.
6	Effect of Helminths on Tuberculosis Severity	JIPMER, BMC, Rutgers, NIRT, NIH	NIH R21	2018	Hochberg NS, Salgame P, Babu S, Ellner JJ, Johnson WE, Parija S, Sarkar S, Mahalakshmy T, Joseph N, Rajkumari N
7	Analysis of IgG-FcR Interactions in TB	Rockefeller, JHU, Emory, BJGMC	Bill & Melinda Gates Foundation	2018	Ravetch J, Ahmed R, Gandhi NR, Gupta A, Mave V, Gupte N
8	RePORT India Tuberculosis Research Training Program	RePORT India	NIH Fogarty: D43	2018	Gupta A, Kornfeld H, Bollinger RC, Christopher DJ, Rodrigues C, Tripathy S, Mehendale S
9	Memory-like NK Cells and Household Contacts of TB Patients	BMMRC, UT	NIH R21	2018	Vankayalapati K, Valluri V, and others
10	RePORT India TB Transmission Training Program	RePORT India	NIH Fogarty: D43	2017	Gupta A, Christopher DJ, Bollinger R, Deluca A, Golub J
11	Systems Approaches for Predicting TB Clinical Outcomes	BJGMC, Emory, Knowledge Synthesis, NIRT, Texas A&M, UTX-Tyler, WITS Health Consortium	NIH: U19	2017	Karakousis P, Bader J, Bharadwaj R, Padmapriyadarsini C, Dutta N, Gupta A, Gupte N, Ioerger T, Kadam D, Hanna LE, Martinson N, Mave V, Pandey A, Rengarajan J, Salamon H, Shivakoti R, Vankayalapati K
12	Developing a Rapid Point-of-Care TB Diagnostic	RePORT International	NIH/NIAID: Ro1	2017	Walt D (Tufts PI), Rushdy A (Broad Institute co-PI), Rolla V, Santos M, Kristi A, Sterling T, Li Y, Mave V, Cristopher DJ, Gupta A, Pim A, Walzl G, Hamilton C, Duffy D, Gillette M
13	Research and Interventions for HIV, Alcohol, Tobacco and Tuberculosis in India and South Africa (The HATT Consortium)	BJGMC, NIRT, JHU	NIH/NIAAA: Ro1	2017	Gupta A, Chander G, Heidi H, Thomas B, Kadam D, Suryavanshi N, Padmapriyadarsini C, Mave V, Gupte N

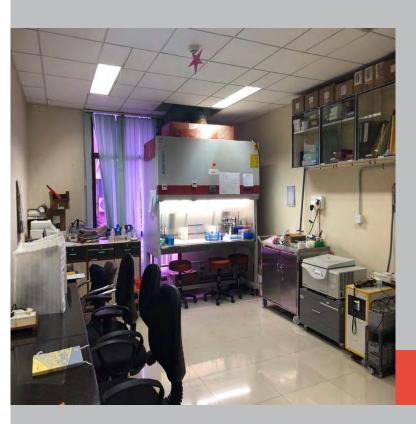
#### **NOT AWARDED**

	TITLE	PARTNERS & IRB SUBS	GRANT SOURCE	START DATE/ DURATION	INVESTIGATORS
14	Bio-markers for Risks of Development of LTBI and TB Disease in a Cohort of Childhood Contacts of Sputum Positive TB Patients	CMC	RePORT India Supplemental Funding	2017	Christopher DJ, Rose W
15	Innate Immune Responses in Household Contacts	BMMRC/LEP RA, BJGMC, NIRT, JHU, UT	NIH/NIAID: Ro1	2017	Vankayalapati K, Valluri V, Gupta A, Mave V, Kadam D, Bharadwaj R, Hanna LE, Shivakumar SVBY, Prudhula, Padmapriyadarsini C, Gupte N
16	Impact of Air Pollution on Inflammation and Anti TB Immunity	BJGMC, NIRT, JHU	RePORT India Supplemental Funding	2016-2017	Shivakoti R, Gupta A, Padmapriyadarsini C, Chandrakumar D, Golub J, Mave V, Babu S, Elf J, Hannah LE, Kulkarni V, Gupte N
17	Characterizing the Host Inflammatory Response, and its Association with Treatment Outcomes and Lung Health in Adult Pulmonary TB Patients Undergoing Treatment in India	BJGMC, NIRT, JHU	RePORT India Supplemental Funding	2016-2017	Gupte A, Padmapriyadarsini C, Gupta A, Babu S, Mave V, Gupte N, Kornfeld H
18	Association of Recent Active Tuberculosis Disease with Significant Coronary Artery Disease at JIPMER, Puducherry: A Hospital-based Case Control Study	JIPMER, BMC	RePORT India Supplemental Funding	2016	Kar S, Sarkar S, Ellner JJ, Santhosh Satheesh
19	Novel Serum Based Biomarkers for Diagnosis of TB and Treatment Monitoring in HIV-infected and Uninfected Children	BJGMC, NIRT, DTTC, Cape Town, JHU	India SA RFA	2016	Valvi C, Hesseling AC, Chandanwale A, Kulkarni R, Paradkar M, Mave V, Gupte N, Chandrasekaran P, Shivakumar SVBY, Danasekaran K, Thiruvenkadam K
20	Pediatric TB Biomarkers for Diagnosis and Treatment Response	BJGMC, NIRT, JHU	NIH/NIAID: Ro1	2016	Karakousis P, Paradkar M, Tornheim JA, Gupta A, Chandrasekaran P, Bader J, Mave V, Gupte N, Kulkarni V, Bharadwaj R, Valvi C, Shivakumar SVBY, Hannah LE, Pandey A
21	Biomarkers for Treatment Response and Disease Recurrence in Pulmonary and Extrapulmonary Tuberculosis Disease	IGIB, BJGMC, SA, NIRT, JHU	India SA RFA	2016	Gokhale R, Kana B, Swaminathan S, Chandrasekaran P, Mave V, Gupta A, Shivakumar SVBY
22	Novel Blood Biomarker to Predict Progression to Active TB Disease Among Recently Exposed Adult and Pediatric Household Contacts of TB Patients in India and South Africa	BJGMC, NIRT, SA, JHU	India SA RFA	2016	Chandrasekaran P,Scriba T, Mave V, Paradkar M, Shivakumar SVBY, Gupte N, Gupta A, Danasekaran K, Khan S, Thiruvengadam S, Tripathy S, Prasad K
23	Memory-like NK Cells and Household Contacts of TB Patients	BMMRC, UT	NIH: 1R21Al127177- 01		Vankayalapati K, Valluri V, and others
24	Annual Screening of Healthcare Personnel Using TST & QGFT and Identification of Bio-markers & the Role of Pet Scan	CMC	RePORT India Supplemental Funding	2016	Christopher DJ, Balamugesh T
25	Radiological Treatment Response in Pulmonary Tuberculosis	CMC	RePORT India Supplemental Funding	2016	Balamugesh T, Christopher DJ
26	Does Tubercular Infection Adversely Affect Cardiovascular Risk?	JIPMER, BMC	RePORT India Supplemental Funding	2016	Kar S, Sarkar Si, Negi VS, Prasanna MD, Roy G, Premarajan KC, Hochberg N, Lakshminarayanan S
27	Geographical and Genotypic Distribution of TB Cases Under RePORT India – Tools for Understanding Epidemiology	JIPMER, BMC, BU	RePORT India Supplemental Funding	2016	Sarkar S, Roy G, Mahalakshmy T, Lakshminaraya S, Joseph NM, Jenkins H, Amsaveni, Hochberg NS





**MVDRC** Freezers



NIRT PBMC Processing Lab



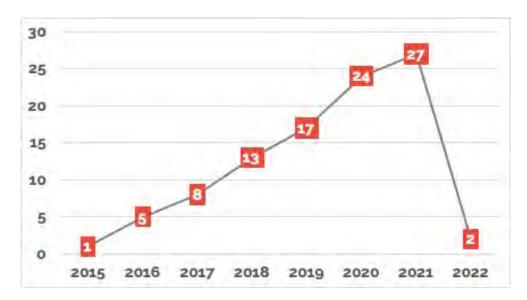


## BMMRC



Hinduja

#### **PUBLICATIONS 2014-2022**



#### **RePORT India Consortium**

1. Building capacity for advances in tuberculosis research; proceedings of the third RePORT International meeting

Van der Heijden YF, Abdullah F, Andrade BB, Andrews JR, Christopher DJ, Croda J, Ewing H, Haas DW, Hatherill M, Horsburgh CR Jr, Mave V, Nakaya HI, Rolla V, Srinivasan S, Sugiyono RI, Ugarte-Gil C, Hamilton C. Tuberculosis (Edinb). 2018;113: 153-162. PMID: 30514497; PMCID: PMC6349374.

2. RePORT International: Advancing tuberculosis biomarker research through global collaboration Hamilton CD, Swaminathan S, Christopher DJ, Ellner J, Gupta A, Sterling TR, Rolla V, Srinivasan S, Karyana M, Siddiqui S, Stoszek SK, Kim P. Clinical Infectious Diseases (CID). 2015 October 15; 61(Suppl 3): S155–S159. PMID: 26409277; PMCID: PMC4583572.

#### Bhagwan Mahavir Medical Research Centre University of Texas Health Science Center at Tyler (CRU 107)

1. Defective expansion and function of memory-like natural killer cells in HIV+ individuals with latent tuberculosis infection.

Kamakshi Prudhula Devalraju, Venkata Sanjeev Kumar Neela, Siva Sai Krovvidi, Ramakrishna Vankayalapati, Vijaya Lakshmi Valluri PLoS One doi: 10.1371/journal.pone.0257185. eCollection 2021.

2. Reduced thyroxine production in young household contacts of tuberculosis patients increases active tuberculosis disease risk

Devalraju KP, Tripathi D, Neela VSK, Paidipally P, Bogam AK, Mallidi V, Sykam A, Singh KP, Ansari MS, Vankayalapati R, Valluri VL. JCI Insight. 2021;6(13):e148271.

3. BCG vaccination reduces the mortality of Mycobacterium tuberculosis-infected type 2 diabetes mellitus mice.

Radhakrishnan RK, Thandi RS, Tripathi D, Paidipally P, McAllister MK, Mulik S, Samten B, Vankayalapati R. JCI Insight. 2020 Mar 12;5(5):e133788. doi: 10.1172/jci.insight.133788. PMID: 32161191; PMCID: PMC7141407.

#### Continued

## Bhagwan Mahavir Medical Research Centre University of Texas Health Science Center at Tyler (CRU 107)

- 4. Metabolites enhance innate resistance to human Mycobacterium tuberculosis infection.

  Deepak Tripathi, Kamakshi Prudhula Devalraju, Venkata Sanjeev Kumar Neela, Tanmoy Mukherjee,
  Padmaja Paidipally, Rajesh Kumar Radhakrishnan, Igor Dozmorov, Mohammad Soheb Ansari,
  Varalakshmi Mallidi, Anvesh Kumar Bogam, Vijaya Lakshmi Valluri, Ramakrishna Vankayalapati. (JCI Insight first revision).
- 5. IL-22 produced by type 3 innate lymphoid cells (ILC3s) reduces the mortality of type 2 diabetes mellitus (T2DM) mice infected with Mycobacterium tuberculosis
  Tripathi D, Radhakrishnan RK, Sivangala Thandi R, Paidipally P, Devalraju KP, Neela VSK, McAllister MK, Samten B, Valluri VL, Vankayalapati R. PloS Pathog. 2019 Dec 6;15(12):e1008140. PMID: 31809521.
- 6. Alcohol enhances type 1 interferon- $\alpha$  production and mortality of young mice infected with Mycobacterium tuberculosis

Tripathi D, Welch E, Cheekatla SS, Radhakrishnan R, Venkatasubramanian S, Paidipally P, Van A, Samten B, Devalraju P, Neela V, Valluri V, Mason C, Nelson S and Vankayalapati R. PloS Pathog. 2018 2 Aug;14(8):e1007174. Doi: 10.1371/journal.ppat.1007174. eCollection 2018 Aug. PMID: 30071107; PMCID: PMC6072099.

- 7. IL-17 and IL-22 production in HIV+ individuals with latent and active tuberculosis Devalraju KP, Neela VSK, Ramaseri SS, Van A, Chaudhury A, Krovvidi SS, Vankayalapati R, Valluri VL. BMC Infect Dis. 2018 11 Jul.;18(1):321. doi: 10.1186/s12879-018-3236-0. PMID: 29996789; PMCID: PMC6042451.
- 8. Defective MyD88 and IRAK4 but not TLR-2 expression in HIV+ individuals with latent tuberculosis infection

Devalraju KP, Neela VSK, Gaddam R, Chaudhury A, Van A, Krovvidi SS, Vankaylapati R, Valluri VL. Cytokine. 2018 Oct;110:213-221. doi: 10.1016/j.cyto.2018.05.005. Epub 201817 May. PMID: 29778672; PMCID: PMC6103807.

9. Interleukin-21 regulates Natural Killer cell responses during Mycobacterium tuberculosis infection

Paidipally P, Tripathi D, Van A, Radhakrishnan RK, Dhiman R, Venkatasubramanian S, Devalraju KP, Tvinnereim AR, Valluri VL, Vankayalapati R. J Infect Dis. 2018 28 Mar.;217(8):1323-1333. doi: 10.1093/infdis/jiy034. PMID: 29390153; PMCID: PMC6018723.

10. IL-21-dependent expansion of memory-like N.K. cells enhance protective immune responses against Mycobacterium tuberculosis

Venkatasubramanian S, Cheekatla S, Paidipally P, Tripathi D, Welch E, Tvinnereim AR, Nurieva R, Vankayalapati R. Mucosal Immunol. 2017 Jul;10(4):1031-1042. doi: 10.1038/mi.2016.105. Epub 20167 Dec. PMID: 27924822; PMCID: PMC5462891.

 NK-CD11c+ cell crosstalk in diabetes enhances IL-6-mediated inflammation during Mycobacterium tuberculosis infection

Cheekatla SS, Tripathi D, Venkatasubramanian S, Nathella PK, Paidipally P, Ishibashi M, Welch E, Tvinnereim AR, Ikebe M, Valluri VL, Babu S, Kornfeld H, Vankayalapati R PLoS Pathog. 2016 Oct 26;12(10):e1005972. doi: 10.1371/journal.ppat.1005972. eCollection 2016. PMID: 27783671; PMCID: PMC5082658.

## 1. Whole Genome Sequencing Assessing Impact of Diabetes Mellitus on Tuberculosis Mutations and Type of Recurrence in India

Mave, V., Chen, L., Ranganathan, U. D., Kadam, D., Vishwanathan, V., Lokhande, R., S, S. K., Kagal, A., Neeta, Shivakumar, S. V. B. Y., Paradkar, M. S., Deshmukh, S., Tornheim, J. A., Kornfeld, H., Farhat, M., Gupta, A., Padmapriyadarsini, C., Gupte, N., Golub, J. E., Mathema, B., & Kreiswirth, B. N. (2022). Clinical Infectious Diseases. https://doi.org/10.1093/cid/ciab1067

#### 2. Measuring Tuberculosis Drugs in Hair in Adults and Children as a Tool to Monitor Exposure and Outcomes

Mave, V., Kadam, D., Gaikwad, S., Kinikar, A., Aguilar, D., Chavan, A., Paradkar, M., Yogendra, S. V. B., Bharadwaj, R., Kagal, A., Suryavanshi, N., Golub, J., Kulkarni, V., Dooley, K. E., Gupta, A., Bacchetti, P., Gerona, R., Gupte, N., & Gandhi, M. (2021). The International Journal of Tuberculosis and Lung Disease, 25(1), 52-60. https://doi.org/10.5588/ijtld.20.0574

#### 3. Diabetes Mellitus and Tuberculosis Treatment Outcomes in Pune, India

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Gupte A, Padmapriyadarsini C, Mave V, Kadam D, Suryavanshi N, Shivakumar SV, Kohli R, Gupte N, Thiruvengadam K, Kagal A, Meshram S, Bharadwaj R, Khadse S, Ramachandran G, Hanna LE, Pradhan N, Gomathy NS, DeLuca A, Gupta A, Swaminathan S; CTRIUMPH Study Team. BMJ Open. 2016 Feb 25;6(2):e010542. doi: 10.1136/bmjopen-2015-010542. PMID: 26916698; PMCID: PMC4769396.

#### Christian Medical College, Vellore University of Cambridge-University of Washington (CRU 101)

1. MTB/RIF Ultra over Xpert® MTB/RIF in the diagnosis of extrapulmonary T.B.

D. J. Christopher, V. Coelho, G. S. Ebby, D. Shankar, R. Gupta, B. Thangakunam, Int J TUBERC LUNG DIS 25(11):939–944 Q 2021. The Union. Nov 2021. DOI: http://dx.doi.org/10.5588/ijtld.21.0280

2. Deep LF-Net: Semantic lung segmentation from Indian chest radiographs including severely unhealthy images

Anushikha Singh a, Brejesh Lall b, B.K. Panigrahi b, Anjali Agrawal c, Anurag Agrawal d, Balamugesh Thangakunam, D.J. Christopher, Biomedical Signal Processing and Control, Apr 2021 DOI: https://doi.org/10.1016/j.bspc.2021.102666

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  Balamugesh Thangakunam, MD, DM, FCCP, Devasahayam Jesudas Christopher, DNB, FCCP. Vellore, India. Chest. Aug 2020. DOI: https://journal.chestnet.org/article/S0012-3692(20)30760-1/fulltext
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Pradip Kumar Arvindbhai Dabhi, Thangakunam Balamugesh, Richa Gupta, Devasahayam Jesudas Christopher. PLoS ONE 15(6):e0233385, June 2020. DOI: 10.1371/journal.pone.0233385.

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Christopher DJ, Jeyaseelan L, Yadav B, Balaji V, Michael JS, Gupta M, Manipadam MT, Sudarsanam TD. May 2020. DOI: 10.4103/lungindia.lungindia\_111\_19

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Christopher DJ, Dinakaran S, Gupta R, James P, Isaac B, Thangakunam B. Respirology. 2018 Jul;23(7):714-717. Epub 2018 Feb 27. PMID: 29486527 DOI: 10.1111/resp.13275.

# Jawaharlal Institute of Postgraduate Medical Education & Research Boston Medical Center/Boston University Rutgers (CRU 102)

1. Development and validation of a parsimonious TB gene signature using the digital NanoString nCounter platform

Kaipilyawar V, Zhao Y, Wang X, Joseph NM, Knudsen S, Babu SP, Muthaiah M, Hochberg NS, Sarkar S, Horsburgh CR, Jr., Ellner JJ, Johnson WE, Salgame P., Clin Infect Dis. 2022. Epub 2022/01/12. doi: 10.1093/cid/ciaco10. PubMed PMID: 35015839.

2. Accuracy of Timika X-ray scoring system to predict the treatment outcomes among tuberculosis patients in India.

Yuvaraj Krishnamoorthy, Selby Knudsen, Sathish Rajaa, Subitha Lakshminarayanan, P.B. Senbagavalli, Jerrold Ellner, Charles Horsburgh, Natasha Hochberg, Padmini Salgame, Sonali Sarkar. IJTB (in press) Received18 Sep. 2020, Accepted 4 Aug. 2021, Available online 11 Aug. 2021. https://doi.org/10.1016/j.ijtb.2021.08.004.

3. Tuberculosis-Learning the Impact of Nutrition (TB LION): protocol for an interventional study to decrease T.B. risk in household contacts.

Cintron C, Narasimhan PB, Locks L, Babu S, Sinha P, Rajkumari N, Kaipilyawar V, Bhargava A, Maloomian K, Chandrasekaran P, Verma S, Joseph N, Johnson WE, Wanke C, Horsburgh CR Jr, Ellner JJ, Sarkar S, Salgame P, Lakshminarayanan S, Hochberg NS. BMC Infect Dis. 2021 12 Oct.;21(1):1058. doi: 10.1186/s12879-021-06734-z.

4. Comparison of profile and treatment outcomes between elderly and non-elderly tuberculosis patients in Puducherry and Tamil Nadu, South India.

Murali S, Krishnamoorthy Y, Knudsen S, Roy G, Ellner J, Horsburgh CR, Hochberg N, Salgame P, Prakash Babu S, Sarkar S. *PLoS One. 2021 Aug 27;16(8): e0256773*.

5. Prevalence and factors associated with diabetes mellitus among tuberculosis patients in South India—a cross-sectional analytical study.

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- 6. 'People listen more to what actors say': A qualitative study of tuberculosis-related knowledge, behaviors, stigma, and potential interventions in Puducherry, India.

  Sabin LL, Thulasingam M, Carwile M, Babu SP, Knudsen S, Dong L, Stephens J, Fernandes P, Cintron C, Horsburgh CR, Salgame P, Ellner JJ, Sarkar S, Hochberg NS. Glob Public Health. 2021 Oct 16:1-13.
- 7. Prevalence and Risk Factors associated with Latent Tuberculosis Infection among Household Contacts of Smear Positive Pulmonary Tuberculosis patients in South India.

Krishnamoorthy Y, Ezhumalai K, Murali S, Rajaa S, Jose M, Sathishkumar A, Govindarajan S, Horsburgh C, Hochberg N, Johnson E, Knudsen S. Tropical Medicine & International Health 2021 Oct 15. https://doi.org/10.1111/tmi.13693

8. Reasons for refusal among patients with tuberculosis and their household contacts to participate in an observational cohort study.

Raghupathy Kalaivani, Knudsen Selby, Ellner Jerrold, Horsburg Charles, Hochberg Natasha, Salgame Padmini, Chinnakali Palanivel, Prakashbabu Senbagavalli, Sarkar Sonali. Perspect Clin Res. 2021 Oct-Dec;12(4):234-235. doi: 10.4103/picr. Epub 202120 Sep. PMID: 34760653; PMCID: PMC8525795.

# Jawaharlal Institute of Postgraduate Medical Education & Research Boston Medical Center/Boston University Rutgers (CRU 102)

- 9. Severe undernutrition in children affects tuberculin skin test performance in Southern India. Reddy D, Ma Y, Lakshminarayanan S, Sahu S, White LF, Reshma A, Roy G, Salgame P, Knudsen S, Cintron C, Ellner JJ, Horsburgh CR Jr, Sarkar S, Hochberg NS. Severe undernutrition in children affects tuberculin skin test performance in Southern India. PLoS One. 2021 Jul 16;16(7):e0250304. doi: 10.1371/journal.pone.0250304. PMID: 34270546; PMCID: PMC8284816.
- 10. Comparing Tuberculosis Gene Signatures in Malnourished Individuals using the T.B. Signature Profiler Johnson WE, Odom A, Cintron C, Muthaiah M, Knudsen S, Joseph N, Jenkins DF, Babu S, Lakshminarayanan S, Zhao Y, Nankya E, Horsburgh CR Jr, Roy G, Ellner JJ, Sarkar S, Salgame P, Hochberg NS. *BMC Inf Dis* 2021; 21(1):106. PMID: 33482742.
- 11. Health-related quality of life and its effect on T.B. treatment outcomes.

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- 13. Alcohol use and tuberculosis clinical presentation at the time of diagnosis in Puducherry and Tamil Nadu, India.

Kan C\*, Ragan EJ\*, Sarkar S, Knudsen S, Muthuraj M, Vinod, Jenkins HE, Forsyth M, Horsburgh CR Jr, Salgame P, Roy G, Ellner JJ, Jacobson, KR, Sahu S\*\*, Hochberg NS\*\*. *PLoS One*; 2020 Dec 17;15(12):e0240595. PMID: 33332367

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Cathrine John Marie, Senbagavalli PB, Komala Ezhumalai, Selby Knudsen, C. Robert Horsburgh, Natasha S. Hochberg, Padmini Salgame, Jerrold Ellner, Sonali Sarkar. European Journal of Pharmaceutical and Medical Research (EJPMR). 2021,8(1), 427-440.

- 16. Household food insecurity among patients with pulmonary tuberculosis and its associated factors in South India: a cross-sectional analysis.
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Ellappan K, Datta S, Muthuraj M, Lakshminarayanan S, Pleskunas JA, Horsburgh CR Jr, Salgame P, Hochberg N, Sarkar S, Ellner JJ, Roy G, Jose M, Vinod Kumar S, Joseph NM. Indian J Tuberc. 2020 Oct;67(4):466-471. doi: 10.1016/j.ijtb.2020.07.016. Epub 202019 Jul. PMID: 33077045.

# Jawaharlal Institute of Postgraduate Medical Education & Research Boston Medical Center/Boston University Rutgers (CRU 102)

#### 19. How much do Indians pay for tuberculosis treatment? A cost analysis

Sinha P, Carwile M, Bhargava A, Cintron C, Acuna-Villaorduna C, Lakshminarayanan S, Kulatilaka N, Locks L, Hochberg NS. *Public Health Action. 2020 Sep 21;10(3):110-117. doi: 10.5588/pha.20.0017. PMID: 33134125; PMCID: PMC7577002.* 

## 20. Interaction of nutritional status and diabetes on active and latent tuberculosis: a cross-sectional analysis

Kubiak R, Sarkar S, Horsburgh CR Jr, Roy G, Kratz M, Reshma, Knudsen S, Salgame P, Ellner JJ, Drain PK, Hochberg NS. BMC Infect Dis. 2019 Jul 16;19(1):627. doi: 10.1186/s12879-019-4244-4. PMID: 31311495; PMCID: PMC6636094.

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#### 22. Existing blood transcriptional classifiers accurately discriminate active tuberculosis from latent infection in individuals from South India

Leong, S, Yue Zhao, Joseph NM, Hochberg NS, Sarkar S, Pleskunas J, HomD, LakshminarayananS, Horsburgh Jr, CR, Roy G, Ellner JJ, Johnson WE, Salgame, P. Tuberculosis (Edinb). 2018 Mar;109:41-51. doi: 10.1016/j.tube.2018.01.002. Epub 2018 31 Jan. PMID: 29559120.

#### 23. Co-morbidities in pulmonary tuberculosis cases in Puducherry and Tamil Nadu, India: Opportunities for intervention

Hochberg NS, Sarkar S, Horsburgh, Jr, CR, Knudsen S, Pleskunas J, Sahu S, Kubiak RW, Govindarajan S, Salgame P, Lakshminarayanan S, Sivaprakasam A, White LF, Joseph NM, Ellner JJ, Roy G. PLoS One. 2017 23 Aug;12(8):e0183195. doi: 10.1371/journal.pone.0183195. eCollection 2017. PMID: 28832615; PMCID: PMC5568341.

#### 24. Predictors of delayed care-seeking for tuberculosis in Southern India: An observational study

Van Ness SE, Chandra A, Sarkar S, Pleskunas J, Ellner JJ, Roy G, Lakshminarayanan S, Sahu S, Horsburgh Jr CR, Jenkins HE, Hochberg NS. BMC Infect Dis. 2017 15 Aug.;17(1):567. doi: 10.1186/s12879-017-2629-9. PMID: 28806911; PMCID: PMC5557420.

JIPMER's first participant in Phase 2 Common Protocol is enrolled

## MV Diabetes Research Centre – NIRT-NIH-ICER University of Massachusetts (CRU 103)

1. Acute Phase Proteins Are Baseline Predictors of Tuberculosis Treatment Failure

Kumar NP, Moideen K, Nancy A, Viswanathan V, Thiruvengadam K, Sivakumar S, Hissar S, Kornfeld H, Babu S.. Front Immunol. 2021 Nov 15;12:731878. doi: 10.3389/fimmu.2021.731878. PMID: 34867953; PMCID: PMC8634481

2. Plasma Chemokines Are Baseline Predictors of Unfavorable Treatment Outcomes in Pulmonary Tuberculosis

Kumar NP, Moideen K, Nancy A, Viswanathan V, Thiruvengadam K, Nair D, Banurekha VV, Sivakumar S, Hissar S, Kornfeld H, Babu S. Plasma Chemokines Are Baseline Predictors of Unfavorable Treatment Outcomes in Pulmonary Tuberculosis. Clin Infect Dis. 2021 Nov 2;73(9):e3419-e3427. doi: 10.1093/cid/ciaa1104. PMID: 32766812; PMCID: PMC8563183.

3. Effect of anti-tuberculosis treatment on the systemic levels of tissue inhibitors of metalloproteinases in tuberculosis - Diabetes co-morbidity

Kumar NP, Moideen K, Viswanathan V, Sivakumar S, Hissar S, Kornfeld H, Babu S. J Clin Tuberc Other Mycobact Dis. 2021 22 Apr.;23:100237. doi: 10.1016/j.jctube.2021.100237. PMID: 33997311; PMCID: PMC8100611.

4. Household food insecurity among patients with pulmonary tuberculosis and its associated factors in South India: a cross-sectional analysis

Reshma Ayiraveetil, Sonali Sarkar, Palanivel Chinnakali, Kathiresan Jayashree, Mathavaswami Vijayageetha, Pruthu Thekkur, Subitha Lakshminarayanan, Selby Knudsen, Natasha S Hochberg, C Robert Horsburgh, Jerrold Ellner, Gautam Roy. Ayiraveetil R, et al. BMJ Open. 2020 Feb 28;10(2):e033798. doi: 10.1136/bmjopen-2019-033798. PMID: 32114470; PMCID: PMC7050349.

- 5. Association of Plasma Matrix Metalloproteinase and Tissue Inhibitors of Matrix Metalloproteinases Levels With Adverse Treatment Outcomes Among Patients With Pulmonary Tuberculosis Kumar, N.P., Moideen, K., Nancy, A., Viswanathan, V., Thiruvengadam, K., Nair, D., Banurekha, V.V., Sivakumar, S., Hissar, S., Kornfeld, H. & Babu, S. (2020). JAMA Netw Open 3(12): e2027754.
- 6. Impact of diabetes and low body mass index on tuberculosis treatment outcomes Kornfeld H, Sahukar BS, Procter-Gray E, Kumar NP, West K, Kane K, Natarajan M, Li W, Babu S, Viswanathan V. Clin Infect Dis 2020 3 Dec.;71(9):e392-e398. doi: 10.1093/CID/ciaa054.PMID: 31955202.
- 7. Heterogeneity in the cytokine profile of tuberculosis-diabetes co-morbidity
  Kumar NP, Moideen K, Nancy A, Viswanathan V, Shruthi BS, Sivakumar S, Natarajan M, Kornfeld H,
  Babu S. Cytokine 2020 Jan;125:154824. PMID: 31472402.
- 8. Systemic RAGE ligands are upregulated in tuberculosis individuals with diabetes co-morbidity and modulated by anti-tuberculosis treatment and metformin therapy

  Kumar NP, Moideen K, Nancy A, Viswanathan V, Shruthi BS, Sivakumar S, Hissar S, Kornfeld H, Babu S.

  BMC Infect Dis 2019 9 Dec.;19(1):1039. PMID: 31818258; PMCID: PMC6902343.
- 9. Plasma chemokines are biomarkers of disease severity, higher bacterial burden, and delayed sputum culture conversion in pulmonary tuberculosis

Kumar NP, Moideen K, Nancy A, Viswanathan V, Shruthi BS, Sivakumar S, Natarajan M, Kornfeld H, Babu S. Sci Rep 2019 3 Dec.;9(1):18217. PMID: 31796883; PMCID: PMC6890773.

10. Plasma eicosanoid levels in tuberculosis and tuberculosis-diabetes co-morbidity are associated with lung pathology and bacterial burden

Kumar NP, Moideen K, Nancy A, Viswanathan V, Shruthi BS, Shanmugam S, Hissar S, Kornfeld H, Babu S. Front Cell Infect Microbiol 2019 1 Oct.;9:335. PMID: 31632923; PMCID: PMC6779700.

## MV Diabetes Research Centre – NIRT-NIH-ICER University of Massachusetts (CRU 103)

- 11. Persistent inflammation during anti-tuberculosis treatment with diabetes co-morbidity Kumar NP, Fukutani KF, Shruthi BS, Alves T, Silveira-Mattos PS, Rocha MS, West K, Natarajan M, Viswanathan V, Babu S, Andrade BB, Kornfeld H. eLife. 2019 4 Jul.;8. PII: e46477. PMID: 31271354; PMCID: PMC6660216.
- 12. Elevated circulating levels of monocyte activation markers among tuberculosis patients with diabetes co-morbidity

Kumar NP, Moideen K, Viswanathan V, Sivakumar S, Natarajan M, Kornfeld H, Babu S. Immunology. 2019 Mar;156(3):249-258. PMID: 30427060; PMCID: PMC6376263.

13. Elevated levels of matrix metalloproteinases reflect severity and extent of disease in tuberculosis-diabetes co-morbidity and are predominantly reversed following standard anti-tuberculosis or metformin treatment

Kumar NP, Moideen K, Viswanathan V, Sivakumar S, Menon PA, Kornfeld H, Babu S. BMC Infect Dis. 2018 25 Jul.;18(1):345. PMID: 30045688; PMCID: PMC6060542.

14. Heightened circulating levels of antimicrobial peptides in tuberculosis-diabetes co-morbidity and reversal upon treatment

Kumar NP, Moideen K, Viswanathan V, Sivakumar S, Menon PA, Kornfeld H, Babu S. PLoS One. 2017 Sep 14;12(9):e0184753. doi: 10.1371/journal.pone.0184753. eCollection 2017. PMID: 28910369; PMCID: PMC5599016.

15. Systems immunology of diabetes tuberculosis co-morbidity reveals signatures of disease complications

Prada-Medina CA, Fukutani KF, Kumar NP, GilSantana L, Babu S, Lichtenstein F, West K, Sivakumar S, Menon PA, Viswanathan V, Andrade BB, Nakaya HI, Kornfeld H. Sci Rep. 2017 May 17;7(1):1999. PMID: 28515464; PMCID: PMC5435727.

16. Defining a research agenda to address the converging epidemics of tuberculosis and diabetes. Part 2: Underlying biological mechanisms

Ronacher K, van Crevel R, Critchley J, Bremer A, Schlesinger LS, Kapur A, Basaraba R, Kornfeld H, Restrepo Bl. Chest. 2017 Jul;152(1):174-180. PMID: 28434937; PMCID: PMC5577357.

17. Defining a research agenda to address the converging epidemics of tuberculosis and diabetes. Part 1: Epidemiology and clinical management

Critchley JA, Restrepo BI, Ronacher K, Kapur A, Bremer AA, Schlesinger LS, Basaraba R, Kornfeld H, van Crevel R. Chest. 2017 Jul;152(1):165-173. PMID: 28434936; PMCID: PMC5989639.

18. Tuberculosis-diabetes co-morbidity is characterized by heightened systemic levels of circulating angiogenic factors

Kumar NP, Moideen K, Sivakumar S, Menon PA, Viswanathan V, Kornfeld H, Babu S. J Infect. 2017 Jan;74(1):10-21. PMID: 27717783; PMCID: PMC5164955.

19. Modulation of dendritic cell and monocyte subsets in tuberculosis-diabetes co-morbidity upon standard tuberculosis treatment

Kumar NP, Moideen K, Sivakumar S, Menon PA, Viswanathan V, Kornfeld H, Babu S. Tuberculosis (Edinb). 2016 Dec; 101:191-200. PMID: 27865391; PMCID: PMC5127284.

20. Effect of standard tuberculosis treatment on naive, memory and regulatory T-cell homeostasis in tuberculosis-diabetes co-morbidity

Kumar NP, Moideen K, Viswanathan V, Kornfeld H, Babu S. Immunology. 2016 Sep;149(1):87-97. PMID: 27289086; PMCID: PMC4981606.

## MV Diabetes Research Centre – NIRT-NIH-ICER University of Massachusetts (CRU 103)

11. Glucose metabolism disorder is associated with pulmonary tuberculosis in individuals with respiratory symptoms from Brazil

Almeida-Junior JL, Gil-Santana L, Oliveira CA, Castro S, Cafezeiro AS, Daltro C, Netto EM, Kornfeld H, Andrade BB. PLoS One. 2016 Apr 14;11(4):e0153590. PMID: 27078026; PMCID: PMC4831681.

12. High prevalence and heterogeneity of diabetes in patients with T.B. in South India: A report from the Effects of Diabetes on Tuberculosis Severity (EDOTS) Study

Kornfeld H, West K, Kane K, Kumpatla S, Zacharias RR, Martinez-Balzano C, Li W, Viswanathan V. Chest. 2016 Jun;149(6):1501-8. PMID: 26973015; PMCID: PMC4944775.

## P.D. Hinduja National Hospital & Medical Research Center Johns Hopkins University (CRU 108)

1. Targeted next-generation sequencing directly from sputum for comprehensive genetic information on drug-resistant Mycobacterium tuberculosis.

Kambli P, Ajbani K, Kazi M, Sadani M, Naik S, Shetty A, Tornheim JA, Singh H, Rodrigues C. Tuberculosis (Edinb). 2021 Mar;127:102051. doi: 10.1016/j.tube.2021.102051. Epub 2021 8 Jan. PMID: 33450448.

2. Whole-genome enrichment approach for rapid detection of *Mycobacterium tuberculosis* and drug resistance-associated mutations from direct sputum sequencing.

Soundararajan L, Kambli P, Priyadarshini S, Let B, Murugan S, Iravatham C, Tornheim JA, Rodrigues C, Gupta R, Ramprasad VL. Tuberculosis Volume 121, March 2020, 101915. https://doi.org/10.1016/j.tube.2020.101915

3. Clinical features associated with linezolid resistance among multidrug-resistant tuberculosis patients at a tertiary care hospital in Mumbai, India

Tornheim JA, Intini E, Gupta A, Udwadia ZF. Journal of clinical tuberculosis and other mycobacterial diseases vol. 20 100175.24 Jul. 2020, doi:10.1016/j.jctube.2020.100175

4. Delamanid central nervous system pharmacokinetics in tuberculous meningitis in rabbits and humans

Tucker EW, Pieterse L, Zimmerman MD, Udwadia ZF, Peloquin CA, Gler MT, Ganatra S, Tornheim JA, Chawla P, Caoili JC, Ritchie B, Jain SK, Dartois V, Dooley KE. Antimicrob Agents Chemother. 2019 23 Sep.;63(10). PII: e00913-19. doi: 10.1128/AAC.00913-19. Print 2019 Oct. PMID: 31383662; PMCID: PMC6761520.

5. Management of drug-resistant tuberculosis

Lange C, Dheda K, Chesov D, Mandalakas AM, Udwadia Z, Horsburgh CR Jr. Lancet. 2019 Sep 14;394(10202):953-966. doi: 10.1016/S0140-6736(19)31882-3. PMID: 31526739.

6. Multi-center study to establish interpretive criteria for clofazimine drug susceptibility testing Ismael N, Said HM, Rodrigues C, Omar SV, Ajbani K, Sukhadia N, Kohl TA, Niemann S, Kranzer K, Diels M, Rigouts L, Rüsch-Gerdese S, Siddiqi S. Int J Tuberc Lung Dis. 2019 May 1;23(5):594-599. doi: 10.5588/ijtld.18.0417. PMID: 31097068.

## P.D. Hinduja National Hospital & Medical Research Center Johns Hopkins University (CRU 108)

- 7. Performance of bioMérieux Lowenstein-Jensen slopes in plastic tube packaging, compared to existing phenotypic methods, for efficient recovery of Mycobacterium tuberculosis (MTB) complex Nambiar R, Bereksi N, Gonzalez R, Anthony de Cozar, Loubet M, Shetty A, Alex van Belkum, Rodrigues C. J Med Microbiol. 2019 Mar;68(3):398-401. doi: 10.1099/jmm.0.000930. Epub 2019 6 Feb. PMID: 30724723.
- 8. Utility of pyrosequencing for rapid detection of tubercular meningitis (TBM) and associated susceptibility directly from CSF specimens
  Ajbani K, Kazi M, Naik S, Soman R, Shetty A, Rodrigues C. Tuberculosis (Edinb). 2018 Jul;111:54-56. doi: 10.1016/j.tube.2018.05.009. Epub 201819 May. PMID: 30029915
- 9. Evaluation of pyrosequencing for extensive drug resistance-defining anti-tuberculosis drugs for use in public healthcare Nambiar R, Shah D, Ajbani K, Kazi M, Sadani M, Shetty A, Keskar P, Kamble S, van Belkum A, Rodrigues C. Tuberculosis (Edinb). 2018 May;110:86-90. doi: 10.1016/j.tube.2018.03.006. Epub 2018 Mar 26. PMID: 29779779
- **10.** Pyrosequencing to resolve discrepant Xpert MTB/RIF and Mycobacterial Growth Indicator Tube 960 Ajbani K, Kazi M, Tornheim J, Naik S, Soman R, Shetty A, Rodrigues C. Lung India. 2018 Mar-Apr;35(2):168-170. doi: 10.4103/lungindia.lungindia\_71\_17. PMID: 29487256; PMCID:PMC5846270.

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## BJGMC





## Hinduja

## JIPMER





# Lectures & Presentations





CMC MV Hospital





BMMRC JIPMER



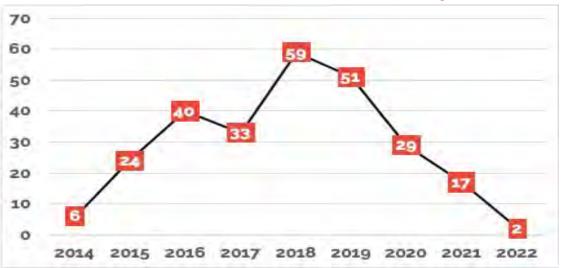
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### **LECTURES & PRESENTATIONS 2014-2022**



**LECTURE**: Individual presentation on a topic of field of expertise. Lectures from prior RePORT India annual conferences are not included in this list but are available upon request.

PRESENTATION | ABSTRACT: Multiple authors, includes poster and oral discussions

#### **RePORT India Consortium**

#### **LECTURES**

- 1. Gupta A. Overview of RePORT. TBVI. Les Diablarets, Switzerland; January 2020.
- 2. Gupta A, Rodrigues C, Christopher DJ, Kornfeld H, Ellner J, Mave V, Devalraju KP. RePORT India Symposium: Biomarkers, diagnostics, and comorbidities. 49th Union World Conference on Lung Health. The Haque, The Netherlands; October 25, 2018.
- 3. Gupta A. RePORT India overview. Presented at: CFAR RePORT International Meeting. Rockville, MD; July 2, 2018.
- 4. Gupta A. Keynote Address: Global health diplomacy: Why it really matters! (RePORT India described) AAAS Science & Technology. Washington, DC; May 31, 2018.
- 5. Gupta, A. Keynote Address: The challenge of eliminating TB in India. (RePORT India described) University of Washington TB Symposium. Seattle, WA; May 18, 2018;
- 6. Gupta A. An Overview of the RePORT India Consortium. Presented at: Annual IeDEA Meeting; National Institutes of Health. June 22, 2016; Rockville, MD, USA.
- 7. Mave V. RePORT India: Objectives and future directions. Presented at: TB Vaccine 4th Global Forum. Shanghai, China; 2015.

#### **ABSTRACT**

Hamilton CD, Ellner J, Swaminathan S, Christopher D, Gupta A, Sterling T, Rolla VC, Stoszek S. Regional Prospective Observational Research for Tuberculosis (RePORT) Consortia using a common protocol to collect specimens for biomarker research. Poster presented at: 45th Union World Conference on Lung Health of the International Union Against TB and Lung Disease. Barcelona, Spain; October 28–November 1, 2014.

## Bhagwan Mahavir Medical Research Centre University of Texas Health Science Center at Tyler (CRU 107)

#### PRESENTATIONS | ABSTRACTS

- Kamakshi Prudhula Devalraju Venkata Sanjeev Kumar Neela, Mohammad Soheb Ansari, Ramakrishna Vankayalapati, Vijaya Lakshmi Valluri. Immune and Hormone Studies in HHCs of TB patients. RePORT India 10th Annual Meeting (Virtual) 9-11 February 2021.
- 2. Buka Samten **The Role of Histone Deacetylase 1 in Immune Responses against Tuberculosis Infection**. RePORT India 10th Annual Meeting (Virtual) 9-11 February 2021.
- 3. Deepak Tripathy **Alcohol Induces Dysbiosis & Type 1 Interferon-A Production in Mice Infected with Mycobacterium Tuberculosis**. RePORT India 10th Annual Meeting (Virtual) 9-11 February 2021.
- 4. Kamakshi Prudhula Devalraju, Venkata Sanjeev Kumar Neela, Mohammad Soheb Ansari, Ramakrishna Vankayalapati, Vijaya Lakshmi Valluri. **Defective expansion and function of memory like natural killer cells in HIV+ individuals with latent tuberculosis infection**. Poster Presented at: RePORT International 2020 Annual Meeting. Mumbai, India; February 10–12, 2020.
- 5. Venkata Sanjeev Kumar Neela, Kamakshi Prudhula Devalraju, Mohammad Soheb Ansari, Ramakrishna Vankayalapati, Vijaya Lakshmi Valluri. **Memory like NK cells and monocytes as Immunological markers for protection in house hold contacts of tuberculosis patients.** Poster Presented at: RePORT International 2020 Annual Meeting. Mumbai, India; February 10–12, 2020.
- 6. Valluri V. Vaccines and immunological markers for TB prevention. Presented at: 50th Annual Union World Conference on Lung Health. Hyderabad, India; October 30–Nov 2, 2019.
- 7. Kumar NV. **T Cell subsets and cytokines in HIV+ individuals with latent and active tuberculosis**. Poster presented at: 50th Annual Union World Conference on Lung Health. Hyderabad, India; October 30–Nov 2, 2019.
- 8. Prudhula DK. **Defective monocyte signalling pathway in HIV+ individuals with latent tuberculosis infection.** Poster presented at: 50th Annual Union World Conference on Lung Health. Hyderabad, India; October 30–Nov 2, 2019.
- 9. Devalraju KP, Neela VSK, Chaudhury A, Vankayalapati R, Valluri VL. **NK cells and memory-like NK cells as immunological markers of protection against latent TB conversion in household contacts of TB patients**. Abstract presented at: 5<sup>th</sup>Global Forum on TB Vaccines. New Delhi, India; February 20–23, 2018.
- 10. Neela VSK, Devalraju KP, Sumnalatha G, Chowdary A, Ansari MS, Vankayalapati R, Valluri VL. CD14+ CD16+ cells as immunological marker for protection in household contacts with latent tuberculosis infection. Abstract presented at: 5<sup>th</sup>Global Forum on TB Vaccines. New Delhi, India; February 20–23, 2018.
- 11. Devalraju KP. **Identify potential biomarkers for development of latent tuberculosis infection (LTBI) by longitudinal follow-up of HHCs of TB patients.** Presented at: Presented at: RePORT International 2016 Annual Meeting. Durban, South Africa; July 14–15, 2016.
- 12. Cheekatla SS, Tripathi D, Venkatasubramanian S, Nathella PK, Paidipally P, Ishibashi M, Welch E, Tvinnereim AR, Mitsuo I, Babu S, Kornfeld H, Vankayalapati R. **NK-DC crosstalk in diabetes enhances Il-6 mediated inflammation during tuberculosis infection**. Poster presented at: Keystone Symposium on Tuberculosis Co-Morbidities and Immunopathogenesis (B6). Keystone, CO, USA; February 28–March 3, 2016.
- 13. Cheekatla SS, Venkatasubramanian S, Tripathi D, Paidipally P, Welch E, Tvinnereim AR, Vankayalapati R. IL-21 is essential for the optimal control of Mycobacterium tuberculosis infection. Presented at: American Association of Immunologist Meeting. New Orleans, LA, USA. May 8–12, 2015.

Bhagwan Mahavir Medical Research Centre University of Texas Health Science Center at Tyler (CRU 107)

- 14. Cheekatla SS, Tripathi D, Venkatasubramanian S, Paidipally P, Welch E, Tvinnereim AR, Kornfeld H, Vankayalapati R. **IL-6 regulates pro- and anti-inflammatory cytokine production and mortality of Mycobacterium tuberculosis infected Type 2 diabetic mice.** Presented at: American Association of Immunologists Meeting. New Orleans, LA, USA. May 8–12, 2015.
- 15. Tripathi D, Venkatasubramanian S, Cheekatla SS, Paidipally P, Welch E, Tvinnereim AR, Vankayalapati R. CD4+CD25+Foxp3+ cells from JNK-/- mice prolong pancreatic allograft survival in type 1 diabetic Mice. Presented at: American Association of Immunologist Meeting. New Orleans, LA, USA. May 8–12, 2015.
- 16. Tripathi D, Venkatasubramanian S, Cheekatla SS, Paidipally P, Welch E, Tvinnereim AR, Vankayalapati R. Liver NK1.1 cells and IL-22 promote pancreatic islets allograft survival in type 1 diabetic mice. Presented at: American Association of Immunologists Meeting New Orleans, LA, USA. May 8–12, 2015.
- 17. Venkatasubramanian S, Dhiman R, Paidipally P, Cheekatla SS, Tripathi D, Welch E, Tvinnereim AR, Brenda Jones B, Theodorescu D, Barnes PF, Vankayalapati R. **A rho GDP dissociation inhibitor produced by apoptotic T-cells inhibits growth of Mycobacterium tuberculosis**. Presented at: American Association of Immunologists Meeting. New Orleans, LA, USA. May 8–12, 2015.
- 18. Venkatasubramanian S, Paidipally P, Cheekatla SS, Welch E, Raghunath A, Tvinnereim AR, Nurieva R, Barnes PF, Vankayalapati R. **IL-21 dependent expansion of memory-like NK cells enhances protective immune responses against Mycobacterium tuberculosis.** Presented at: NK 2015—15<sup>th</sup> Meeting of the Society for Natural Immunity. Montebello, Canada; May 2-6, 2015.

Byramjee Jeejeebhoy Government Medical College National Institute for Research in Tuberculosis Johns Hopkins University (CRUs 106 & 105)

#### **LECTURES**

- 1. Mave V. **Metabolomics and tuberculosis in Indian context**. Presented at RePORT South Africa 2019 Annual Meeting. Johannesburg, South Africa; May 2019.
- 2. Mave V. **VPM TB vaccine trial, TB sequencing study**. Presented at: RePORT India Tuberculosis Consortium Meeting. Chennai, India. March 2019.
- 3. Gupta A. Panelist. Leveraging collective Impact to promote India's development: The role of the Indian diaspora in the fight against tuberculosis. The Role of the Indian Diaspora in the Fight Against Tuberculosis. Georgetown University. Washington, DC, USA; October 2, 2018.
- 4. Kinikar A. **Update on RICC pediatric transcriptomic study—India component**. RePORT International Annual Meeting. Szouchou, China; September 12–14, 2018.
- 5. Chandrasekaran P. **TB research in India**. Presented at: 1<sup>st</sup> BRICS TB Research Network Meeting. Rio de Janeiro, Brazil; September 14–15, 2017.
- 6. Mave V. **Diabetes and drug levels: Rifampin + other drugs**. Presented at: RePORT International 2017 Annual Meeting. Rio de Janeiro, Brazil; September 2017.

Byramjee Jeejeebhoy Government Medical College National Institute for Research in Tuberculosis Johns Hopkins University (CRUs 106 & 105)

- Chandrasekaran P. Ongoing research and research priorities for India on LTBI. Presented at: WHO
  Global TB Programme Technical Consultation Meeting on Programmatic Management of Latent
  Tuberculosis Infection (LTBI). Seoul, Republic of Korea; August 31–September 1, 2017.
- 8. Mave V. **Impact of DM and HIV on TB drug resistance and recurrence**. Presented at: RePORT India 2017 Joint Leadership Meeting. Hyderabad, India; February 2017.
- 9. Mave V. **Participant recruitment and retention strategies**. Presented at: Investigator meeting of TB vaccine. Chennai, India: December 2016.
- 10. Mave V. **RePORT India**. Presented at: Common Protocol and TB Vaccine Studies Integration Meeting. Chennai, India; November 2016.
- 11. Mave V. **Updates on the recombinant BCG vaccine trial in India.** Presented at: RePORT International 2016 Annual Meeting. Durban, South Africa; July 2016.
- 12. Gupta, A. Conducting HIV and TB research in India: Challenges and opportunities. University of Texas Health Science Center. Tyler, TX, USA; June 23, 2016.
- 13. Gupta A. **TB in pregnancy**. Presented at: RePORT India 2016 Joint Leadership Meeting: Advancing TB Research. CMC Vellore, India; February 2, 2016.
- 14. Gupta A. **TB in pregnancy**. Presented at: RePORT India TB Workshop. March 5, 2015; Mumbai, India.
- 15. Gupta, A. Conducting HIV and TB research in India: Challenges and opportunities. Emory University. Atlanta, GA, USA; August 27, 2015.
- 16. Mave V. Therapeutic drug monitoring (TDM) of TB in young children: The role of hair assays. Presented at: IMPAACT Network Annual Meeting. Washington DC, USA; June 2015.
- 17. Mave V. **RePORT India: Objectives and future directions**. Presented at: TB Vaccine 4th Global Forum. Shanghai, China; April 2015.

#### **ABSTRACTS | POSTERS | PRESENTATIONS**

- Tornheim JA, Paradkar M, Fukutani F, Kinikar A, Mave V, Andrade BB, Gupta A, Karakousis PC. Blood-Based Biomarkers of Tuberculosis in Children Integrating Metabolomic and Transcriptomic Data. TB Science. Virtual. October 2020.
- 2. Tornheim, JA. **Identification of Blood-Based Biomarkers for Tuberculosis in Children using Integration of Metabolomics and Transcriptomics.** TB RiCC Virtual Meeting. 29 September 2020.
- 3. Queiroz ATL, Kulkarni V, Sangle S, Cordeiro-Santos M, Andrade BB, Sterling T, Gupta A, Ellner J, Kadam D, Rolla VC, Salgame P, Mave V. **Transcriptome signature of tuberculosis in persons with advanced HIV from India.** TB RiCC Virtual Meeting. 29 September 2020.
- 4. Tornheim JA, Madugundu AK, Paradkar M, Fukutani KF, Queiroz ATL, Gupte N, Gupte AN, Kinikar A, Kulkarni V, Balasubramanian U, Sreenivasamurthy S, Raja R, Pradhan N, Shivakumar SVBY, Valvi C, Hanna LE, Andrade BB, Mave V, Pandey A, Gupta A. **Transcriptomic Profiles of Confirmed Pediatric Tuberculosis Patients and Household Contacts Identifies Active Tuberculosis, Infection, and Treatment Response among Indian Children.** Presented at: Johns Hopkins Department of Medicine Research Retreat. 28 February 2020. Baltimore, MD.

- 5. Cox SR, Chandrasekaran P, Gaikwad S, Kinikar A, Shivakumar SVBY, Paradkar M, Sekar K, Gupte A, Seth B, Thiruvengadam K, Raskar S, Pradhan N, Kulkarni V, Hanna LE, Gupte N, Bollnger RC, Mave V, Gupta A, for the CTRIUMPH-RePORT India Study Team. Causes and timing of death among patients treated for tuberculosis in Pune and Chennai, India. Presented at: RePORT India Conference. 10-12 February 2020. Mumbai, India & Johns Hopkins Department of Medicine Research Retreat. 28 February 2020. Baltimore, MD.
- 6. Paradkar M, Chandrasekara P, Jain D, Shivakumar SVBY, Thiruvengadan K, Gupte AN, Thomas B, Kinikar A, Sekar K, Bharadwaj R, Dolla CK, Gaikwad S, Elilarasi S, Lokhande R, Reddy D, Murali L, Kulkarni V, Pradhan N, Hanna LE, Pattabiraman S, Kohli R, Nayagam R, Suryavanshi N, Shrinivasa BM, Cox SR, Selvaraju S, Gupte N, Mave V, Gupta, Bollinger RC, for the CTRIUMPH-RePORT India Study Team. Tuberculosis preventive therapy should be considered for all household contacts of pulmonary TB patients in India. RePORT India 2020 Joint Leadership Meeting. Mumbai, India. February 2020.
- 7. Alexander M, Bhosale R, Mathad J, Naik S, Divya A, Gupte N, Patil N, Gupta A. **Inappropriate** postpartum weight loss may predict development of active TB. Presented at: 50th Union World Conference on Lung Health. Hyderabad, India. October 20–November 2, 2019.
- 8. Baliashvili D, Gandhi NR, Kim S, Gupta A, Churchyard G, Swindells S, Hesseling A, Hughes M, Shah S for the ACTG 5300/IMPAACT I2003 PHOENIx Feasibility study team. **Resistance to Mycobacterium tuberculosis infection among household contacts of MDR TB patients.** Presented at: 50th Union World Conference on Lung Health. Hyderabad, India. October 20-November 2, 2019.
- 9. Bhosale R, Graham H, Alexander M, Kinikar A, Khwaja S, Patil N, Gupta A, Mathad J, Shivakoti R. Association of latent TB infection in pregnancy with maternal and infant health outcomes in an Indian cohort. Presented at: 50th Union World Conference on Lung Health. Hyderabad, India. October 20-November 2, 2019.
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- 43. Chandrasekaran P, Thiruvengadam K, Gupte N, Luck EH, Mave V, Gupte A, Gupta A, Swaminathan S. **Household contact tracing of adult pulmonary TB patients in India: Prevalence of TB disease and infection.** Presented at: RePORT India 2017 Joint Leadership Meeting. Hyderabad, India; February 3, 2017.
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- 46. Mave V, Pradhan R, Kagal A, Bharadwaj R, Gupte N, Gupta A, Meshram S, Golub J. **Third anti-TB drug in continuation phase for TB patients: Is it the need of the hour for India?** Presented at: 47th Union World Conference on Lung Health. Liverpool, UK; October 27, 2016.
- 47. Mave V, Gupte N, Meshram S, Kagal A, Gupta A, Bharadwaj R, Pradhan R, Golub J. **Xpert® MTB/RIF** assay for pulmonary tuberculosis diagnosis in patients with pre-diabetes mellitus and diabetes mellitus. Presented at: 47th Union World Conference on Lung Health. Liverpool, UK; October 27, 2016.
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- 52. Gupte A, Meshram S, Selvaraju S, Gupte N, Shivakumar SVBY, Paradkar M, Kohli R, Thiruvengadam K, Suryavanshi N, Chandrasekaran P, Mave V, Swaminathan S, Gupta A, Golub J, Checkley W. **Host factors associated with poor respiratory health-related quality of life in pulmonary tuberculosis**. Presented at: RePORT International 2016 Annual Meeting. Durban, South Africa; July 14, 2016.
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#### **LECTURES**

- 1. Risk TB in Diabetic patients and its management' in webinar titled 'Management of Diabetes and Tuberculosis' under the aegis of the Indian Chest Society, held on 30 Jan 2022.
- 2. Christopher DJ. "Evidence for Lung Injury from the Real World on Impairment after Clinical Cure of Pulmonary TB." Presented at webinar by DBT (RePort India) from 9th Feb 2021 to 11th Feb 2021.
- 3. Christopher DJ. **COVID TB WEBINAR. Trajectory of the Pandemic and Projected Disease Burden**. Presented at: Webinar session Live on July 27, 2020.
- 4. Christopher DJ, **Post TB bronchiectasis**. Presented at: Nexplore Bronchiectasis Conclave. Candolim, Goa, India; December 14, 2019.
- 5. Christopher DJ. Experiences with LTBI screening of healthcare workers in an Indian referral hospital. Presented at: 50th Annual Union World Conference on Lung Health. Hyderabad, India; October 30–November 2, 2019.
- 6. Christopher DJ. **TB-diabetes link**. Presented at: Prof. Dr. M. Viswanathan Oration at the Research Society for the study of Diabetes in India, Annual Conference. Dindigul, Tamil Nadu, India; August 10, 2019.
- 7. Christopher DJ. **PET scan in TB meningitis.** Presented at: RePORT India 2019 Joint Leadership Meeting: Biomarkers and Beyond. Chennai, India; February 4–6, 2019.
- 8. Christopher DJ. **Xpert PCR ultra and transcriptional signatures in pleural tuberculosis.** RePORT India 2019 Joint Leadership Meeting: Biomarkers and Beyond. Chennai, India; February 4–6, 2019.

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#### **LECTURES**

- 9. Christopher DJ. **Is India's endeavor to end TB by 2025 achievable?** Presented at: 36th AP Tuberculosis & Chest Diseases Conference. Madanapally, Andhra Pradesh, India; November 10–11, 2018.
- 10. Christopher DJ. Addressing diagnostic challenges for TB meningitis—From clinical staging to PET Scanning. Presented at: 49th Union World Conference on Lung Health. The Hague, The Netherlands; October 24–27, 2018.
- 11. Christopher DJ. Is India's endeavor to end TB by 2025 achievable? How can RePORT align with this? Presented at: RePORT International 2018 Annual Meeting. Suzhou, China; September 12–14, 2018.
- 12. Christopher DJ. **Determination of efficacy of expert PCR ultra and transcriptional signatures in the diagnosis of pleural tuberculosis.** Presented at: RePORT International 2018 Annual Meeting. Suzhou, China; September 12–14, 2018.
- 13. Christopher DJ. **Healthcare personnel TB—Fact of life in high burden countries.** Presented at: RePORT International 2018 Annual Meeting. Suzhou, China; September 12–14, 2018.
- 14. Christopher DJ. **Point of care diagnostics and need for triage test in a high prevalence setting.** Presented at: Investigators Meeting: Understanding the Resources and Gaps in DAIDS funded TB Research. NIAID Conference Center. Rockville, MD, USA; July 2–3, 2018.
- 15. Christopher DJ. **Battling the white plague (TB) in our campuses.** Presented at: The Quality Circle, Christian Medical College. Vellore, India; April 14, 2018.
- 16. Christopher DJ. **State of TB control in India.** Presented at: RePORT India 2018 Joint Leadership Meeting: Catalyzing Discoveries toward TB Elimination. Delhi, India; February 15, 2018.
- 17. Christopher DJ. **Prevalence of latent TB infection (LTBI) among undergraduate nursing trainees in a rural secondary care hospital in Southern India.** Presented at: RePORT India 2018 Joint Leadership Meeting: Catalyzing Discoveries toward TB Elimination. Delhi, India; February 15, 2018.
- 18. Christopher DJ. **Targeted LTBI testing.** Presented at: LTBI Knowledge Seminar. Hyderabad, India; January 11, 2018.
- 19. Christopher DJ. **LTBI screening in high TB prevalence setting.** Presented at: Qiagen Knowledge Seminar. Bangalore, India; November 2, 2017.
- 20. Christopher DJ. **LTBI Screening: A clinician's perspective.** Presented at: CME organized by Qiagen. New Delhi; India. April 5, 2017.
- 21. Christopher DJ. **LTBI: To screen or not to screen.** Presented at: Three T's of TB Prevention: Test, Treat, and Track Symposium. Asia Pacific Regional Conference; International Union against Tuberculosis. Tokyo, Japan; March 23, 2017.
- 22. Christopher DJ. **Advances in the management of drug resistant TB.** Presented at: TB Symposium. Convened by Krishna Medical College in collaboration with McGill University (Canada). Manipal, India; December 21, 2016.
- 23. Christopher DJ. **Healthcare worker TB: A Panel Discussion.** Presented at: TB Symposium. Convened by Krishna Medical College in collaboration with McGill University (Canada). Manipal, India; December 21, 2016.
- 24. Christopher DJ. **Evolution of drug resistant TB in India.** Presented at: Annual Update in Tuberculosis. Convened by CMC Vellore, Vellore, India; November 19, 2016.

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- 25. Christopher DJ. **Screening for LTBI in healthcare personnel to assess TB risk—Lessons from India.** Presented at: 5th Meeting of Asian Experts Community. Taipei, Taiwan; August 26–28, 2016.
- 26. Christopher DJ. **TB risk in healthcare workers: Myth or reality?** Presented at: RePORT International 2016 Meeting. Durban, South Africa; July 14–15, 2016.
- 27. Christopher DJ. **From lab to clinic: Optimizing the importance of new diagnostics.** Presented at: Advancing TB Research—An Exploration of Opportunities. Convened by PD Hinduja Hospital and NIH (USA). Mumbai, India; March 23–24, 2016.
- 28. Christopher DJ. **Lessons from healthcare—TB research in India.** Presented at: CMC Winter Symposium and the RePORT India 2016 Joint Leadership Group Meeting. Vellore, India; February 12–13, 2016.
- 29. Christopher DJ. **Pleural tuberculosis.** Presented at: Association of Physicians of India Meeting. Hyderabad, India; January 29–31, 2016.
- 30. Christopher DJ. **TB in healthcare workers.** Presented at: National Update in Respiratory Medicine. Convened by PD Hinduja Hospital. Mumbai, India; November 27–29, 2015.
- 31. Christopher DJ. **Road for TB elimination in India.** Presented at: 4th Meeting of Asian Experts Community. Bali, Indonesia; August 7–9, 2015.
- 32. Christopher DJ. **Newer diagnostics in TB.** Presented at: Institute of Thoracic Medicine, MMC, CME Program for the PG Students of Southern States. Chennai, India; September 2014.
- 33. Christopher DJ. **Relevance of TST and IGRA in current day practice.** Presented at: ASHRAICON Conference 2014. Ahmedabad, India; July 27, 2014.

#### PRESENTATIONS | ABSTRACTS

- 1. D. J. Christopher, Dhivya Roy, Deepa Shankar, Balamugesh T **Advance lung function testing: Lung Volumes(TLC) & Diffusing Capacity(DLco) diagnoses substantial pulmonary function impairment in treated Pulmonary Tuberculosis patients (24071)** Presented at Virtual ERS International Congress 2020, Barcelona, Spain; September 7 to 9 2020.
- D. J. Christopher, Coelho Victor, Dr. Ebby Simon, Deepa Shankar, Balamugesh T Incremental Yield of Xpert MTB/RIF Ultra over Xpert MTB/RIF in the diagnosis of xtrapulmonary tuberculosis (25062) Presented at Virtual ERS International Congress 2020, Barcelona, Spain; September 7 to 9 2020.
- 3. D. J. Christopher, Dhivya Roy, Deepa Shankar, Balamugesh T **Total lung and diffusing capacity in treated pulmonary tuberculosis patients** Presented at: RePORT India 2020 Joint Leadership Meeting. PD Hinduja, Mumbai; February 9 to 12, 2020.
- 4. D. J. Christopher, Rajasekar. S, Balamugesh T **Is smear microscopy obsolete in the era of Xpert MTB/Rif?** Presented at: RePORT India 2020 Joint Leadership Meeting. PD Hinduja, Mumbai; February 9 to 12, 2020.
- 5. Samuel Santhosh, D. J. Christopher, Blessed Winston, Ratna Prabha, Sumith Mathew, Deepa Shankar, Binu Susan Mathew **Dried plasma spots as a replacement for conventional plasma rifampicin concentration for use in resource limited settings** Presented at: RePORT India 2020 Joint Leadership Meeting. PD Hinduja, Mumbai; February 9 to 12, 2020.

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- 6. Daniel Schwartz David, Aparna Irodi, binita Riya Chacko, Leena RV, D J Christopher, Richa Gupta. **Effectiveness of digital chest radiograph as a Triage tool among patients with clinical suspicion of pulmonary tuberculosis**. Annual conference of the society of chest imaging and interventions (SCII-CON Apr 2019)
- 7. Christopher DJ, Kuruvilla L, Sarangi PK, Irodi A, Chacko B, Leena RV, Shankar D, Thangakunam B. **Comparison of chest radiographic pattern in diabetic and non-diabetic patients with pulmonary tuberculosis.** Presented at: 29<sup>th</sup> ERS International Congress, IFEMA. Madrid, Spain; September 28–October 2, 2019.
- 8. Christopher DJ, Deva J, Thangakunam B, Mathew BS, Winston B. **Anti-tubercular drug** concentrations in pulmonary tuberculosis patients—Diabetics vs non-diabetics. Presented at: 29<sup>th</sup> ERS International Congress, IFEMA. Madrid, Spain; September 28–October 2, 2019.
- Christopher DJ. Experiences with LTBI screening of healthcare workers in an Indian referral hospital. Presented at: 50th Union World Conference on Lung Health. Hyderabad, India; October 30– Nov 2, 2019.
- 10. Christopher DJ. **Chest radiologic pattern in Diabetic patients with Pulmonary Tuberculosis (PTB)**. Abstract presented at: ERS International Congress 2019, September 2019.
- 11. Christopher DJ . **Anti-tubercular drug concentrations in Pulmonary Tuberculosis patients - Diabetic vs Non-Diabetic groups**. Abstract presented at: ERS International Congress 2019, September 2019; DOI: 10.1183/13993003.congress-2019.PA2999
- 12. Christopher DJ, Christopher SA, Balamugesh. T, Hephzibah J, David T, Sathyendra S, Abraham OC, Ramya I, Mathuram A. **Role of PET CT scans in tuberculous meningitis.** Presented at: RePORT India 2019 Joint Leadership Meeting. Chennai, Tamil Nadu, India; February 4–6, 2019.
- 13. Christopher DJ, Deva J, Thangakunam B, Mathew BS, Winston B. **Plasma drug concentrations of isoniazid and rifampicin in pulmonary tuberculosis patients with diabetes.** Presented at: RePORT India 2019 Joint Leadership Meeting. Chennai, Tamil Nadu, India; February 4–6, 2019.
- 14. Christopher DJ, Shankar D, Hemanth Kumar AK, Thangakunam B, Kannan T, Ramachandran G. **Pharmacokinetics of rifampicin, isoniazid and pyrazinamide during daily and intermittent dosing.** Presented at: RePORT India 2019 Joint Leadership Meeting. Chennai, Tamil Nadu, India; February 4–6, 2019.
- 15. Christopher DJ, Arjun AC, Balamugesh T, David T, Sathyendra S, Ramya I, Abraham OC, Mathuram A, Ramakrishnan L. **Predictors of mortality in a TB meningitis cohort.** Presented at: RePORT India 2019 Joint Leadership Meeting. Chennai, Tamil Nadu, India; February 4–6, 2019.
- 16. Christopher DJ, Arjun AC, Balamugesh T, Shankar D. **Respiratory and non-respiratory comorbidities in tuberculosis.** Presented at: RePORT India 2019 Joint Leadership Meeting. Chennai, Tamil Nadu, India; February 4–6, 2019.
- 17. Christopher DJ, Thangakunam B, Shankar D, Samuvel S, Oliver A, Deepak A. **Empirical treatment of smear negative 'supposedly' pulmonary tuberculosis patients—Is it right?** Presented at: RePORT India 2018 Joint Leadership Meeting. Delhi, India; February 15–17, 2018.
- 18. Christopher DJ, Thangakunam B, Samuvel S, Deepak A, Shankar D, Mathuram A, David T, Sathyendra S, Abraham OC, Ramya I, Ramakrishnan L. **Comparison of profile of Indian patients with tubercular meningitis in the CMC, Vellore, cohort with other cohorts.** Presented at: RePORT India 2018 Joint Leadership Meeting. Delhi, India; February 15–17, 2018.

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- 19. Christopher DJ, Shankar D, Micheal JS, Thangakunam B, Ramakrishnan L. **Factors affecting time to sputum smear and culture conversion in adults with pulmonary tuberculosis: A prospective cohort study from CMC RePORT data.** Presented at: RePORT India 2018 Joint Leadership Meeting. Delhi, India; February 15–17, 2018.
- 20. Christopher DJ, Dinakaran S, Gupta R, Prince J, Isaac B, Thangakunam B. Large thoracoscopic pleural biopsy improves yield of Xpert MTB/RIF for diagnosis of pleural tuberculosis. Presented at: BRONCOCON, CMC Vellore. Vellore, India; March 2–4, 2017.
- 21. Christopher DJ, Balamugesh T, Dhabi P. **The prevalence of active and latent tuberculosis infection in patients with type 2 diabetes mellitus in a tertiary care hospital of South India**. Presented at: RePORT India 2016 Joint Leadership Meeting. Vellore, India; February 12–14, 2016.
- 22. Christopher DJ, Balamugesh T, Rohit KO, James P, Gupta R. **Diagnostic yield of various** microbiologic and histopathologic tests in TB pleural effusion diagnosed with thoracoscopy and outcomes of such patients on 6 months follow up. Presented at: RePORT India 2016 Joint Leadership Meeting, Vellore, India; February 12–14, 2016.
- 23. Christopher DJ, Mitra S, Saroini JS, Balaji V, Gupta M, Therese M, Yadav B, Jeyaseelan L. **Burden of diabetes among patients with tuberculosis: Ten-year experience from an Indian tertiary care teaching hospital**. Presented at: 45<sup>th</sup> Union World Conference on Lung Health. Barcelona, Spain; October 28–November 1, 2014.
- 24. Christopher DJ, Denkinger C, Thangakunam B, Sarojini JS, Pai M, Schumacher S. **Point-of-care** implementation of Xpert: Evaluating the impact of product and process innovation in TB diagnosis. Presented at: 45<sup>th</sup> Union World Conference on Lung Health. Barcelona, Spain; October 28–November 1, 2014.

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#### **LECTURES**

- 1. 2021 American Society of Tropical Medicine and Hygiene. (virtual meeting). Symposium: **Recipe for disaster: undernutrition and infectious diseases. "Undernutrition and TB."**
- 2. 2021 Indian Public Health Association IPHACON 2021 Symposium Organizer, Moderator, and Speaker. "Untapped Solutions for India's Tuberculosis Epidemic" (virtual meeting) -- "Tuberculosis: Learning the Impact of Nutrition"
- 3. 2022. Tufts University. Global Health Seminar. **"Food as Medicine: Addressing Undernutrition to end TB"**
- 4. Hochberg, NS. **Tuberculosis: The fundamentals and the sea changes**. Presented at: MPH Course: Global Health Priorities & Approaches. Tufts University School of Medicine. Boston, MA, USA; 2019.
- 5. Hochberg, NS. **Malnutrition and tuberculosis**. World TB Day, National Regional Conference, Albany, NY, USA; 2019.

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- 6. Hochberg, NS. **Malnutrition and tuberculosis**. Providence/Boston CFAR TB/HIV Scientific Working Group TB Interest Group Round Table. Boston, MA, USA; 2019
- 7. Hochberg, NS. **The skinny on tuberculosis: Why malnutrition matters**. Infectious Diseases Grand Rounds. Presented at: Boston Medical Center. Boston MA, USA; 2019.
- 8. Hochberg NS. **Indo-U.S. TB cohort: Study design and preliminary results**. Presented at: TB Research Unit (TBRU) Investigators Meeting. Boston, MA, USA; September 2017.
- 9. Hochberg NS. **Updates in tuberculosis: The era of sea changes**. Medicine Grand Rounds. Presented at: Carney Hospital. Dorchester, MA. USA; March 2017.
- 10. Hochberg NS. Indo-U.S. **TB Cohort: Study design and preliminary results.** Invited speaker, JIPMER. February 8, 2017; Puducherry, India.
- 11. Hochberg NS. **Malnutrition and TB in India: Intersection and implications.** Presented at: Northeastern World TB Day Symposium. Boston, MA, USA. March 6–7, 2017.

#### PRESENTATIONS | ABSTRACTS

- 1. Kaipilyawar V. **Development and validation of a parsimonious TB gene signature using the digital NanoString nCounter platform.** Presented at Rutgers Data Operating & Maintenance Center Meeting. Jan 2022.
- 2. Kaipilyawar V. **Identification of a six-cytokine biosignature discriminating active TB from latent TB infection.** Presented at Rutgers NJMS Dept of Medicine Research Virtual Symposium. May 2021.
- 3. Kaipilyawar V, Zhao J, Joseph N, Sarkar S, Horsburgh CR, Hochberg NS, Ellner JJ, Johnson WE, and Salgame P. **Evaluating TB gene signatures using the digital NanoString nCounter platform.** Rutgers Graduate School Symposium. March 2021.
- 4. Kaipilyawar V, Zhao J, Joseph N, Sarkar S, Hochberg NS, Salgame P, Johnson WE, Ellner JJ. **Identification of a six-cytokine biosignature discriminating active TB from latent TB infection.** RePORT India 2021 Virtual Joint Leadership Meeting. February 2021.
- 5. Kaipilyawar V, Zhao J, Joseph N, Sarkar S, Hochberg NS, Salgame P, Johnson WE, Ellner JJ. **Identification of a six-cytokine biosignature discriminating active TB from latent TB infection.** Rutgers NJMS Dept of Medicine Research Virtual Symposium. February 2021.
- 6. Kaipilyawar V. **Malnutrition leads to distinct gene expression patterns in immune pathways and tuberculosis risk signatures in latent tuberculosis infection.** Presented at Rutgers Dept. of Oral Biology Seminar Series. February 2021.
- 7. Sinha P, Lönnroth K, Bhargava A, Sarkar S, Salgame P, Heysell SK, and Rudgard **W Food for thought:** *Undernutrition and Tuberculosis*. Symposium, 50<sup>th</sup> Union World Lung Health Conference, October 2020., Hyderabad, India.
- 8. Kaipilyawar V, Verma S, Stringari LL, Ellner JJ, Alland D, Dietze R, Rodrigues RR, Salgame P. **Innate** immune mechanisms of protection against Mycobacterium tuberculosis infection. RePORT India 2020 Joint Leadership Meeting. Mumbai, India; February 10-12, 2020.

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- 9. Kaipilyawar V. **Evaluating biosignatures to predict the risk of TB in latently infected individuals using the Nanostring Platform.** Presented at RePORT India 2020 Joint Leadership Meeting. Mumbai, India; February 10-12, 2020.
- 10. VanValkenburg A, Kaipilyawar V, Sarkar S, Lakshminarayanan S, Cintron C, Babu S, Knudsen S, Joseph N, Horsburgh CR, Babu P, Ellner J, Johnson WE, Salgame P, Hochberg NS. Malnutrition is associated with increased inflammation and increased tuberculosis risk signatures in individuals with latent Mycobacterium tuberculosis infection
- 11. Abilasha N, Bharath B, Priyanga J, Senbagavalli P, Prakash B, Vinod K, Subitha L, Roy G, Salgame P, Muthuraj M, Roy G, Sarkar S, Hochberg NS, Noyal J. **Effect of diabetes prevalence on circulating components of blood, disease severity and drug susceptibility in patients with pulmonary tuberculosis**. Presented at: 50th Union World Conference on Lung Health. Hyderabad, India. October 30–November 2, 2019.
- 12. Chua A, Mowry WB, Sahu S, Roy G, Ellner JJ, Horsburgh Jr CR, Pleskunas J, Sarkar S, Hochberg NS, Reddy D. Does the form of tobacco product used by smokers influence pulmonary tuberculosis severity? Presented at: ATS 2018. San Diego, CA, USA; May 18–23, 2018.
- 13. Abilasha N, Bharath B, Priyanga J, Senbagavalli P, Prakash B, Vinod K, Subitha L, Roy G, Salgame P, Muthuraj M, Roy G, Sarkar S, Hochberg NS, Noyal J. Effect of diabetes prevalence on circulating components of blood, disease severity and drug susceptibility in patients with pulmonary tuberculosis. Presented at: RePORT India 2018 Joint Leadership Meeting. Chennai, India; February 14-16, 2018.
- 14. Schenk NM, Sahu S, Roy G, Ellner JJ, Horsburgh Jr CR, Pleskunas J, Sarkar S, Hochberg NS, Reddy D. **Influence of type of tobacco product on chest X-ray findings in pulmonary tuberculosis patients in India**. Presented at: RePORT India 2018 Joint Leadership Meeting. Chennai, India; February 14-16, 2018.
- 15. Hoyt K. White L, Sarkar S, Pleskunas J, Zhou T, Noyal J, Muthuraj M, Vinod K, Roy G, Ellner JJ, Horsburgh Jr CR, Hochberg NS. **Effect of malnutrition on tuberculosis mycobacterial burden and chest radiographic findings**. Presented at: RePORT India 2018 Joint Leadership Meeting. Chennai, India: February 14-16, 2018.
- 16. Reddy D. **Wood fuel usage is associated with a higher leukocyte count in pulmonary tuberculosis patients**. Presented at: RePORT India 2018 Joint Leadership Meeting. Chennai, India; February 14-16, 2018.
- 17. Forsyth M. Alcohol use and clinical presentation of tuberculosis at time of diagnosis in Puducherry and Tamil Nadu, India. Presented at: RePORT India 2018 Joint Leadership Meeting. Chennai, India; February 14-16, 2018.
- 18. Johnson WE, Knudsen S, Hochberg N, Joseph N, Roy G, Sarkar S, Ellner J, Salgame P. **Optimizing** parsimonious gene signatures defining the spectrum of tuberculosis infection. Presented at: 48<sup>th</sup> Union World Conference on Lung Health. Hyderabad, India; October 2017.
- 19. Johnson WE. **Parsimonious gene signatures for TB outcomes**. Presented at: JIPMER. Pondicherry, India: November 2017.
- 20. Johnson WE. Addressing unwanted heterogeneity in genomic data: Applications in RNA-sequencing and prediction. Presented at: Department of Statistics, University of Connecticut. Storrs, CT, USA; November 2017.

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- 21. Svadzian A, Sahu A, Pleskunas JA, Sarkar S, Roy G, Ellner JJ, Hochberg NS, Reddy D. **Association** between wood fuel usage and disease severity among pulmonary tuberculosis cases. Presented at: American Society of Tropical Medicine & Hygiene Meeting. Atlanta, GA, USA; November 2016.
- **22. Stigma as a barrier to tuberculosis care: A literature review.** Presented at: Evans Department of Medicine Research Days, Boston University School of Medicine. Boston, MA, USA; October 2016.
- 23. Roy G, Sivaprakasam A, Kubiak R, Govindarajan S, Salgame P, Ellner J, Hochberg N, Sarkar S. **Description of new pulmonary tuberculosis cases in Southern India**. Presented at: Evans Department of Medicine Research Days, Boston University School of Medicine. Boston, MA, USA; October 2016.
- 24. Svadzian A, Sahu A, Pleskunas JA, Sarkar S, Roy G, Ellner JJ, Hochberg NS, Reddy D. **Association** between wood fuel usage and disease severity among pulmonary tuberculosis cases. Poster presented at: Evans Department of Medicine Research Days, Boston University School of Medicine. Boston, MA, USA; October 2016.
- **25. Conversion among pulmonary tuberculosis cases in India**. Presented at: Evans Department of Medicine Research Days, Boston University School of Medicine. Boston, MA, USA; October 2016.
- **26. Predictors of 2 month sputum conversion among tuberculosis patients in India**. Presented at: Evans Department of Medicine Research Days, Boston University School of Medicine. Boston, MA, USA: October 2016.
- **27. Prolonged cough among tuberculosis patients in Tamil Nadu and Pondicherry, India**. Presented at: Evans Department of Medicine Research Days, Boston University School of Medicine. Boston, MA, USA: October 2016.
- 28. Reddy D, Sahu S, Roy G, Ellner JJ, Horsburgh Jr CR, Pleskunas JA, Sarkar S, Hochberg NS. **Association between biomass fuel, tobacco use and two-month sputum smear conversion among pulmonary tuberculosis cases in India.** Presented at: American Thoracic Society Conference. San Francisco, CA, USA; May 2016.
- 29. Roy G, Sivaprakasam A, Kubiak R, Govindarajan S, Salgame P, Ellner J, Hochberg N, Sarkar S. **Description of new pulmonary tuberculosis cases in Southern India**. Presented at: 46th Union World Conference on Lung Health. Cape Town, South Africa; December 1–5, 2015.
- 30. Sarkar S, Fernandes P, Lakshminarayanan S, Kubiak R, Horsburgh CR, Ravikumar T, Ellner J, Hochberg N. **Age and gender distribution of latent tuberculosis infection cases in a household contact study**, India. Presented at: 46th Union World Conference on Lung Health. Cape Town, South Africa; December 1–5, 2015.
- 31. Reddy, D, Sahu S, McIntosh A, Kubiak R, Roy G, Ellner J, Sarkar S, Hochberg N. **Association between latent tuberculosis infection and indoor air pollution among household contacts of pulmonary tuberculosis cases**. Poster presented at: 46th Union World Conference on Lung Health of the International Union Against TB and Lung Disease. Cape Town, South Africa; December 1–5, 2015.

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- Arutselvi Devarajan, Satyavani Kumpatla, Mythili Dhanasekaran, Shruthi Basavaradhya Sahukar, Subash Babu, Hardy Kornfeld, Vijay Viswanathan. Glycaemic status in Screen Detected versus Known cases of DM TB patients and its effect on treatment outcomes - EDOTS Study from South India. Presented at 10<sup>th</sup> Annual meeting of RePORT India; Feb 9-11, 2021
- Vijay Viswanathan, Arutselvi Devarajan, Satyavani Kumpatla, Mythili Dhanasekaran, Subash Babu, Hardy Kornfeld. Having Prediabetes before the detection of TB: Does it have a negative influence?. Presented at American Diabetes Association (ADA) 80th Scientific Sessions June 12 - 16, 2020 (Chicago, IL - A Virtual Experience)
- 3. TB and diabetes from bench to bedside and back. Presented at: 2<sup>nd</sup> International Symposium on Frontiers in Biomedical Science of Infection Control Convergence Medical Research Center, MMRC. Chungnam National University. Daejeon, Korea; October 15, 2019.
- 4. Shruthi BS, Sivakumar S, Arutselvi D, Kumar NP, Babu S, Menon PA, Natarajan M, Sathyavani K, Kornfeld H, Viswanathan V. **Association of diabetes mellitus with INH monoresistance.** Presented at: RePORT India 2019 Joint Leadership Meeting. Chennai, India; February 4–6, 2019.
- 5. Kumar NP, Moideen K, Sivakumar S, Menon P, Viswanathan V, Kornfeld H, Babu S. **Altered circulating levels of eicosanoids in tuberculosis-diabetes co-morbidity and reversal upon standard tuberculosis treatment.** Presented at: Keystone Symposia -Tuberculosis: Mechanisms, Pathogenesis and Treatment. Banff, Alberta, Canada; January 17–21, 2019.
- 6. Kumar NP, Moideen K, Sivakumar S, Menon P, Viswanathan V, Kornfeld H, Babu S. **Elevated** circulating levels of monocyte activation markers among tuberculosis patients with diabetes comorbidity Presented at: IMMUNOCON 2018 45th Annual Meeting of Indian Immunology Society. TSHTI, Faridabad, India; November 1–3, 2018.
- 7. Kornfeld H. **AMP kinase activation as host-directed therapy for tuberculosis**. 49<sup>th</sup> Union World Conference on Lung Health. The Hague, Netherlands; October 23–26, 2018.
- 8. Kumar NP, Moideen K, Sivakumar S, Menon P, Viswanathan V, Kornfeld H, Babu S. **Effect of standard tuberculosis treatment on circulating levels of pro-inflammatory cytokines in tuberculosis-diabetes comorbidity**. Presented at Keystone Symposia -Tuberculosis: Translating Scientific Findings for Clinical and Public Health Impact. Whistler, BC, Canada; April 15–19, 2018.
- 9. Kornfeld H. **TB and diabetes from bench to bedside and back**. Presented at: American Thoracic Society International Conference ATS San Diego, CA, USA; March 22, 2018.
- 10. Kornfeld H. **Diabetic immunopathy and TB**. Presented at: TB Conference. The Union-North American Region, Chicago, IL, USA; March 3, 2018.
- 11. Kumar NP, Moideen K, Sivakumar S, Menon P, Viswanathan V, Kornfeld H, Babu S. **Effect of anti-tuberculosis treatment on the systemic levels of matrix metalloproteinases and tissue inhibitors of MMP in tuberculosis-diabetes comorbidity.** Presented at: 5th Global Forum on TB Vaccines. New Delhi, India; February 20–23, 2018.
- 12. Moideen K, Kumar NP, Bethunaickan R, Sivakumar S, Menon PA, Viswanathan V, Shruthi BS, Kornfeld H, Babu S. **Altered systemic levels of neutrophil and mast cell granular proteins in tuberculosis-diabetes comorbidity and changes following treatment**. Presented at: 5th Global Forum on TB Vaccines. New Delhi, India; February 20–23, 2018.
- 13. Shruthi BS. **Impact of metformin use on TB severity in diabetes.** Presented at: RePORT India 2018 Joint Leadership Meeting: Catalyzing Discoveries toward TB Elimination. Delhi, India; February 15, 2018.

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- 14. Moideen K. Effect of anti-tuberculosis treatment on the systemic levels of matrix metalloproteinases and tissue inhibitors of MMP in tuberculosis—diabetes comorbidity. Presented at: RePORT India 2018 Joint Leadership Meeting: Catalyzing Discoveries toward TB Elimination. Delhi, India; February 15, 2018.
- 15. Kumar NP. Effect of standard tuberculosis treatment on circulating levels of monocyte activation markers and RAGE ligands in tuberculosis-diabetes comorbidity. Presented at: RePORT India 2018 Joint Leadership Meeting: Catalyzing Discoveries toward TB Elimination. Delhi, India; February 15, 2018.
- 16. Shruthi BS. **Impact of metformin use on TB severity in diabetes.** Presented at: RePORT India 2018 Joint Leadership Meeting: Catalyzing Discoveries toward TB Elimination. Delhi, India; February 15, 2018.
- 17. Kornfeld H. **TB and diabetes from bench to bedside and back**. Presented at: Division of Infectious Disease, Boston University School of Medicine. Boston, MA, USA; January 25, 2018.
- 18. Kornfeld H. **TB and diabetes from bench to bedside and back**. Presented at: Division of Endocrinology, University of Massachusetts School of Medicine. Worcester, MA, USA; January 9, 2018.
- Kornfeld H. Clinical and immunological findings from the Effect of Diabetes on TB (EDOTS) study in India. Presented at: 48th Union World Conference on Lung Health. Guadalajara, Mexico; October 11– 14, 2017.
- 20. Kornfeld H. **Impact of diabetes and hyperlipidemia on host defense.** Presented at: 48<sup>th</sup> Union World Conference on Lung Health. Guadalajara, Mexico; October 11–14, 2017.
- 21. Kornfeld H. **Sugar, fat, and consumption**. Presented at: Infectious Diseases Grand Rounds, Perelman School of Medicine, University of Pennsylvania. Philadelphia, PA, USA; September 28, 2017.
- 22. Kornfeld H. **Intersection between TB & diabetes**. Presented at: New England TB Clinicians' Conference, University of Massachusetts Medical School. Worcester, MA, USA; May 11, 2017.
- 23. Kornfeld H. **Diabetic immunopathy and TB**. Presented at: Rollins School of Public Health, Emory University. Atlanta, GA, USA; April 20, 2017.
- 24. Kornfeld H. **Diabetic immunopathy & TB**. Presented at: Meakins-Christie Laboratories, McGill University. Montreal, Canada; April 10, 2017.
- 25. Kornfeld H. **Diabetic immunopathy and TB**. Presented at: National TB Conference. Atlanta, GA, USA; 21 April 2017.
- 26. Kornfeld H. **Tuberculosis and diabetes: From bench to bedside and back**. Presented at: Workshop on Integrated Care and Research for Tuberculosis, Diabetes, and HIV/AIDS: Challenges, Strategies, and Clinical Solutions. NIAID, International Union for Tuberculosis and Lung Disease, Bill and Melinda Gates Foundation. Liverpool, UK.; October 24, 2016.
- 27. Kornfeld H. **Diabetic immunopathy**. Presented at: Boston University School of Medicine Inflammation Symposium. Boston, MA, USA; May 23, 2016.
- 28. Kornfeld H. **Developing a comprehensive therapeutic research strategy for the converging epidemics of TB, T2DM, and HIV**. Co-Organizer and Speaker. NIAID Workshop. Rockville, MD, USA; May 10–11, 2016.
- 29. Kornfeld H. **Workshop on advancing TB research: TB, diabetes, and host-directed therapies**. Presented at: P.D. Hinduja Hospital. Mumbai, India; April 23–24, 2016.

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- 30. Kornfeld H. **The impact of Mycobacterium tuberculosis immune evasion on protective immunity: Implications for TB vaccine design**. Co-Organizer, NIAID TB Workshop. Rockville, MD, USA; March 7–8, 2016.
- 31. Kornfeld H. **Symposium on Tuberculosis Co-Morbidities & Immunopathogenesis**. Organizer and Speaker, Keystone, CO, USA; February 28–March 2, 2016.
- 32. Kornfeld H. **Sugar, fat, and consumption**. Presented at: Pulmonary Center, Boston University School of Medicine. Boston, MA, USA; January 16, 2016.
- 33. Kornfeld H. **Environmental epigenetics—Diabetes and tuberculosis**. Presented at: Joint Retreat for the Centres for Biodiscovery & Molecular Development of Therapeutics and Biosecurity and Tropical Infectious Diseases (Australian Institute of Tropical Health & Medicine). Port Townsend, Australia; September 22, 2015.
- 34. Kornfeld H. **Determinants of TB severity**. Presented at: Shenzhen-Hong Kong Institute of Infectious Diseases. Shenzhen, China; November 20, 2015.
- 35. Kornfeld H. **Tuberculosis: The rise of comorbidities**. Presented at: Medical Grand Rounds. University of Massachusetts Medical School. Worcester, MA, USA; June 4, 2015.
- 36. Kornfeld H. **TB and diabetes**. Presented at: Singapore Immunology Network. Singapore; February 27, 2015.
- 37. Kornfeld H. **Keystone Symposium on Granulomas in Infectious and Non-Infectious Disease: TB and Diabetes**. Invited speaker, Santa Fe, NM, USA; January 22–27, 2015.
- 38. Kornfeld H. **The effects of diabetes on the susceptibility**. Presented at: No.4 People's Hospital of Nanning, Nanning, China; January 12, 2015.
- 39. Kornfeld H. **Sugar, fat, and consumption**. Presented at: University of Texas, Health Science Center at Tyler, TX, USA; August 22, 2014.

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#### PRESENTATIONS | ABSTRACTS

- Prerna R. Arora, Rohan V. Lokhande, Prasad Naik1, Alpa J. Dherai1, Zarir F. Udwadia, Ashok A. Mahashur, Lancelot Pinto, Mullerpattan Jai, Ayesha Sunavala, Rajeev Soman, Camilla Rodrigues, Amita Gupta, Jeffrey A Tornheim, Neil Martinson, Ebrahim Variava, Lubbe Wiesner, Anton Joubert, Tester F. Ashavaid. Development & validation of plasma Bedaquiline levels presented at MSACL 2021, Virtual Meet
- 2. Ishita Gajjar, Jeffrey A. Tornheim, Nisha Kharat , Prerna R Arora, Namrata Sawant, Megha Karane, Samridhi Sharma, Lancelot Pinto, Jai Mullerpattan, Ashok Mahashur, Ayesha Sunavala, Camila Rodrigues, Tester F Ashavaid, Amita Gupta, Zarir F. Udwadia. Impact of Covid-19 lockdown on Mental Health of patients with Multi-Drug Resistant Tuberculosis in Tertiary Care Center, Mumbai. Presented at ACBM Academic Carnival; October 2, 2021, Virtual Meeting

- 3. Ishita Gajjar, Jeffrey A. Tornheim, Nisha Kharat , Prerna R Arora, Namrata Sawant, Megha Karane, Samridhi Sharma, Lancelot Pinto, Jai Mullerpattan, Ashok Mahashur, Ayesha Sunavala, Camila Rodrigues, Tester F Ashavaid, Amita Gupta, Zarir F. Udwadia. Impact of Covid-19 lockdown on Mental Health of patients with Multi-Drug Resistant Tuberculosis in Tertiary Care Center, Mumbai. Presented at 34thAnnual Research Day of P. D. Hinduja National Hospital & MRC, Mumbai, India; August 7, 2021, Virtual Meeting
- 4. Heeral Pandya, Prerna Arora, Nisha Kharat, Ishita Gajjar, Jeffery Tornheim, Sanjana Valecha, Zarir F. Udwadia, Lancelot Pinto, Ashok Mahashur, Amita Gupta, Camilla Rodrigues, Tester Ashavaid Comparison of Tuberculin Skin Test & QuantiFeron Tuberculosis Gold Plus in House-hold Contacts of Multi-Drug Resistant Tuberculosis Patients. Presented at 34th Annual Research Day of P. D. Hinduja National Hospital & MRC, Mumbai, India; August 7, 2021, Virtual Meeting
- 5. Heeral Pandya, Prerna Arora, Nisha Kharat, Ishita Gajjar, Jeffery Tornheim, Sanjana Valecha, Zarir F. Udwadia, Lancelot Pinto, Ashok Mahashur, Amita Gupta, Camilla Rodrigues, Tester Ashavaid Comparison of Tuberculin Skin Test & QuantiFeron Tuberculosis Gold Plus in House-hold Contacts of Multi-Drug Resistant Tuberculosis Patients. Presented at 2021 Global Tb Clinical and Educational Summit (Virtual Meeting) and awarded as the Best Poster.
- 6. Udwadia ZF. India's COVID response: The Good and The Bad. Presented at: COVID TB Webinar, RePORT India, on 27 July 2020.
- 7. Chawla PK, Keny Bhamini, Dherai AJ, Udwadia ZF, Mahashur AA, Pinto L, Soman R, Sunavala A, Mullerpattan J, Rodrigues C, Gupta A, Tornheim JA, Martison N, Ebraham V, Ashavaid TF. **Serum linezolid levels in MDRTB patients.** Abstract submitted at: RICC 2020, September 2020
- 8. Chawla PK, Naik PR, Lokhande RV, Dherai AJ, Udwadia ZF, Mahashur AA, Pinto L, Mullerpattan J, Sunavala A, Soman R, Rodrigues C, Gupta A, Tornheim JA, Martinson N, Variava E, Wiesner L, Joubert A, Ashavaid TF. **Development & validation of plasma Bedaquiline levels.** Presented at: 33<sup>rd</sup> Annual Research Day, P.D. Hinduja Hospital and MRC. Mumbai, India; June 30, 2020. (Awarded 1<sup>st</sup> Prize for Best Laboratory paper)
- 9. Naik PR, Chawla PK, Lokhande RV, Dherai AJ, Udwadia ZF, Mahashur AA, Pinto L, Mullerpattan J, Sunavala A, Soman R, Rodrigues C, Gupta A, Tornheim JA, Martinson N, Variava E, Wiesner L, Joubert A, Ashavaid TF. **Plasma moxifloxacin levels in Indian MDR-TB patients.** Presented at: 33<sup>rd</sup> Annual Research Day, P.D. Hinduja Hospital and MRC. Mumbai, India; June 30, 2020. (Awarded 2<sup>nd</sup> Prize for Best Laboratory paper)
- 10. Tornheim JA, Gajjar I, Shivakumar SVBY, Gupte AN, Gutpe N, Kishore G, Karane M, Rodrigues C, Gupta A, Udwadia ZF. Increased Moxifloxacin Dosing among MDR-TB Patients with Low-Level Resistance to Moxifloxacin did not Improve Treatment Outcomes in a Tertiary Care Center in Mumbai, India. Presented at: Johns Hopkins Department of Medicine Research Retreat. 28 February 2020. Baltimore, MD.
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