

RePCoRT

INDIA

COMMEMORATING

1 YEARS OF
TB RESEARCH



सत्यमेव जयते

DEPARTMENT OF BIOTECHNOLOGY
Ministry of Science & Technology
Government of India

2025 ANNUAL JOINT LEADERSHIP MEETING

HOSTED BY

**Bhagwan Mahavir Medication Research Centre (BMMRC)
and the Centre for Cellular & Molecular Biology**

Hyderabad, India

April 10-12, 2025

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Dr. Rajesh S. Gokhale
Secretary, Department of Biotechnology,
Director General, BRIC & Chairman BIRAC

“The knowledge gained and the capacities developed through this collaboration will continue to serve not only India and the U.S., but the broader global community in its fight against complex public health challenges!”

It is with great pride and a deep sense of purpose that I present this foreword on the Indo-U.S. Vaccine Action Program (VAP) and one of its most impactful initiatives, RePORT India. For nearly four decades, the Indo-U.S. VAP has stood as a shining example of bilateral cooperation between India and the United States—driving scientific progress and contributing meaningfully to global health. This unique partnership has fostered cutting-edge vaccine research, strengthened institutional linkages, nurtured scientific talent, and helped build a robust ecosystem for sustainable vaccine development.

Among its many contributions, RePORT India (Regional Prospective Observational Research for Tuberculosis) stands out as a flagship initiative. Launched in 2013, RePORT India has created a strong, multi-institutional platform for tuberculosis research. It has enabled the systematic and ethical collection of high-quality clinical data and specimens, and today, it is the largest among the six global RePORT consortia. RePORT India has become a cornerstone of India's TB research strategy—catalysing collaborations, enhancing research capacity, and generating critical insights that support the country's goal of eliminating TB.

In an era marked by emerging and re-emerging infectious diseases, the importance of initiatives like VAP has never been more evident. This program stands as a model of mutual respect, sustained commitment, and scientific excellence. I extend my heartfelt appreciation to all collaborators, researchers, institutions, and partners who have contributed to this remarkable journey.

I hope this document not only reflects our shared achievements but also serves as an inspiration for future endeavours that harness science and technology for the advancement of global public health.





Dr. Jyoti M Logani
Scientist F, DBT



Dr. Peter Kim
Director of Therapeutics
Research Program, DAIDS/NIH



Dr. Fatima Jones,
Chief of Laboratory & Clinical
Sciences Branch, NIH

RePORT India has made significant strides in tuberculosis (TB) research since its establishment in 2013 under the Indo-U.S. Vaccine Action Program. As the largest among six regional consortia—including China, Brazil, Indonesia, the Philippines, and South Africa—RePORT India has focused on several key areas:

Establishment of a Central Biorepository: A pivotal achievement of RePORT India is the creation of a Central Biorepository at the National Institute of Research in Tuberculosis (NIRT) in Chennai and manages biological specimens, providing invaluable resources for TB research.

Development of Common Protocols: The RePORT India consortium has successfully developed standardized protocols to streamline and unify tuberculosis (TB) research efforts across the country. The Phase I Common Protocol was designed to generate high-quality data and biological specimens to enhance understanding of the prognosis of TB disease and the biological mechanisms underlying progression from TB exposure to active disease. Building on this foundation, Phase II emphasizes leveraging the archived Phase I samples to pursue focused and impactful TB science. This phase includes the addition of new clinical research sites at PGIMER Chandigarh and NEIGRIHMS Shillong, and introduces a novel Presumptive TB Cohort, further expanding the scientific reach and relevance of the RePORT India platform

Contributions to Vaccine and Diagnostic Development: RePORT India has supported the advancement of new TB vaccines and diagnostics including the VPM 1002 trial.

Strengthening Research Capacity and Collaboration: By fostering collaborations among Indian and international researchers, RePORT India has bolstered TB research capacity and infrastructure within the country. This collaborative approach has facilitated the sharing of knowledge, resources, and best practices, contributing to more effective TB research and control strategies.

Our program officers remain committed to supporting and advancing this critical scientific mission, ensuring that the consortium continues to serve as a model for international collaboration in TB research.

Dr. Sonali Sarker
JIPMER, EC Chair, India

TB has remained a challenge for the medical community, India being one of the worst affected. RePORT India was a giant leap in collaborative research, an amalgamation of knowledge, experience and expertise of the US and Indian investigators from reputed institutions to facilitate the understanding of various aspects of this complex disease. Aligning with the national goals, RePORT India is helping find answers to questions which have implications on the control of TB in India, and also globally.

A decade-long journey has witnessed many challenges and also proven that perseverance is essential to sustain the scientific temperament needed to match the tenacity and irresoluteness of this dreaded disease. We are indebted to the team from DBT and NIAID, NIH, which conceived the idea of RePORT India and to those who made it happen including the Chairs at its inception Drs. Jerrold Ellner and Sowmya Swaminathan. I take this opportunity to thank all the PIs and staff at the sites, who made RePORT India what it is today. Finally the TB patients community, which allows and supports our research activities despite their suffering. We hope to bring changes in their lives through our research.



“This programme has strengthened the capacity for research, positioning India as one of the leading knowledge hubs on TB.”

Dr. Amita Gupta
Johns Hopkins University, EC Chair, US

In 2010, when I joined the NIH/NIAID delegation to India to meet with leading investigators and institutions to explore TB collaborations, I was 7 months pregnant and had no idea what would transpire thereafter. Low and behold it was the birth of RePORT India, now an incredible, bilaterally-funded consortium dedicated to studying disease diagnosis, outcomes, transmission, and responses to exposure in the Indian setting. Now celebrating our 10th year, we have invested in strengthening early stage and mid-stage investigators in India and in the US, and have significantly strengthened the research infrastructure among 9 clinical sites throughout India and 6 US institutions.



“What I am most proud of are the incredible people who have come together to create a real research family and community that is RePORT India. Our 10 year journey has so much to be proud of, and our best days ahead of us!”

Together, we have built incredible capacity for high quality cohorts of people with TB and their household contacts and a central repository housing >500,000 samples, published more than 200 papers, some of which have changed India and WHO policies such as for TB preventive therapy and nutrition guidelines for people living with TB, and garnered more than 30 grant awards totaling more than ₹26,117,900 (\$30 million USD).



Dr. Vijaya Valluri
BMMRC, EC Co-Chair, India

On behalf of the Executive Committee, it is my privilege to welcome you to the *14th Annual RePORT India Meeting*. This gathering represents a cornerstone of collaboration and innovation in advancing Tuberculosis research and public health not only in India but also internationally. Over the years, *RePORT India* has grown into a pulsating platform for fostering partnerships, sharing scientific breakthroughs, and driving impactful solutions.

“The work of RePORT India exemplifies the power of collaboration in transforming research into real-world impact.”

The theme of this year's meeting “Progress towards ending TB – Contributions from RePORT India” underscores our collective commitment to addressing the challenges posed by tuberculosis through cutting-edge research and multidisciplinary approaches. We are proud to host a diverse group of experts, researchers, and policymakers who bring unparalleled dedication and expertise to this mission. Our scientific aims, sample banks, publications and contributions to policy making are ineluctable indicators of our hard work, effort and unparalleled vision. As we reflect on the progress made, we also acknowledge the road ahead. The work of RePORT India exemplifies the power of collaboration in transforming research into real-world impact. Together, let us continue to push boundaries, inspire innovation, and strengthen our resolve to combat tuberculosis.

We extend our heartfelt gratitude to all participants, sponsors, and partners for their unwavering support. Your contributions are invaluable in shaping the future of TB research and care. This year's scientific line-up as always, is better than ever and we look forward to an engaging and fruitful meeting.



Dr. Padmini Salgame
Rutgers University, EC Co-Chair, U.S.

In the last 10 years, RePORT India has built a strong partnership with a large group of scientists from India and the United States to advance TB research to end the global TB epidemic. A 10th year anniversary is no small accomplishment for such a large multi-institutional consortium!

“RePORT India has witnessed a decade of outstanding research, amazing collaborations, and unwavering dedication—a well-deserved congratulations to our incredibly amazing team on reaching our 10th anniversary!”

We should be immensely proud of the impactful contributions we have made together in tuberculosis research. RePORT India has also played an immense role in nurturing and training the next generation of scientists dedicated to TB research. I am excited for the ground-breaking discoveries they will make in the coming decade to make “ending TB” a reality. I am honored to have been part of RePORT India right from its inception. It has been a pleasure to have shared this inspiring, challenging, exciting and fun-filled 10-year journey with all its twists and turns with my vast RePORT India family! I look forward to continuing this journey together and wish the RePORT India team continued success and many more achievements.

Dr. Jerrold Ellner Rutgers University

As a career TB investigator, I always hoped to conduct collaborative research in India because of the disease burden and the chance to study comorbidities. The opportunity arose when the NIH and DBT issued a joint request for proposals. The choice of JIPMER as a collaborative site occurred through serendipity. At a rare Sunday meeting I met Dr. Ganguly, then president of JIPMER who embraced the idea of a collaboration. Through him, I met Dr. Ravikumar, the Director-designate of JIPMER and through "Ravi", Drs. Guatham Roy and Sonali Sakar. After several phone calls, I invited Sonali to Boston to work on the grant proposal. We had the necessary ingredients for a collaboration, funding and outstanding collaborators, good ideas and most of all determination. There was skepticism at first because the critical infrastructure for clinical and translational research had to be reinforced JIPMER. But we prevailed. And Sonali now is Chair of RePORT India, and JIPMER is the site of the administrative and data hubs. I want to thank my collaborators at JIPMER and in the US (Padmini Salgame, Natasha Hochberg, and Rachel Kubiak) and the support of NIH program (Peter Kim and Sudha Srinivasan). I had the honor of serving as the first US Chair of RePORT India. We agreed to a term limit of 2-years. There was a peaceful transition and I stepped aside.



“India is the 'crown jewel' of RePORT International.”

By all objective criteria RePORT India has become a force in global research on tuberculosis—the publications, the biorepository, the related research funding and the training. RePORT India has unlimited potential as long as governmental interest and funding continues. Of course this is not a given. On the other hand, the requirement for funding can drive academic excellence.

In my view, RePORT India must have greater communication and collaboration with leading basic scientists in India (and the US) and with governmental programs. Given the dire public health threat of TB, RePORT India must do more than observational research; the addition of implantation science and of diagnostic studies will be key and, in itself, assist in the collaboration with programme. We also need more sentinel publications and, of course, sustained funding. We need to be proactive in developing collaborations that utilize existing data and specimens.

I currently serve as Director of the RePORT International Coordinating Center. India is the "crown jewel" of RePORT International. It was the first RePORT network and arguably the most productive (of course there was a head-start). I am thankful that Sonali is Co-Chair of the Executive Committee of RePORT International. The overlap in leadership assures coordination of activities.

To close, "Never underestimate the power of a small group of committed people to change the world. In fact, it is the only thing that ever has." Margaret Mead. RePORT India has succeeded in part because of the small group of committed people with good ideas. Let's keep it up!



Apurva Sarin, PhD

Professor Apurva Sarin is the Chief Executive Officer of the DBT-Wellcome Trust India Alliance, bringing over 25 years of leadership experience in scientific research and institutional management. Prior to this role, she served as Senior Professor and Dean of Faculty at the DBT Institute for Stem Cell Science & Regenerative Medicine (inStem), Bengaluru and was appointed its Director in 2019. Her

“RePORT India harnesses the power of collaboration and shared expertise to advance the prevention, diagnosis, and treatment of TB, underpinning the urgency to accelerate innovation, and bring us closer to a world free of tuberculosis.”

research has focused on the regulation of immune homeostasis in health and disease. She led a laboratory at the National Centre for Biological Sciences (NCBS), Tata Institute of Fundamental Research (TIFR), Bengaluru (1998-2015), before continuing this work at inStem.

Professor Sarin holds a Master's degree in zoology from the University of Delhi and a PhD from Jawaharlal Nehru University, New Delhi. Following postdoctoral training at the Experimental Immunology Branch of the National Cancer

Institute, NIH, USA, she began her independent research career at NCBS in 1998. Her contributions to biosciences have been recognized by the DBT National Bioscience Award for Career Development (2005-06). Her research was supported by the Wellcome Trust, UK (Senior Research Fellowship, 2002-2007), the Department of Science & Technology (Swarnajayanti Fellowship in Biology, 2002-2007), the Department of Science & Technology (Swarnajayanti Fellowship in Biology, 2003-2008), and the Department of Biotechnology (Centre of Excellence Award, 2015-2022) amongst others. Professor Sarin is a Fellow of the Indian Academy of Sciences, Bengaluru, and has represented India on the Council of Scientists and the Board of Trustees of the Human Frontier Science Program



Robert Modlin, MD

Robert Modlin is the Klein Professor of Dermatology, Professor of Microbiology, Immunology, and Molecular Genetics at UCLA. He served as the Chief of the Division of Dermatology and Vice Chair for Cutaneous Medicine and Dermatologic Research in the Department of Medicine for 25 years. Dr. Modlin's interest in leprosy began during his dermatology residency at the Los Angeles County/ University of Southern California Medical Center. The research in the Modlin lab is centered on the study of leprosy and tuberculosis as models to learn about mechanisms of host

defense in humans. As such, Dr. Modlin's laboratory has made fundamental insights into T cell subsets, cytokine patterns, antigen presentation, innate immunity and antimicrobial mechanisms in the human immune response to infection. Key discoveries include the role of Th1/Th2 cytokines in disease outcomes in humans, identification of structurally defined nonpeptide antigens presented by CD1 to T cells, identification of granulysin as mediating CD8+ T cell antimicrobial activity, identification of the first ligands for Toll-like receptor 2, and elucidating the role for vitamin D in human antimicrobial responses.

Dr. Modlin has published more than 200 articles, including 14 papers in *Science* and *Nature*, and 6 in *Nature Medicine*. He completed his undergraduate studies at Johns Hopkins University, received his medical degree at the New York University School of Medicine, was a pediatrics intern at NYU, and a dermatology resident at Los Angeles County/University of Southern California School of Medicine

Dr. Soumya Swaminathan

Dr. Soumya Swaminathan is an esteemed Indian pediatrician and clinical scientist renowned for her extensive research on tuberculosis and HIV. Born on May 2, 1959, in Chennai, India, she is the daughter of Dr. M.S. Swaminathan, celebrated as the "Father of the Green Revolution in India," and educationalist Mina Swaminathan. Dr. Swaminathan earned her M.B.B.S. from the Armed Forces Medical College in Pune and an M.D. in Pediatrics from the All India Institute of Medical Sciences in New Delhi. She further honed her expertise with a post-doctoral fellowship in neonatology and pediatric pulmonology at the Children's Hospital Los Angeles. Throughout her illustrious career spanning over four decades, Dr. Swaminathan has been pivotal in bridging scientific research and policy implementation. She served as the Director General of the Indian Council of Medical Research (ICMR) from 2015 to 2017, where she played a crucial role in advancing medical research in India. In 2017, she joined the World Health Organization (WHO) as Deputy Director-General for Programmes and was later appointed as the organization's first Chief Scientist in 2019. In this capacity, Dr. Swaminathan was instrumental in leading global scientific efforts during the COVID-19 pandemic. After her tenure at WHO, she assumed the role of Chairperson at the M.S. Swaminathan Research Foundation in February 2023, continuing her dedication to research and development in agriculture and health. Dr. Swaminathan's unwavering commitment to public health and her significant contributions to medical science have solidified her reputation as a leading figure in global health.



“The Report consortium and collaboration has advanced our understanding of TB pathogenesis, treatment and prevention. We should build on the bio repository and clinical databases to further our understanding of the risk factors for disease progression and outcomes, through international collaborative studies. It's a good example of multidisciplinary and cross border collaboration and should be strengthened so that global TB elimination goals can be achieved.”



Dr. Anurag Bhargava

Anurag Bhargava is a Professor in the Department of Medicine at Yenepoya Medical College, Mangalore, Karnataka, and an Adjunct Professor in the Department of Medicine at McGill University. He is a clinician-researcher with extensive experience in delivering healthcare across all levels of care in India, including working in the underserved areas in Central India, where he ran an award-winning patient-centered TB treatment program for a decade.

“In a decade alone, the RePORT India Consortium has grown in scope and stature in the landscape of TB research in India. The work of its outstanding and committed investigators is playing an important role in addressing the knowledge gaps in epidemiology, basic science, and clinical aspects of TB infection, active disease, and its outcomes in India. These should inform the development of improved strategies and interventions for TB prevention and TB care in India, and globally.”

He coordinated the development of the National TB Elimination Programme's (NTEP's) Guidance Document on Nutritional Care and Support that led to the launch of the direct benefit transfer scheme to all patients with tuberculosis in India in 2018, which has resulted in improved outcomes in patients with TB. Dr. Bhargava was the Principal Investigator of the RATIONS, a field-based cluster-randomized trial conducted in 2800 households affected by TB in Jharkhand. The nutritional supplementation with an inexpensive food basket and micronutrients resulted in a nearly 50% reduction in the incidence of lung TB in TB household members with an index person with microbiologically confirmed TB, as well as improved outcomes in persons with TB. The Lancet, in its 200th anniversary issue, mentioned the RATIONS trial as one of the key events in its publication history. Dr. Bhargava is a member of the WHO Strategic Technical Advisory Group for TB (STAG-TB) at regional and global levels. He was awarded the inaugural Dr. K.V. Desikan Memorial Award by the LEPRAS Society and the Dr. P.R.J. Gangadharam Endowment Award 2021, awarded by the Mahatma Gandhi Institute of Medical Sciences and Kasturba Health Society, Sevagram, Wardha for his lifetime contributions to TB control in India.

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)
- Prof. M. Viswanathan Diabetes Research Centre (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
- St. Louis University School of Medicine (SLU)
- University of California—San Francisco (UCSF)
- University of Massachusetts (UMass)

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 Science and Education (IISER), Pune, 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

SPONSORS

Department of Biotechnology, Government of India
National Institute of Allergy and Infectious Diseases, United States
Indo-US Vaccine Action Program

This conference is supported by Department of Biotechnology, Government of India, and the U.S. NIH administered through CRDF Global. The views expressed in written conference materials or publications and by speakers and moderators do not necessarily reflect the official policies of the Government of India or the Department of Health and Human Services, nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. or Indian Government.



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RePCORT

INDIA

OVERVIEW

1 YEARS OF
TB RESEARCH

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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 1 – 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 1 – 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 1 – 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

BMMRC & SLU

- **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, St Louis University School of Medicine, St. Louis, MO, 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. PIs:** 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. PIs:** 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

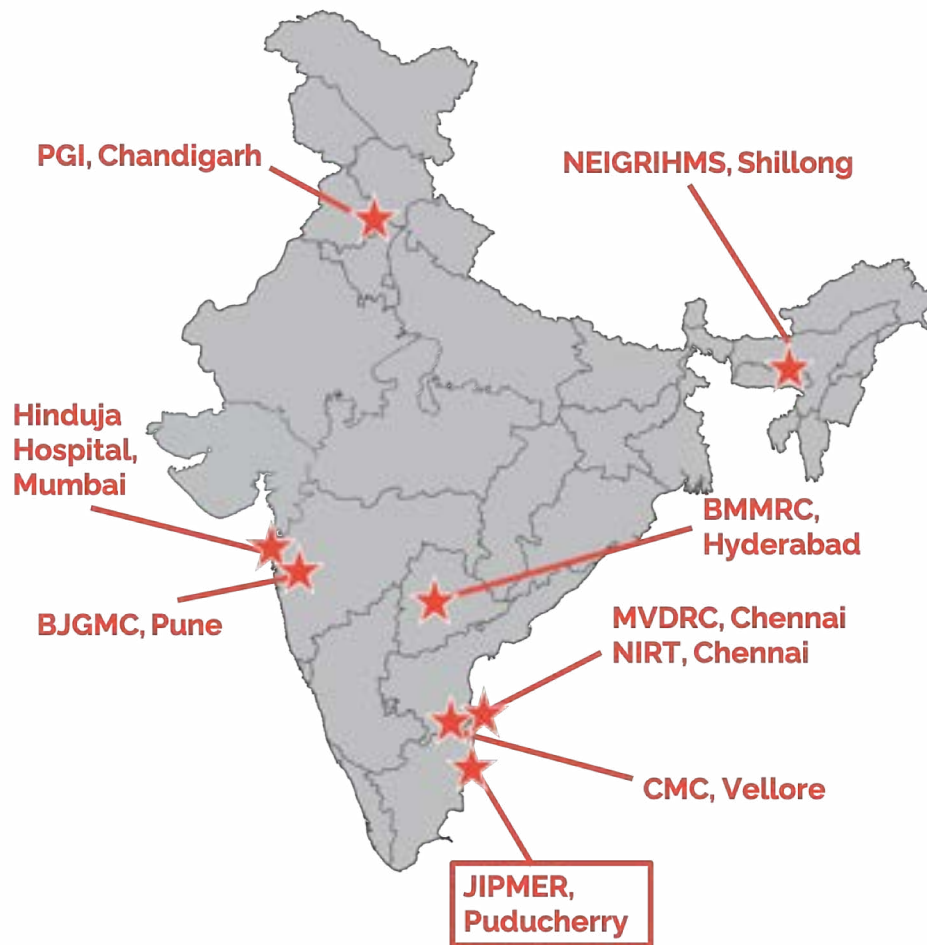
MVDRC, NIRT-ICER, & UMass

- **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)

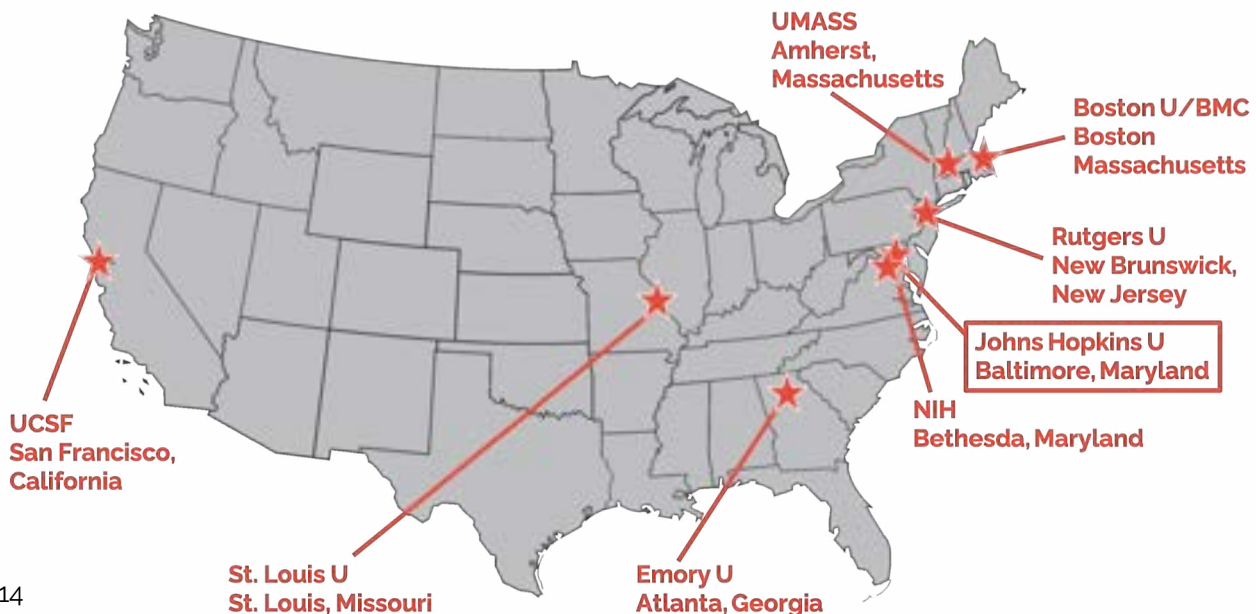
Phase 2 – Common Protocol

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 outside the 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.

RePORT India Phase 2



Under a Phase 2 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 1 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 2 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.



Phase 2 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 (BU)

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 (SLU)

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.



SITE UPDATES



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VISION

The Christian Medical College, Vellore seeks to be a witness to the healing ministry of Christ, through excellence in education, service, and research.

MISSION

The primary concern of the Christian Medical College, Vellore, is to develop through education and training, compassionate, professionally excellent, ethically sound individuals who will go out as servant-leaders of health teams and healing communities. Their service may be in promotive, preventive, curative, rehabilitative, or palliative aspects of healthcare, in education, or in research.

ABOUT THE INSTITUTION & CAMPUS

Christian Medical College (CMC) is a leading medical training institution in India whose clinical network includes primary, secondary, and tertiary care clinics and hospitals in and around Vellore. Founded in 1900 by an American missionary, Dr. Ida S. Scudder, CMC provides care to over 2,800 inpatients and 8,300 outpatients daily across 67 inpatient wards and 92 clinics. Christian Medical College is also a leading medical research institution, publishing over 400 research articles in peer-reviewed journals each year, making it the second-largest medical research institution in India. The largest expansion of CMC, is the Ranipet Campus featuring Level 1 trauma care and multi-specialty facilities.

RESEARCH FOCUS AREAS

1. Host determinants in the eicosanoid pathway in PTB & TBM (RePORT India)
2. Rapid Research in Diagnostics Development for TB (R2D2 TB)
3. Airway injury risk mechanisms and IL-6 (AIR-MAIL)
4. TB Diagnostics : Aptamer based assays, CAD validation, multiplexed POC tests (GCC-Bill Gates funded), validation of TruNat, XPERT ULTRA Extrapulmonary TB and Pediatric TB
5. Clinical Trials for TB Vaccines (VPM1002 and INDIGO (H2020))

PARENT PROTOCOL

TB Meningitis Protocol: Prospective, observational cohort of persons with TB meningitis treated with standard of care anti-TB drugs and adjunctive corticosteroids.

PULMONARY TB PROTOCOL

Prospective, observational cohort of persons with smear-positive pulmonary TB treated with standard of care anti-TB drugs.

RePORT INDIA STUDIES

1. CAD Validation for Pulmonary TB
2. PET Scan for Extra-cranial TB Meningitis
3. PPD TST Antigen Solutions for Latent TB
4. Xpert PCR ULTRA for Pleural TB
5. POCUS Study for TB Diagnosis
6. R2D2 TB Network



CMC Campus
Vellore



Dr. DJ Christopher, MBBS, DTCD
Professor of Pulmonary Medicine



Dr. Balamugesh T, MBBS, MD, DM
Professor and Head of Pulmonary Medicine



CMC Team

CMC Lab





Dr. Aditya Cattamanchi

Professor and Chief of the Division of Pulmonary Diseases & Critical Care Medicine at UC Irvine



Dr. Akshay Gupte

Assistant Professor
Boston University School of Public Health



UCSF Team



CMC Repository

RiCC FUNDED STUDIES

1. AIR-MAIL Study: IL-6 and airway injury mechanisms
2. Long TB: Long-term cardiac and pulmonary consequences of TB

PERSONNEL TRAINING

- Regulatory & Clinical Training: HSP, GCP, GCLP, Common Protocol Training, Laboratory Training
- Technical Training: BD MGIT Culture, DST Training, PBMC Training, GeneXpert Training
- Lung Health Training: Includes spirometry, 6 minutes' walk test and related techniques; the site also trains others in lung health management

KEY ACHIEVEMENTS

CMC has been at the forefront of tuberculosis diagnostics, playing a key role in validating a variety of point-of-care molecular tests. This has increased substantially in collaboration with University of California, San Francisco (UCSF), USA. CMC is part of NIH U01-funded R2D2 TB Network, with Dr. D. J. Christopher serving on the steering committee. CMC's key contributions include:

INFRASTRUCTURE DEVELOPMENT

Pulmonary Medicine Research Lab Equipment:

- Cepheid GeneXpert System XVI for rapid TB detection.
- 10-color Xpert MTB/XDR assay on the Ranipet campus for detecting drug-resistant TB.
- Adequate storage with multiple -20°C and -80°C freezers for study sample preservation.

Computers, Filing, Backup & Office Infrastructure:

- CHIPS (Computerized Hospital Information System) for seamless data management.
- Dedicated filing and archiving systems for research documentation.

CMC continues to expand its research, diagnostics, and infrastructure to improve TB care and outcomes nationally and globally.

IMPACT & RECOGNITION

RePORT India in News

Dr. D. J. Christopher, led a landmark study that identified long-term lung function impairment and persistent symptoms among a significant proportion of Indians recovering from COVID-19. The study also highlighted a higher prevalence of comorbidities such as diabetes and hypertension in Indian subjects compared to their Chinese and European

counterparts. These findings provided crucial insights into post-COVID recovery and contributed to improved clinical management strategies in India.

CMC collaborates with University of California San Francisco

The UCSF Center for Tuberculosis, part of the Institute for Global Health Sciences, aims to improve TB patient outcomes through research, training, and policy advancements. In collaboration with CMC Vellore and global partners,

RePORT diagnostic studies, conducted in partnership with CMC Vellore and global sites, have led to 20 abstract presentations at Union conferences (2022–2024). The main study has screened over 11,000 participants and enrolled more than 8,000 across five sites, including 1,477 in India. Research includes evaluations of novel TB tests, AI-driven diagnostics, and patient preferences and findings have been published in journals like *Lancet Global Health* and *Clinical Infectious Diseases*.

MISSION & VISION

Providing the required infrastructure as a central facility dedicated to TB research

Fostering multidisciplinary collaboration across all aspects of TB research to strengthen TC clinical research in India

ABOUT THE INSTITUTION & CAMPUS

JIPMER can trace its origins to the 'Ecole de Medicine de Pondicherry' established by the French Government in 1823. JIPMER became an institution of national importance under the Ministry of Health and Family Welfare, in 2008 and spreads over 192 acres. The model of providing free specialty health care while maintaining quality and safety makes JIPMER a unique model in the country. JIPMER has expansion in Karaikkal and Yanam, regions in the UT of Puducherry and conceptual plans for Puducherry second campus is ongoing.

JIPMER has been part of RePORT India since 2014 and an active member of RePORT International, collaborating across seven countries on tuberculosis (TB) research. The multidisciplinary team—comprising clinicians, microbiologists, pharmacologists, pulmonologists, epidemiologists, and immunologists—has contributed significantly to community-based studies, molecular research, basic science, and epidemiology. JIPMER collaborates with national and international institutions such as AIIMS, IGIB, FMR, NII, CCMB, ICGEB, NITRD, Rutgers University, and Boston Medical Center. Partnerships with the State TB Health System facilitate community-based enrollments through Government Community Centers, Primary Health Centers, and Community Clinics.

RESEARCH FOCUS AREAS

Epidemiological & Community-Based Studies, TB Biomarkers & Host Response Studies, Clinical & Translational Research and Advanced Laboratory & Data Science and the impact of Nutrition and parasitic infection in TB disease.

PARENT PROTOCOL

The study on Biomarkers for Risk of TB and for TB Treatment Failure and Relapse is a collaborative effort between researchers in India and the U.S., led by Drs. Gautam Roy and Sonali Sarkar (JIPMER) and Drs. Jerrold Ellner, Padmini Salgame (Rutgers), Robert Horsburgh, and Natasha Hochberg (Boston).

RePORT INDIA STUDIES

- Impact of Pregnancy on Tuberculosis,
- Role of Iron Deficiency in Resistance of Women of Child-Bearing Age to Tuberculosis
- Comparison of PPD Tuberculin Skin Test Antigen Solutions in Detecting Latent TB
- Host and Microbiome Transcriptional Profiling in Upper Airways for TB Susceptibility
- Mycobacterium Tuberculosis Mediated Host Metabolomics & Disease Severity Correlation
- RePORT India Phase II Common Protocol



JIPMER Campus
Puducherry



Dr. Sonali Sarkar, MBBS, MD
Professor & Principal Investigator
RePORT India Chair



Dr. Senbagavalli Prakash Babu, Ph.D.
RePORT India Program Manager



Komala Ezhumalai, M.Sc., M.phil
RePORT India Data Manager

- Whole Genome Sequencing of MTB Clinical Strains for Drug Resistance & Strain Lineage
- Predictors of Resistance Emergence in Multidrug-Resistant TB Patients (PREEMPT)- JIPMER & BU
- TB Learning Impact of Nutrition (TB-LION) – JIPMER & BMC
- TB Learning Effect of Parasites & Reinforcing Diets (TB-LEOPARD) – JIPMER & BMC
- Nutritional Interventions to End Tuberculosis (TB) among persons with HIV in India (Ko1Al167733-01 AI) – JIPMER & BMC

RiCC FUNDED STUDIES

- Dynamics and Immune Mechanisms of QFN Response in Close Contacts of TB Cases - study of protective immune mechanisms in the context of the dynamics of IGRA conversion and reversion - at JIPMER, BJGMC, Johns Hopkins University and Rutgers University.
- Impact of latent TB infection and trained immunity on susceptibility to SARS-CoV2 infection in India and the Philippines - Addresses the questions of whether latent TB infection is associated with decreased risk of acquisition of SARS-CoV2 infection, and if acquired a decreased risk of severe COVID-19 disease manifestations - at JIPMER, the University of the Philippines - Manila and Rutgers University.
- Epidemiologic factors associated with TB treatment outcomes across RePORT International consortia - Data harmonized across five countries, including sites at BJGMC and JIPMER on co-morbidities and other factors related to TB treatment success - at JIPMER, BJGMC, Johns Hopkins, Vanderbilt University and Rutgers University.
- Analysis of Host Biomarkers Associated with Adverse TB Treatment Outcomes Across RePORT International Sites - Expand the validation studies of host biomarkers associated with TB treatment failure proposed at several RePORT International Consortia (India, South Africa, Brazil, the Philippines and Indonesia) - University of Cape Town, FioCRUZ and Rutgers University.
- TB - RiCC 3.0 - Data harmonized across five countries, advancing global TB research through innovative data approaches and capacity-building to refine insights into TB progression and co-morbidities.
- Prevalence, Incidence, and Biomarkers of Subclinical Tuberculosis (TB) in Close TB Contacts in the RePORT International Consortium - A two-phase study leveraging prospective and retrospective samples from RePORT sites to investigate SCTB cases and household contacts.

ACHIEVEMENTS & DEVELOPMENT

JIPMER joined RePORT India in 2013 and has expanded from four staff members to 59 researchers by 2024, overseeing nine Clinical Research Sites (CRS) as the Coordinating Hub and Data Coordinating Center for RePORT India Phases I & II.

PERSONNEL TRAINING

- Ethics & Regulatory Training: HSP, GCP, GCLP.
- RePORT India-Specific Training: Common Protocol Training, Laboratory Training.
- Clinical & Laboratory Skills: BD MGIT Culture, DST Training, PBMC Training, GeneXpert Training.



JIPMER CRS is fortunate to collaborate with two US Institutes: the Rutgers New Jersey Medical School and Boston University School of Medicine

KEY ACHIEVEMENTS

- NIH-RICC funded 'Junior Investigator Program' to Dr Prakash Babu, receiving in-person training in Brazil and South Africa
- Awardee of TB-RICC Laboratory Enhancement and Capacity Building and has Seahorse, 10X genomics chromium controller, electroporator, thermal cycler, luminometer, nanodrop, incubators and centrifuges.
- Obtained CRDF grant for building sample storage capacity at RePORT India CRS
- NIH-RICC funded 'Junior Investigator Program' to obtain in-person training in Brazil and South Africa
- Understanding Mycobacterium tuberculosis mediated host metabolomics in pulmonary tuberculosis: correlation with disease severity and treatment course.' – PEER Women Mentorship award to Dr Senbagavalli Prakash Babu by, NIAID, USA

LABORATORY FACILITIES

JIPMER's Research Lab for Tuberculosis (RLTB) is a state-of-the-art 1,800 sq. ft. facility with NIH-funded enhancements. Key features include:

- BSL-2 & BSL-3 Facilities: Plasma, serum, PBMC isolation, IGRA testing, MTB culture, strain identification.
- Advanced Equipment: Bio-safety cabinets, -80°C deep freezers, ELISA readers, spectrofluorometer, qPCR.
- Specialized Research Tools: 10X Genomics Controller, Seahorse Agilent Metabolomics Analyzer.
- Collaborations in EQA Programs: PBMC-EQA (NIRT), Quantiferon EQA (CAP), Parasitology (WSLH Proficiency Testing), Sputum (p-Smile).

ACHIEVEMENTS IN TRANSLATIONAL TB RESEARCH

JIPMER's research has contributed significantly to TB diagnosis, treatment, and prevention:

- Gene Signatures for TB Diagnosis & Treatment Monitoring (Published in Tuberculosis, 2018).
- Impact of Co-Morbidities on TB Treatment Outcomes (Transcriptome risk profiling study ongoing).
- Cost-Effective Diagnostic Approaches: TST-positive & negative sample analysis at Rutgers.
- TB & Pregnancy Study: 29 pregnant TB index cases and 82 non-pregnant index cases enrolled.
- Malnutrition & TB Susceptibility Study: 266 index cases analyzed; samples shipped for immunological assays.
- VPM1002 TB Vaccine Trial: Phase IIb completed with high participant retention rates.

PUBLICATIONS

JIPMER along Rutgers and BU team has contributed to 36 publications since 2014. A key publication includes:

Leong S, Zhao Y, Joseph NM, Hochberg NS, Sarkar S, Pleskunas J, Hom D, Lakshminarayanan S, Horsburgh CR Jr, Roy G, Ellner JJ, Johnson WE, Salgame P. Tuberculosis (Edinb). **Existing blood transcriptional classifiers accurately discriminate active tuberculosis from latent infection in individuals from south India.** 2018 Mar;109:41-51. doi: 10.1016/j.tube.2018.01.002. Epub 2018 Jan 31. PMID: 29559120.

This publication is highlighted because of the sentinel observation that transcriptional signatures for tuberculosis discovered in Africa perform well in India. Subsequent publications describe the development of the TB signature profiler and a parsimonious optimized signature of TB in South India.





Jerrold J. Ellner trained in Medicine, Infectious Diseases, and Immunology at Johns Hopkins and the NIH. He held faculty positions at Case Western Reserve and Boston University and is now a Professor of Medicine at Rutgers New Jersey Medical School. His research focuses on TB's natural history, immunopathogenesis, and host biomarkers. He collaborates on TB studies using immunology, microbiology, and virology (for TB-HIV) within clinical and epidemiologic frameworks. He has led multiple NIH-funded global research programs and currently directs the TB Research Unit and FEND for TB. Dr. Ellner oversees TB cohort studies in Pondicherry, India, within the RePORT-India Consortium, where he was the first U.S. Chair, and is a Principal Investigator at the RePORT International Coordinating Center at Rutgers.

Rutgers Medical School

The Rutgers research group (Ellner, Johnson, and Salgame) focuses on discovering TB biomarkers and immune mechanisms. RePORT India enables rigorous study of TB co-morbidities, infection risk, disease progression, and treatment response. After Drs. Ellner and Johnson moved from Boston University to Rutgers, malnutrition studies continued at BU under Natasha Hochberg and Pranay Sinha.

In collaboration with JIPMER, Rutgers studied TB in pregnancy, anemia, alcoholism, COVID-19, and IGRA conversion/reversion in close contacts. The JIPMER partnership thrives through Drs. Sonali, Roy, Sen, Prakash, and their students. Rutgers leads RePORT India studies on TB diagnostics, infection resistance, and the Basic Science Working Group. Dr. Salgame serves as U.S. Co-Chair of RePORT India.

RePORT India and the RePORT International Coordinating Center (RICC) are based at Rutgers New Jersey Medical School in Newark, alongside the Public Health Research Institute, Center for Emerging Pathogens, and Global TB Institute. Rutgers is part of two NIH-funded TB networks—the TB Research Unit and FEND-TB (diagnostics)—and conducts TB-related diagnostic and treatment research while providing patient care. Rutgers Health Sciences is the state of New Jersey's largest and oldest academic health and science institute. It has several pre-professional programs, such as medicine, nursing, pharmacy, and allied health, as well as graduate and post-graduate training in the biomedical sciences. Through basic, clinical, population, and translational research—spanning the life sciences, physical sciences, and social sciences—Rutgers Health drives professional education, biomedical breakthroughs, and economic development while improving lives close to home and globally.



Padmini Salgame, PhD is Professor in the Department of Medicine, Center for Emerging and Re-Emerging Pathogens at Rutgers New Jersey Medical School. She is the Director of the MD/PhD Program and the Graduate Medical Research Program. Her research focuses on *Mycobacterium tuberculosis* and host immune mechanisms that protect against infection and progression to disease. Her research team also studies the biology and host response of clinical strains of *M. tuberculosis* with differing transmissibility. Her group conducts these investigations in humans and in animal models. She and her collaborators also perform biomarker studies at several international sites. Dr. Salgame is on the Editorial Board of *Infection and Immunity* and is also Associate Editor for *PLOS Pathogens*. In addition to her research pursuits, Dr. Salgame has managed and led various science training programs. She is Program Director on a T32 training grant in Infection, Immunity, and Inflammation and is regularly invited to teach national and international immunology courses.

Boston University School of Public Health (BUSPH)

Boston University School of Public Health is currently among the top Schools of Public Health in the US.. Its mission is to improve the health of local, national and international populations, particularly the disadvantaged, underserved and vulnerable, through excellence and innovation in education, research and service. BUSPH currently has 159 full-time faculty members and 669 students from over 40 countries.

RESEARCH FOCUS AREAS

Key research domains of Dr. Horsburgh are TB transmission, community engagement, stigma reduction, rapid diagnostics and prevention and treatment of drug resistance. The BU Center for Tuberculosis Research has a TB clinical trials unit that is currently conducting a duration-randomized clinical trial of fluoroquinolone-susceptible MDR-TB treatment. Dr. Sinha's primary interest is the relationship between undernutrition and TB, which he explores through epidemiological and health-economic studies stationed in India, Benin, and Togo.

KEY ACHIEVEMENTS

Dr. Horsburgh authored the qualitative study "People listen more to what actors say", aimed to understand TB-related stigma (perceived, enacted, and internalised) and found possible interventions to inform future interventions to reduce TB-related stigma in India. Dr. Sinha used RePORT India data to spearhead discussions on policy change with the Indian Ministry of Health and Family Welfare. As of October 1, 2024, the Ministry has enacted several major changes such as doubling of cash transfers, introduction of energy dense nutritional supplement to underweight PWTB and allowance of nutritional support for household contacts of PWTB.



Dr. Bob Horsburgh, Professor of Medicine & Epidemiology, has 30 years of experience in public health and medicine. He currently holds faculty positions in the Departments of Epidemiology, Biostatistics, Global Health and Medicine. Dr. Horsburgh teaches courses in the Epidemiology of AIDS, the Epidemiology of Tuberculosis and Vaccine Epidemiology. His research focuses on tuberculosis, nontuberculous mycobacterial infections and opportunistic infections in AIDS. Currently, he is involved in research in Brazil, India, South Africa, Tanzania, Vietnam and the Philippines. He is a member of the Board of Directors of the International Union Against Tuberculosis and Lung Disease (IUATLD) and Chairman of the Steering Committee of RESIST-TB, an international organization dedicated to improving MDR-TB treatment through Clinical Trials and dissemination of best practices (www.resisttb.org).



Dr. Pranay Sinha is an Assistant Professor at Boston University School of Medicine, specializing in the link between undernutrition and tuberculosis (TB). He conducts epidemiological research in India, Benin, and Togo and uses health economic modeling to shape policies. Since 2014, he has been involved in TB research with field experience in India and South Africa. Clinically, he works as an Infectious Diseases physician at Boston Medical Center, mentoring trainees and treating TB patients. He is dedicated to addressing social determinants of health, particularly undernutrition, in global TB elimination efforts. His research highlights the impact of nutrition on TB treatment and prevention. He collaborates with experts worldwide to advance TB policy and intervention strategies. Through his work, he aims to use nutritional policies to help end TB.



MVDRRC Campus
Chennai



Dr. Vijay Viswanathan, MD, PhD
Head & Chief Diabetologist



MVDRRC Team



NIRT-ICER Team

MISSION

To support individuals with diabetes in leading long, healthy lives through advanced research and comprehensive healthcare. NIRT is dedicated to training researchers and healthcare professionals in both basic and clinical sciences.

VISION

To be a leading institution for diabetes and TB research, driving innovations in patient care, training, and advocacy for better disease management and prevention.

ABOUT THE INSTITUTION & CAMPUS

MV Hospital for Diabetes was founded by Prof. M. Viswanathan in 1954 as one of Asia's first hospitals dedicated to diabetes care. Over the years, it has evolved into a Center of Excellence, treating over 400,000 patients and training more than 1,000 healthcare professionals. Recognized by India's Department of Science and Technology and the International Diabetes Federation, the hospital is at the forefront of diabetes research and management. MVDRRC works in collaboration with NIAID-ICER and ICMR-NIRT for RePORT India studies.

RESEARCH FOCUS AREAS

- Diabetes & TB Research – Investigating the interaction between diabetes and tuberculosis.
- Epidemiology & Prevention – Identifying risk factors and developing strategies to prevent diabetes-related complications.
- Molecular & Immunological Studies – Understanding immune responses in TB-DM patients to improve treatment approaches.
- Clinical Trials & Drug Development – Evaluating new treatments, vaccines, and biomarker-based diagnostics.

KEY RESEARCH FINDINGS

- High Diabetes Prevalence in TB Patients – Over 50% of adult TB patients in Chennai have diabetes.
- Impact of Diabetes on TB Severity – Poor glycemic control worsens TB outcomes.
- Prolonged Inflammatory Response – TB-DM patients show sustained immune activation even after treatment.
- Novel Biomarkers for TB Severity – Chemokines and cytokines identified as potential markers for treatment outcomes.
- TB-Diabetes Interaction & Metabolic Classification – Identifying high-risk patient groups based on BMI and glucose metabolism.

TRAINING & CAPACITY BUILDING

The research project has trained medical officers, scientists, lab managers, data analysts, and social workers, equipping them with expertise in molecular biology, immunology, microbiology, and bioinformatics.

INFRASTRUCTURE & TECHNOLOGICAL ADVANCEMENTS

The NIRT-ICER facility is equipped with:

- Advanced lab instruments – Flow cytometers, genetic analyzers, RT-PCR, and sequencing systems.
- Clinical research infrastructure – Secure clinical trial databases, IRB-accredited study sites, and GLP/GCP-trained staff.
- Electronic Data Systems – Secure platforms like DataFax and REDCap for efficient data management.

ACHIEVEMENTS & PUBLICATIONS

- 30+ international publications in indexed journals.
- Research cited in The Hindu for its impact on TB and diabetes management.
- Contributions to RePORT India studies and global TB-DM research collaborations.

Key Publications:

- The study titled **"High Prevalence and Heterogeneity of Diabetes in Patients With TB in South India" from the Effects of Diabetes on Tuberculosis Severity (EDOTS) study**, published in Chest (2016), underscored the significant intersection between diabetes and TB, calling attention to the need for better management of diabetes in TB patients to enhance disease control and treatment efficacy.
- The study titled **"Plasma Chemokines Are Baseline Predictors of Unfavorable Treatment Outcomes in Pulmonary Tuberculosis,"** published in Clinical Infectious Diseases (2021), highlighted the importance of chemokine monitoring as a potential tool to improve TB treatment outcomes and help identify patients at risk for unfavourable outcomes.

IMPACT & RECOGNITION

- Research findings contribute to shaping TB and diabetes management policies.
- RePORT India studies influencing national and global TB control programs.
- Infrastructure developments enhancing clinical and translational research in India.

REPORT INDIA IN NEWS

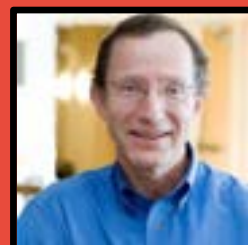
Dr. Asha Fredrick was honoured with Prof. M Viswanathan honour award at M V Hospital for Diabetes & Prof. M Viswanathan Diabetes Research Centre, Royapuram Chennai.



MVDRC-NIRT ICER Lab



Dr. Subhash Babu, MD, PhD, is Head & Scientific Director, NIH-ICER and a physician-scientist (MD/PhD) with expertise in the pre-clinical, clinical development and clinical trials arena. He is the Scientific Director of the India NIAID-International Center for Excellence in Research (ICER) program, based out of Bethesda, MD. As a Staff Scientist at the National Institutes of Health (NIH), he has led numerous translational research initiatives addressing global health challenges, including infectious diseases, metabolic diseases, and immune disorders. He has served as Principal Investigator or Co-PI in over 30 clinical trials and authored 260+ publications and 13 book chapters.



Dr. Kornfeld, MD, is a Professor of Medicine at the University of Massachusetts Medical School. He earned his medical degree from Boston University and trained in Internal Medicine, Infectious Diseases, Pulmonary Medicine, and Molecular Virology. His research focuses on macrophage cell death in TB, immunometabolism, TB susceptibility in diabetic mouse models, and host-directed therapy. Clinically, he is involved in RePORT India Phase 2, studies on lung function in HIV/TB patients, and a trial of metformin as adjunctive therapy in HIV/TB.

**MVDRC collaborates with
NIH-ICER and UMass**

INDIAN COUNCIL OF MEDICAL RESEARCH- NATIONAL INSTITUTE FOR RESEARCH IN TUBERCULOSIS: CRS 105



NIRT Campus
Chennai



Dr. Bhavani PK, MBBS, MPH, PG
Diploma in Bioethics & Medical Ethics
Scientist E, ICMR-NIRT, Chennai
Research Scientist



NIRT Team



MISSION & VISION

ICMR-NIRT aims to advance tuberculosis research through high-impact clinical trials, diagnostics, and treatment strategies. Our vision is to contribute to global TB eradication by translating research findings into policy and practice.

ABOUT THE INSTITUTION & CAMPUS

The National Institute for Research in Tuberculosis (ICMR-NIRT), Chennai, is a premier research institute dedicated to TB studies. Established in 1956, the institute has been pivotal in shaping national TB policies. With state-of-the-art laboratories and clinical research facilities, NIRT has contributed to over 55 randomized controlled trials and several landmark studies.

RESEARCH FOCUS

- Randomized controlled trials (RCTs) on high-dose Rifampicin and TB treatment shortening
- TB preventive therapy (TPT) for household contacts of TB patients
- Post-TB lung disease and pulmonary rehabilitation
- Pharmacokinetic studies and drug trials for TB and HIV

ABOUT ICMR-NIRT

- Revolutionized domiciliary treatment of TB – Madras Study, done in 1950's showed that TB could be effectively treated at home
- Conducted largest BCG vaccine trial ever (Chingelput BCG trial)
- Conducted National TB Prevalence Survey -
- Released Indian M.tb mutations catalogue
- 4 National COVID sero surveys coordinated & implemented by ICMR-NIRT
- Systematic Screening for TB (disease & infection) among the Orphaned and other vulnerable Population in Selected Districts of Tamil Nadu

ACHIEVEMENTS & DEVELOPMENT

- Coordinated multi-centric TB & HIV drug trials influencing national policies
- Established evidence for TB preventive therapy (TPT) for all household contacts of pulmonary TB patients
- Demonstrated the safety and efficacy of high-dose Rifampicin in pulmonary TB

PERSONNEL TRAINING & CAPACITY BUILDING

- The pharmacokinetic lab in-charge Dr Jeyakumar has trained report project staff on the performance of drug assay and serves as a nodal site for performing PK assays for the RePORT India study.
- The NIRT bacteriology lab serves as a common lab to all the 3 Report India sites- ICMR-NIRT, MVDRC and CMC Vellore

- All the RePORT India clinic project staff involved in Lung health aims underwent training on Spirometry thrice – First at CMC, Vellore, second at Rajiv Gandhi Government General Hospital, Chennai (Madras Medical College) and again 2024 they were trained by Prof Rupak Singla, NITRD
- Study investigators and project Medical Officer undertook training Chest X-ray reading and scoring.
- Lab trainings – All study staff undertook basic GCP, GCLP, HSP, protocol training and SOP reading before study initiation. With respect to lab work of RePORT study all lab staff and staff nurse were trained on freezer pro manual, Iso screen testing and sample handling, testing and processing. Protocol refresher trainings were given every time any amendments were made to the protocol.

INFRASTRUCTURE DEVELOPMENT

- Upgraded pharmacokinetic and bacteriology laboratories
- Established a central lab for RePORT India studies
- Enhanced facilities for drug assays and sample processing

RECENT SIGNIFICANT CLINICAL TRIAL PUBLICATIONS

- **Daily regimen superior to Intermittent regimen in HIV infected** (JAMA Intern Med. 2018;178(4): 485-93)
- **4-Months regimen of moxifloxacin had non-inferior outcomes to 6 months** (Trop med and international health 2020;25(4): 483-95)
- **Metformin With Anti-Tuberculosis Drugs for Early Sputum Conversion in Adults With Pulmonary Tuberculosis** (Clin Infect Dis 2022;75(3):425-34)
- Ascertained safety of High dose Rifampicin in pulmonary TB: HICON-R [https:// doi.org /10.1093/ofid/ofae034](https://doi.org/10.1093/ofid/ofae034)
- **Shorter Treatment for Non-severe Tuberculosis in African and Indian Children (SHINE trial)** (N Engl J Med 2022; 386:911-922)
- **Randomized Clinical Trial of High Dose Rifampicin with or without Levofloxacin versus Standard of Care for Paediatric Tuberculous Meningitis: The TBM-KIDS Trial** (Clin Infect Dis 2022 Mar 15;ciac208)

IMPACT & RECOGNITION

RePORT India in News

- Featured in national and international media for TB research breakthroughs
- Recognized for contributions to TB preventive therapy and high-dose Rifampicin studies

NIRT Team



Spirometry Training



NIRT Lab Team



Key Publications

Tuberculosis preventive treatment should be considered for all household contacts of pulmonary TB patients in India

Paradkar M, Padmapriyadarsini C, Jain D, Shivakumar SVBY, Thiruvengadam K, Gupte AN, Thomas B, Kinikar A, Sekar K, Bharadwaj B, Dolla CK, Gaikwad S, Elilarasi S, Lokhande R, Reddy D, Murali L, Kulkarni V, Pradhan N, Elizabeth Hanna L, Pattabiraman S, Kohli R, Nayagam R, Suryavanshi N, Shrinivasa BM, Cox SR, Sriram Selvaraju S, Gupte N, Mave V, Gupta A, Bollinger RC, for the CTRIUMPH-RePORT India Study Team. PLOS One. 2020 July 29;15 (7):e0236743. <https://doi.org/10.1371/journal.pone.0236743>. PMID: 32726367; PMCID: PMC7390377

This study results provided additional evidences supporting the WHO recommendation on offering TPT to all HHC of PTB patients residing in a high TB burden country such as India. This study results provided evidence to revise the TPT guidelines in India and currently TPT is offered to all HHCs of pulmonary TB patients in India irrespective of TBI status. <https://tbcindia.mohfw.gov.in/wp-content/uploads/2023/05/Guidelines-for-Programmatic-Management-of-Tuberculosis-Preventive-Treatment-in-India.pdf>

Pharmacokinetics of rifampicin, isoniazid & pyrazinamide during daily & intermittent dosing: A preliminary study

Ramachandran G, Hemanth Kumar AK, Kannan T, Thangakunam B, Shankar D, Christopher DJ. Indian J Med Res. 2023 Feb-Mar; 157(2&3):211-215. doi: 10.4103/ijmr.IJMR_1835_19. PMID: 36861539; PMCID: PMC10319390.

First PK study from India to compare drug levels of first line drugs given as intermittent and daily dosing and reported that INH doses used currently in the daily ATT resulted in suboptimal concentrations suggesting that INH doses may need to be increased in case of a daily regimen. The authors also recommended larger studies using higher INH doses along with therapeutic drug monitoring.



NIRT Team

ACHIEVEMENTS

GRANT TITLE	PARTNERS	GRANT SOURCE	START DATE
Airway Injury Risk Mechanisms and Interleukin -6 (AIRMAIL)	Boston University, BJGMC, CMC, JHU	NIH R01	2024
Evaluating the clinical utility of a novel RNA-based assay for predicting TB treatment outcomes and diagnosing paucibacillary TB	Weil Cornell, BJGMC, JHU, Makerere University	RICC	2024
Local Capacity Building to Develop Novel Drug-Resistant TB Testing and High-Throughput Multiplex Protein Measurement Programs in Pune, India	BJGMC	RICC	2023
RePORT India Consortium Strengthening Equipment Funding	BJGMC, Hinduja	RICC	2023
TB-RICC Laboratory Enhancement and Capacity Building	BJGMC	RICC	2023
T Cell Biomarkers and T-Regulatory Responses to Pediatric TB	Emory, JHU, BJGMC, NIRT	RICC	2020
Pregnancy Associated Immune Responses to TB and HIV in India and South Africa (PARTHISA study)	JHU, BJGMC, Wits Health Consortium, Cornell	RICC	2020
Pharmacokinetic Assessment of MDR-TB Drugs in the Treatment of TB Meningitis	JHU, PD Hinduja, Beijing Chest Hospital, BJGMC, Wits Health	RICC	2020



BJGMC Campus
Pune



Dr. Sanjay Gaikwad is Professor & Head of the Department, Respiratory Medicine, Byramjee Jeejeebhoy Government Medical College, Pune. He has more than 35 years of expertise in tuberculosis. He serves as the Zonal Task Force OR (Operational Research) Chairman for the West Zone NTEP. He is involved in Post Graduation Teaching, provide Guidance, and he is also an Examiner for the Master's Degree Doctor of The Medicine - Pulmonary Medicine Subject. He is also a Pulmonologist, Intensive Respiratory Care Medicine and Sleep Medicine. Dr. Gaikwad holds a strong background in clinical medicine, particularly in respiratory medicine. He specializes in training in identifying and managing TB, he understands its complex clinical presentation, diagnostic methods, and treatment strategies. He is also associated with several clinical and operational research activities at the International, State/National levels.



Dr. Aarti Kinikar, Professor & Head of the Department, Paediatric, is an expert in pediatric infectious diseases with a special focus on tuberculosis in children. She is a member of various government Task Forces and Advisory Committees, Chairperson of the State Operational Research on Tuberculosis Committee as well as Maharashtra University of Health Sciences, Nashik. She has over 35 years of experience diagnosing and treating pediatric TB, particularly in high-risk populations, including HIV-positive children and those with malnutrition. She collaborates with global health organizations to implement TB screening programs in under-resourced areas, providing education to healthcare professionals on the early identification of pediatric TB. Dr. Kinikar is also involved in research focused on better understanding the interaction between TB and HIV in children and how to tailor treatment strategies for this vulnerable population.



Dr. Rajesh Karyakarte is Professor & Head of the Department, Microbiology at BJGMC. With over 35 years of experience in the field, he has focused much of his research on the pathogenesis, diagnosis, and treatment of TB, particularly through innovative microbiological techniques. His research has played a key role in developing faster, more accurate methods to diagnose TB, especially in resource-limited settings where timely diagnosis is critical to reducing transmission. In addition to his research, Dr. Karyakarte has been involved in training healthcare professionals and laboratory technicians in the latest TB diagnostic techniques, as well as on the importance of quality control in microbiological testing. Dr. Karyakarte has become a leading expert in the field of tuberculosis microbiology, contributing to both the scientific community and the broader global health efforts to combat TB.

GRANT TITLE	PARTNERS	GRANT SOURCE	START DATE
Inflammasome Genetics and TB Treatment Outcomes	UPenn, JHU, UMass, NIRT, MVDRC, BGJMC	RICC	2020
Host RNA Expression for Diagnosis and Monitoring of Pediatric TB in Africa and India	NIRT, BGJMC, JHU, Univ. Cape Town, Imperial College, London	RICC	2019
Characterization of Genomics and Metabolomics among Individuals (TB-GWAS)	Emory, JHU, BJGMC, JIPMER, BMMRC, NIRT, PHRU, McGill	NIH/NIAID R01	2018
Measuring TB Drugs in Hair as a Tool to Monitor Adherence, Exposure and Response	BJGMC, NIRT, JHU	NIH/NIAID : R21	2016-2018
Impact of Immune Changes of HIV and Stages of Pregnancy on TB (Prachiti)	BJGMC, NIRT, JHU	NIH/NICH D R01	2015-2020
Understanding of Tuberculosis Infection and Preventive Therapy Among Skin-Test Positive Household Contacts of Tuberculosis Cases	BJGMC, NIRT, JHU	NIH CFAR Fogarty D43	2015



Dr. Rohidas Borse is Professor & Head of the Department, General Medicine. He is a distinguished medical expert with extensive experience in infectious diseases, particularly tuberculosis (TB). With over 36 years in the field of medicine, Dr. Borse has specialized in the diagnosis, treatment, and management of TB & HIV in adults, across a wide range of settings, from urban hospitals to resource-limited regions. Dr. Borse's work spans several critical areas, including clinical research, epidemiology, and public health interventions for TB control. He has been instrumental in designing and implementing TB treatment regimens, particularly for multi-drug-resistant (MDR) and extensively drug-resistant (XDR) TB, and developing protocols for early diagnosis.



Dr. Amita Gupta is the Florence Sabin Professor of Infectious Diseases and Director of the Division of Infectious Diseases at the Johns Hopkins School of Medicine, and she holds a joint appointment in the Department of International Health at the JH Bloomberg School of Public Health. Dr. Gupta's work focuses on international clinical research, public health, and education in infectious diseases, with specialties in HIV/AIDS, tuberculosis (TB), and antimicrobial resistant infections. Since 2003, her research has focused primarily on low- and middle-income settings and in India, where she leads several JHU research collaborations. Dr. Gupta is an author of more than 300 peer-reviewed research publications and 7 book chapters on prevention and treatment of HIV, TB, and other infectious diseases, primarily in low- and middle-income settings.

KEY ACHIEVEMENTS

- One of the highest enrolling sites in both- phase I and II RePORT India protocols
- Successful completion of initial targets in adult diagnostic cohort (PTB suspects, n= 115) and Cohort A (adult PTB cases, n=120)
- Resumed the phase II Common Protocol version 3.0 based enrollments in both:
 - Cohort A advanced lung health aim (adult TB cases, n=8/50) and,
 - Pediatric Diagnostic Cohort (n=61/150).
- Enrolled household contacts of pulmonary TB patients in Quantiferon study led by Rutgers University- (100% target of 500 enrollments achieved in 15 months, follow ups completed).
- Ongoing participation in the DBT led 'Indian Tuberculosis Genomics Consortium' (Whole genomic sequencing study).
- Assays completed for the study of proteomic markers of TB recurrence and death in collaboration with IIT-Mumbai, data analysis ongoing.
- Ongoing participation in several phase I and phase II-based RePORT India and RePORT International adult and pediatric substudies.
- Site has contributed to about 30 indexed journal publications.
- The following CTRIUMPH-RePORT India Study Team led publication contributed to the "Guidelines for Programmatic Management of Tuberculosis Preventive Treatment in India (National Tuberculosis Elimination Programme (NTEP) under the Ministry of Health and Family Welfare, India)"- Tuberculosis preventive treatment should be considered for all household contacts of pulmonary tuberculosis patients in India. PLoS One. 2020 Jul 29;15(7):e0236743. doi: 10.1371/journal.pone.0236743.

INFRASTRUCTURE (CAMPUS & EQUIPMENT)

BJGMC Mycobacteriology Laboratory (Department of Microbiology)

We have established TB microbiology laboratories (BSL-2+ as well as a BSL-3) with the help of BJGMC administration and the NIH-funded AIDS Clinical Trials Network (ACTG) and IMPAACT networks.

The laboratory is validated and approved for the following tests:

1. AFB smear microscopy- (ZN & FM)
2. MGIT- liquid culture
3. MGIT-First line Drug Susceptibility Testing
4. MGIT- Second line Drug Susceptibility Testing
5. Gene Xpert
6. Gene Xpert Ultra
7. LJ-Solid Culture.
8. Line Probe Assay (1st Line and 2nd Line)



Dr. Bob Bollinger, MD, MPH is the Raj and Kamla Gupta Professor of Infectious Diseases at the Johns Hopkins University (JHU) School of Medicine, and he holds joint appointments in International Health at the Johns Hopkins (JH) Bloomberg School of Public Health, and in Community Public Health at the JH School of Nursing. He is also Associate Director for Medicine of the Johns Hopkins Center for Global Health. From 2005 to 2022, he was the Founding Director of the CCGHE. Dr. Bollinger and has been on the faculty at Johns Hopkins School of Medicine for >30 years, where he has been an educator, researcher and clinician. He has more than 40 years of experience in clinical and epidemiologic research and education in many countries including India, Bangladesh, Pakistan, Uganda, Tanzania and Ethiopia, in a broad range of global health priorities, including HIV, TB and emerging infections. He serves as the protocol Chair of RePORT India.



Dr. Vidya Mave is Co-Director of Johns Hopkins Center for Infectious Diseases in India. Based in Pune, India, she is Leader and Director of Byramjee-Jeejeebhoy Government Medical College-Johns Hopkins University (BJGMC-JHU) Clinical Research Site in Pune, India as well as Associate Professor of Johns Hopkins University School of Medicine. Dr. Mave has nearly 20 years of experience in clinical practice, education, and research in infectious diseases. Her research interests include HIV and co-morbid infections such as TB as well as comorbidities (HIV), the use of novel tools (Hair PK, whole genome sequencing, host biomarkers), and TB vaccine clinical trials to optimize HIV and TB treatment outcomes.



Dr. Nishi Suryavanshi is Clinical Research Site Coordinator and Deputy Director of the BJGMC Clinical Research site. She has more than 25 years of experience working in the NIH-funded studies as a protocol team member, site co-investigator and lead for social - behavioral science studies in TB, HIV, mental health, substance use, and women's health. She received her MSc and PhD in medical anthropology from the University of Pune.



Dr. Mandar Paradkar is trained in Pediatrics (DCH) and Public Health (MPH, Commonwealth Scholar). He is currently a RICC Postdoctoral Fellow (2024-26), and an early career investigator and Operations working group chair for RePORT India. He has extensive experience in conducting TB studies in adults and children at the BJGMC JHU CRS. Dr. Paradkar has contributed over past decade to implementation of RePORT India studies and other pediatric clinical trials at the site. His publication with CTRIUMPH-RePORT team (PLOS ONE, 2020), contributed to the Indian programmatic TB Preventive Therapy Guidelines.



CRS Repository Facility

The CRS repository has 17 -80° C freezers of approx. 500L capacity, 2 -20° C freezers, and 8 LN2 canisters including 1 automatic filling LN2 freezer. There are approximately 300,000 specimens currently banked in freezers from several studies.



Dr. Nikhil Gupte is a PhD Biostatistician from Johns Hopkins University. He is Director of biostatistics and data management at Johns Hopkins Center for Infectious Diseases India. Dr. Gupte has spent over 25 years collaborating with researchers in public health, epidemiology, and clinical trials to design robust studies and analyze complex data sets. Dr. Gupte is also a sought-after educator and mentor, having taught biostatistics and mentored numerous graduate students in statistical methodology. Their commitment to advancing the field extends beyond research, having authored more than 150 peer-reviewed publications.



Neeta Pradhan is a medical microbiologist and Tuberculosis Laboratory Manager at BJGMC, who has worked in the laboratory field for more than 25 years.



Vandana Kulkarni is Laboratory Manager at BJGMC. She is responsible for operations of the research laboratory and for supervision of laboratory supervisors and technicians, and she evaluates personnel competency and proficiency as well as waste management, vendor development for instrument purchase, and maintenance contracts. She also is responsible writing and revising all laboratory standard operating procedures (SOPs), for training staff in new methodologies as required, and for ensuring that laboratory and staff operate under Good Clinical Laboratory Practices.

CRS Laboratory Team



BJGMC Team



Molecular Virology Facility



Illumina MiSeq Sequencer



BSL 2 & 2 Facilities

Mycobacteriology Lab Team



PBMC Processing Lab



Sample Processing Lab





BMMRC Campus
Hyderabad



Dr. Vijaya Lakshmi Valluri
India PI



Dr. Ramakrishna Vankayalapati
US PI



Prudhula Kamakshi



Sanjeev Kumar

MISSION & VISION

- Immunologic and genetic aspects of diseases like tuberculosis, HIV and leprosy.
- Identifying biomarkers for TB progression in household contacts (promising leads from Phase I)
- Evaluation of efficacy of vaccines and investigation of in vitro correlates of protection
- Gaining an insight into the underlying mechanisms of immune deficiencies resulting in active TB infection in TB households.

ABOUT THE INSTITUTION & CAMPUS

Mahavir Hospital and Research centre (MHRC) a charitable hospital, was started in 1978 by Bhagwan Mahaveer Memorial Trust (BMMT) to offer affordable medical care to economically backward patients. It is the first private charitable hospital in the state for initiating and conducting research on chest diseases about 35 years ago. Bhagwan Mahavir Medical Research centre (BMMRC): a non-profit seeking research centre was started in 1988 by BMMT. It was in the early 1980s that Dr. KJR Murthy (late), a well-known chest physician and pioneer, envisaged the importance of an effective vaccine to fight tuberculosis. Dr. Murthy and his team gained international recognition for the PPM DOTS model and later was integrated in the National TB Control Programme. PPM DOTS model was internationally accepted and is known as MAHAVIR MODEL. > 200 papers were published in national and international journals of repute and 45 students were awarded Ph.D degree from this centre.

RESEARCH FOCUS AREAS

- Immunology of infectious diseases: Tuberculosis, HIV and leprosy.
- Genetics and association studies on Tuberculosis, HIV and leprosy.

The main aim of the research centre is to contribute towards an effective booster vaccine and identify biomarker for early detection of TB infection among high-risk individuals in the society. Dr Vijaya along with her mentor worked extensively on childhood TB, and were the first to report that the effect of BCG vaccine wanes with age, a booster is required for continued protection against TB.

PARENT PROTOCOL

Title: Identify immunologic markers of persons at highest risk of Progression of latent tuberculosis infection to tuberculosis

Overall goal of the project. The goal of the project was to find novel biomarkers that will identify persons with latent tuberculosis infection (LTBI) who are at increased risk for progression to active tuberculosis (TB).

RePORT INDIA STUDIES

S NO	PROJECT TITLE	PI/CO-PI	FUNDING AGENCY
1	RePORT India Phase II COMMON PROTOCOL (5 yrs) Indo US TB VAP	Dr. Vijaya L Valluri - Indian PI Dr. Ramakrishna V, University of Texas, Tyler - US PI	DBT, Govt & CRDF Global, USA
2	Innate Immune Response of LTBI+HIV+ Children (R01 grant)	Dr. Vijaya L Valluri - Indian PI Dr. Ramakrishna V, University of Texas, Tyler - US PI	NIH, University of Texas, Tyler USA
3	Memory like NK cells as biomarkers for risk of activation of latent TB in HIV+ individuals	Dr. N.V. Sanjeev Kumar –PI Dr. D K Prudhula Co-I Dr. Vijaya L Valluri - Co-I	ICMR, Govt

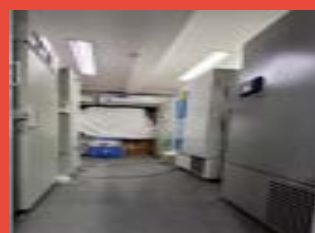
ACHIEVEMENTS & DEVELOPMENT**Personnel Training**

The following scholars received financial support from RePORT study (DBT) during their PhDs:

- Dr. Sudheer Pydi (Awarded)
- Dr RS Sharada (Awarded)
- Dr. Lavanya Joshi (Awarded)
- Dr. Sanjeev Kumar NV (Awarded)
- Dr. Prudhula DK (Awarded)

Grants and honours to young investigators associated with the study:**Dr. Kamakshi Prudhula Devalraju, has received the following as a part of this project:**

Future leader fellowship 2025: RePORT International Coordinating Center's (RICC) Future Leaders Program (FLP) is intended to develop the capacity of investigators within RePORT International institutions to assume leadership positions within RePORT country networks. Travel support to attend and present "Memory-like NK cells as immunological markers of protection against latent TB conversion in house hold contacts of TB patients" at 5th Global Forum on TB vaccines, 20-23rd February 2018 New Delhi, India.



50000 USD grant from NIH as a young investigator grant to explore "TH17 cell subsets as potential risk markers of latency and active TB infection in house hold contacts". Awarded in December 2016. Project initiated in July 2017. Duration of the grant- One year.

Travel grant from NIAID to attend and present my work (Identify potential Bio markers for development of Latent Tuberculosis Infection (LTBI) by longitudinal follow-up of HHC's of TB patients) at the RePORT International meeting, in Durban, South Africa, July 14-16, 2016.

She is also currently serving as Co-Chair for RePORT India consortium common protocol.

Dr NV Sanjeev Kumar & DK Prudhula received a 3-year project titled "Memory like NK cells as biomarkers for risk of activation of latent TB in HIV+ individuals" funded by Indian Council of Medical Research (ICMR) [2020-2023]

KEY ACHIEVEMENTS

Highlights of the results from our cohort:

Technology developed:

- Determination of latent TB: We designed an in-house IGRA to detect LTBI in our cohort, this assay is on par with the conventional QFT-TB test commercially available with over 95% specificity and sensitivity.
- Determination of conversion to latent TB and Biomarkers for progression to ATB
- From our RNA Seq studies we identified five genes which may be involved in resistance to Mtb infection or development of LTBI and are currently validating the results.

INFRASTRUCTURE DEVELOPMENT

The laboratory has procured an 8 colour flow cytometer BD Canto II, three deep freezers, CO2 incubator, MGIT 960 system liquid nitrogen (LN2) setup for cryopreservation of cells sponsored by DBT, Gol, BIRAC and CRDF Global, USA.

BMMRC Team



BMMRC and CCMB sites have joined forces to develop a combined **"Hyderabad site"** in the RPT Phase II common protocol.

Dr. Vinay Nandicoori, Director CCMB, is a Molecular and Cellular Biologist who has contributed to delineating the signalling networks in *Mycobacterium tuberculosis* (*Mtb*). He did his Masters in Biotechnology at the Indian Institute of Technology, Bombay and his Ph.D. in Molecular and Cellular Biology from the Indian Institute of Science, Bangalore. He was a Postdoc at Texas A&M University for 3 years and the University of Virginia for three and half years before returning to India in 2004. In 2021 he moved to the Centre for Cellular and Molecular Biology, Hyderabad, India as the Director, where he established his lab. His research interest is to delineate the kinase-mediated signalling networks in *Mtb*. In addition, his lab is also interested in identifying novel drug-resistant mechanisms, deciphering transcription regulation and identifying novel targets for host-directed therapy. He has 85 research papers to his name in international journals of high repute. He is the recipient of NASI-Scopus Young Scientist Award. He is an elected fellow of all three Science Academies in India.

Dr Nandicoori, is known chiefly for his studies on the kinase-mediated signaling networks in *Mtb* infection has been working to understand the molecular basis of *Mtb* pathogenesis, drug resistance for quite some time and therefore brings in excellent expertise on pathogen-host interaction. CCMB is a premier research organization in frontier areas of modern biology. The objectives of the centre are to conduct high quality basic research and training in areas of modern biology, and promote centralized national facilities for new and modern techniques in the inter-disciplinary areas of biology.



CCMB Main Building



Dr Vinay Kumar Nandicoori
Director, CCMB

CCMB Lab



Dr. Vinay's Team at CCMB

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MISSION & VISION

P.D. Hinduja Hospital and MRC follows a vision of providing "Quality Healthcare for All". The hospital is a 520 bed tertiary care multi-speciality hospital with dedicated consultants and staff delivering quality medical care to all patients, as well as continuous medical education to all the doctors & training of nurses and by undertaking basic & clinical research with the focus on the needs of the country. The hospital is recognised by ICMR as a Centre of Excellence for Tuberculosis and has several dedicated research studies (funded nationally and internationally) ongoing in the field of TB. The hospital serves with a vision to provide affordable, value based, ethical and transparent services to all patients.

ABOUT THE INSTITUTION & CAMPUS

P.D. Hinduja Hospital and Medical Research Centre's healthcare journey commenced in 1951 by the late Shri P. D. Hinduja, with a vision to provide quality healthcare for all. Over the last seven decades, the hospital has passionately followed this philosophy and today the hospital is regarded as one of the top hospitals in Mumbai and one of the best hospitals in India. We commit to move forward with greater zeal and determination to set new benchmarks in medical excellence and patient care. Along with the medical patient care wing, the hospital has a strong pillar for academics awarding M.Sc, Ph.D and DNB degrees in affiliation to University of Mumbai and Maharashtra University of Health Sciences. The hospital also has the College the Nursing providing graduation and post-graduation courses in Nursing. The hospital has a vast dedicated wing in research and has dedicated facilities for research in several areas including Cardiovascular diseases, Cancer, Tuberculosis (TB) etc and is now also an ICMR Centre of Excellence in Tuberculosis. The microbiology laboratory is the TB referral lab for the city and the biochemistry lab providing Therapeutic drug monitoring (TDM) services of 28 drugs including for both first and second line TB drugs.

RESEARCH FOCUS AREAS

Research has been one of the core focus point for the institute adopting the state of art techniques and high throughput outcome work. The institute has dedicated skillful researchers with their expertise in fields of Biochemistry, Microbiology, Molecular Biology, Pharmacology with their experience in high throughput sequencing, Microarray, Multi-omics approach, Pharmacokinetics, Pharmacodynamics, Pharmacogenetics, and a strong clinical wing with a few clinical trials ongoing on site. The institute has R01 grants funded by National Institute of Health (NIH, USA) focussed on TB treatment and outcomes, Department of Biotechnology and Department of Science and Technology funded research studies on development and validation of Therapeutic Drug Monitoring assays for TB drugs using Tandem Mass Spectrometry and has also been a major site for a few other international funded Global collaborative studies like CRYPTIC consortium.

PARENT PROTOCOL: MDR-TB Free: Monitoring adverse effects, Utilizing resources optimally, Knowing resistance patterns, and Treatment strategy (MDR-TB MUKT)

Overall Objective

To establish well-characterized prospective cohorts of active MDR-TB cases and their household contacts with associated biorepositories.



Principal Investigators
Dr. Camilla Rodriguez
Dr. Tester Ashavaid
Dr. Zarir Udawadia

Hinduja Campus
Mumbai





Dr. Jeffrey Tornheim
JHU PI



Hinduja Team



Primary Objectives

- Cohort A: To document participant outcomes including early treatment response, MDR-TB treatment-associated adverse events, mortality, and loss to follow-up.
- Cohort B: To assess rates of prevalent and incident TB infection and disease in household contacts of MDR-TB cases.

Establishing a Biorepository for sputum, saliva, M.tb isolate, Whole blood, Paxgene, Plasma, Urine, QFT, PK (Plasma EDTA, Plasma Hep and Serum)

RePORT INDIA STUDIES

1. MDR-TB Free: Monitoring adverse effects, Utilizing resources optimally, Knowing resistance patterns, and Treatment strategy (MDR-TB MUKT) – as RePORT India Parent Protocol for Phase I
2. Therapeutic Outcomes with Second-Line Drug Exposures in a Cohort of South African and Indian Patients with Drug Resistant TB: A Pharmacokinetic-Pharmacodynamic Assessment
3. The Regional Prospective Observational Research for Tuberculosis (RePORT) India Phase II Common Protocol
4. Predictors of Resistance Emergence Evaluation in MDR-TB Patients on Treatment - (PREEMPT)
5. Validation of Indigenously Developed Technology (TruNat MTB) for Diagnosis of Extra-pulmonary Tuberculosis: Multi-centric Validation
6. Whole Genome Sequencing of Drug Resistant Tuberculosis in India: Genotype-Phenotype Correlation, Clinical Impact of Resistance, and Sequencing Directly from Sputum

RICC FUNDED STUDIES

1. Pharmacokinetic Assessment of MDR-TB Drugs in the Treatment of TB Meningitis: The study is completed and data analysis is ongoing. The Study aimed to look at pharmacokinetics of drugs in CSF samples and evaluate biomarkers in extra pulmonary TB patients.
2. RePORT India Consortium Strengthening Equipment Funding: This shovel ready grant has helped build in capacity of performing Spirometry in TB patients on site (currently being used for smear / culture negative patients and is being optimised for the use in positive TB patients), perform MIC testing, Vicell counter and liquid nitrogen storage tanks for PBMC counts and storage of biospecimens in LN2.
3. Baseline pRescription According to direct from Sputum Sequencing and Targeted Drug Concentration Strategy (BRASS TaCS): This study evaluates the combination of real-time next generation sequencing (NGS), video-based direct observation of therapy (vDOT), therapeutic drug monitoring (TDM), and expanded drug susceptibility testing (DST) within minimum inhibitory concentration (MIC) testing for rifampin-resistant or multidrug-resistant tuberculosis (RR/MDR-TB). This study will assess whether the combined strategy can reduce toxicity and improve RR/MDR-TB treatment outcomes.

4. Multiplexed detection of cell-free M. Tuberculosis DNA and its drug-resistant variants in blood (CRISPR-TBD): In this study we expect to prove that MTB-cfDNA retains high sensitivity and specificity using a both universal and resistance profile-specific genetic targets as per WHO mutation catalogue. We intend to demonstrate that this tool can be easily implemented in a high-burden lab in an endemic setting.

ACHIEVEMENTS & DEVELOPMENT

Personnel Training

- All site staffs have been certified online with a GCP/HSP certification course
- All lab staffs are also certified online with GCLP and Dangerous Goods Training
- All site staffs are trained with the updated RePORT India Phase II protocol & MOP
- All study clinicians are certified X-Ray readers
- Other training courses include PBMC isolation and cryopreservation training, Quantiferon training, Freezer Pro training and CITI conflict of interest certificate program

Key Achievements

The studies have resulted in several publications and new opportunities to get national and international grants. The site has enriched in capacity building and technology transfer across and provide the tests developed with these new technologies as a diagnostic service available for direct patient care. The new tests include Therapeutic Drug Monitoring of second line TB drugs, targeted next generation sequencing, customised sensititre plate panels and is also involved with ongoing research on Transcriptomics, Pharmacogenomics, pharmacokinetics models, whole genome sequencing etc.

Infrastructure Development

The continued participation has given us the opportunity to be a part of Shovel ready grant where in we could build in our infrastructure with new spirometers, Customised sensititre plates, Vicell cell viability counter and liquid nitrogen containers for PBMC extractions and storage through direct funding with NIH.

Method development and transfer to develop pharmacokinetic studies for second line TB drugs in our TDM lab through an India South Africa collaborative grant.

Publications

1. **Pharmacokinetic analysis of linezolid for multidrug resistant tuberculosis at a tertiary care centre in Mumbai, India.** Resendiz-Galvan JE, Arora PR, Abdelwahab MT, Udwadia ZF, Rodrigues C, Gupta A, Denti P, Ashavaid TF, Tornheim JA. Front Pharmacol. 2023 Jan 4;13:1081123. doi: 10.3389/fphar.2022.1081123. PMID: 36686664; PMCID: PMC9846493.
2. **Swimming against the STREAM: Why STREAM 2 data cannot be easily applied to MDRTB patients across India** Udwadia ZF, Patel JM, Batyala M, Tornheim JA, Rodrigues C. Lung India. 2023 May-Jun;40(3):290-291. doi: 10.4103/lungindia.lungindia_74_23. PMID: 37148033; PMCID: PMC10298808.
3. **Cycloserine did not increase depression incidence or severity at standard dosing for multidrug-resistant tuberculosis.** Tornheim JA, Udwadia ZF, Arora PR, Gajjar I, Gupte N, Sharma S, Karane M, Sawant N, Kharat N, Blum AJ, Shivakumar SV. Eur Respir J. 2022 Mar 24;59(3):2102511. doi: 10.1183/13993003.02511-2021. PMID: 34949698; PMCID: PMC8943271.
4. **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.** Jeffrey A. Tornheim, Zarir F Udwadia, Prerna R Arora, Ishita Gajjar, Samridhi Sharma, Megha Karane, Namrata Sawant, Nisha Kharat, Alexander J Blum, Shri Vijay Bala Yogendra Shivakumar, Akshay N Gupte, Nikhil Gupte, Jai B Mullerpattan, Lancelot M Pinto, Tester F. Ashavaid, Amita Gupta, Camilla Rodrigues. Open Forum Infectious Diseases, 2021; ofab615, <https://doi.org/10.1093/ofid/ofab615>



NEIGRIHMS Campus
Shillong



Dr. Valerie W. Lyngdoh
Assistant Professor



Team NEIGRIHMS
Shillong, Meghalaya

MISSION & VISION

Tuberculosis research requires global cooperation and knowledge sharing in developing solution to complex tuberculosis challenges. To conduct innovative, interdisciplinary research that addresses the challenges of tuberculosis (TB), with the goal of developing effective prevention, diagnosis, and treatment.

INSTITUTION'S HISTORY & CAMPUS

NEIGRIHMS (North Eastern Indira Gandhi Regional Institute of Health and Medical Sciences) is an autonomous institute established by the Government of India in 1987 under the Meghalaya Registration of Societies Act (1983). With a mission to enhance healthcare in the North Eastern region, it serves as an apex center for policy guidance, capacity building, and international health collaborations. NEIGRIHMS provides postgraduate and postdoctoral teaching in 35 disciplines, houses a 252-bed Regional Cancer Centre, a medical and nursing college, emergency medicine services, and a 594-bed hospital. Proposed expansions include a Trauma Centre, College of Pharmacy and Dental Sciences, a Patient Rest House, and air ambulance services to improve healthcare accessibility in remote areas. Site is part of Common protocol phase II and activated on June 12, 2024.

RESEARCH FOCUS AREAS:

The research domains on tuberculosis (TB) are:

1. TB Diagnostics: Developing rapid, accurate, and affordable diagnostic tools for active TB and latent TB infection.
2. TB Epidemiology and Transmission Dynamics: Investigating the social, environmental, and biological factors driving TB transmission.
3. TB and HIV Co-infection: Understanding the interactions between TB and HIV, and developing effective interventions for co-infected individuals.
4. Implementation Science and Operational Research: Evaluating the effectiveness of TB programs and interventions, and identifying strategies to improve TB control.
5. TB treatment adherence: Investigating strategies to improve TB treatment adherence and retention in care.
6. Research domains are interconnected and require a multidisciplinary approach to address the complex challenges of TB.

ACHIEVEMENTS & DEVELOPMENT

Personnel Training

1. Medical Social Worker/Site Coordinator: Trained in DAIDS Human Subjects Protection (HSP)/Good Clinical Practice (GCP), Laboratory Training, and FreezerPro.
2. Lab Technician: Completed HSP/GCP, Source Documentation, Risk Management, Dangerous Goods Handling, Good Clinical Laboratory Practice (GCLP), and FreezerPro Specimen Management.

Workshops & Capacity-Building

- Organized sessions on research methodology, data analysis, scientific writing, presentation skills, and time management.
- Training in TB program management, implementation, surveillance, and monitoring.
- Mentorship programs and collaborative research participation.
- Supported staff attendance at conferences and workshops.

Key Achievements

Despite initial delays due to technical issues and funding, enrollment has commenced. Samples collected (sputum, saliva, urine, blood) were processed per protocol, with sputum sent to Nazareth Hospital for culture. Of 13 samples tested, 11 were TB-sensitive (rifampicin & isoniazid). The site is progressing toward the six-month follow-up (end of treatment) and anticipates completing enrollment as scheduled with continued funding.

Infrastructure Development

The Mycobacteriology Laboratory (NEIGRIHMS) received financial and technical support, enabling installation of:

- -80° Freezer
- Barcode Label Printer
- Room Temperature Monitor
- Miscellaneous culture and LPA supplies





PGIMER
Chandigarh



Dr. A. N. Aggarwal, MBBS, MD, DM, Professor and Head, Principal Investigator, is full-time faculty, and heads the Department of Pulmonary Medicine. He has published more than 500 scientific papers in national and international journals that have been cited more than 23000 times with a h-index of 79. He is a Fellow of the American College of Chest Physicians, Indian Chest Society, and National College of Chest Physicians (India). He has been awarded the Fogarty Fellowship under AIDS and TB International Training Program (AITRP), and is a recipient of the JALMA Trust Fund Orator Award of the Indian Council of Medical Research.

MISSION

To advance pulmonary medicine through research, innovation, and clinical excellence, enhancing diagnostics and patient care in pulmonary function testing, bronchoscopy, sleep medicine, and respiratory intensive care.

VISION

To be a global leader in pulmonary medicine, shaping the future of respiratory healthcare through transformative research and the development of innovative diagnostic protocols and treatment strategies.

ABOUT THE INSTITUTION & CAMPUS

The Postgraduate Institute of Medical Education and Research (PGIMER) is a renowned public medical university located in Chandigarh, India. As a premier institute, it offers comprehensive educational, medical research, and training facilities across all specialties, super-specialties, and sub-specialties. PGIMER is recognized as the leading tertiary care hospital in northern India. At present there are 160 speciality and super-speciality OPDs and numerous laboratory facilities serving patients nation-wide from all walks of society. PGIMER has satellite centers in Sangrur, Punjab, and Una, Himachal Pradesh.

PGIMER focuses on research addressing rural and community health issues, tackling diseases such as malaria, TB, HIV, leprosy, cancer, and more. Advanced techniques like flow cytometry, chromatography, and genetic studies are used for research. A BSL-III lab for mycobacteria is being built, and new bio techniques like LC-MS and genome sequencing have been introduced in the CSIC research block.

RESEARCH FOCUS AREAS

Department of Pulmonary Medicine is the "WHO Collaborating Center for Research and Capacity Building in Chronic Respiratory Disease" Particular focus on pulmonary function testing, interventional pulmonology, diffuse lung disorders, chronic respiratory diseases, respiratory intensive care, and pulmonary infections (including tuberculosis).

RePORT INDIA STUDIES

- RePORT India Phase II Common Protocol

ACHIEVEMENTS & DEVELOPMENT**Personnel Training**

All Project staffs were trained on HSP, GCP. Laboratory staffs were trained on MGIT culture, GeneXpert, PBMC isolation, sample transportation and shipment.

Laboratory Facilities

State of the art technologies for various diagnostic modalities are available in PGIMER like 384 slice dual source CT scan, Advanced PET and CT facilities, Advanced Metabolic and Genetic laboratories, Advanced Mycobacteriology laboratories, etc.

Publications

1. Development and assessment of a novel magnetic nanoparticle antibody-conjugate and aptamer-based assay (MNP-Ab-Ap assay) for the rapid diagnosis of pleural tuberculosis
2. MPT51-based assay performed the best with 66.6% sensitivity and 95.4% specificity for diagnosing pleural tuberculosis provided an incremental advantage over the existing diagnostic algorithm.
3. Evaluation of Mycobacterium tuberculosis derived cell-free DNA using pleural fluid and paired plasma samples for the diagnosis of pleural tuberculosis
4. A novel cell-free M. tuberculosis DNA probe-based-qPCR assay was developed for the diagnosis of pleural tuberculosis. This provided incremental advantage over existing diagnostic algorithms.
5. Xpert MTB/RIF Ultra versus Xpert MTB/RIF for diagnosis of tuberculous pleural effusion: A systematic review and comparative meta-analysis
6. Meta-analysis and meta-regression were performed through hierarchical summary receiver operating characteristic (HSROC) modeling to evaluate comparative performance of the two tests in diagnosing pleural tuberculosis. Xpert MTB/RIF Ultra provides superior diagnostic accuracy over Xpert MTB/RIF, mainly because of its higher sensitivity.
7. Active pulmonary tuberculosis and coronavirus disease 2019: A systematic review and meta-analysis
8. The pooled estimate for proportion of active pulmonary tuberculosis was 1.07% among COVID-19 patients. COVID-19 patients with active tuberculosis have a significantly higher risk of severe disease (1.46 times) and mortality (1.93 times).
9. Diagnostic accuracy of TB-LAMP assay in patients with pulmonary tuberculosis: a case-control study in northern India
10. TB-LAMP and Xpert MTB/RIF were positive in 21.1% and 22.5% of the samples, respectively. The TB-LAMP assay showed a good sensitivity (82%) and specificity (96.8%) for detection of M. tuberculosis.

PGI Team





Department of Virology & Biotechnology ICMR-NIRT

MISSION & VISION

The vision of the Central Biorepository is to serve as a central hub for storing well-characterized, high-quality biological specimens to facilitate groundbreaking medical research leading to the development of new diagnostics, therapeutics, and personalized medicine approaches for tuberculosis. The mission is to provide invaluable biospecimens to a broad research community for undertaking path-breaking research in tuberculosis while maintaining rigorous quality control and ethical principles.

ABOUT THE INSTITUTION & CAMPUS

ICMR-National Institute for Research in Tuberculosis, a permanent Institute under the Indian Council of Medical Research (ICMR), is an internationally recognized institution for Tuberculosis (TB) research. As the fight against tuberculosis continues, it is expected that the efforts of ICMR-NIRT will continue to throw light on the changing principles of chemotherapy and allied aspects of tuberculosis.

The RePORT India Central TB Biorepository was initially set up within the main campus of the ICMR-National Institute for Research in Tuberculosis (NIRT), Chennai, during Phase I of Common Protocol. The Central Biorepository subsequently moved to its permanent location in a new composite research facility at ICMR-NIRT Thiruvallur campus, which was dedicated to the service of the Nation on 25 February 2024.

OBJECTIVES OF THE CENTRAL BIOREPOSITORY

- To receive, curate, store and manage samples received from the RePORT India Clinical Research Units across India in appropriate storage conditions.
- To retrieve and disburse samples to researchers with approved concept sheets and required regulatory approvals.
- To implement a quality management system to achieve the defined objectives of the Central Biorepository.



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HOD, Dept. of Virology & Biotechnology, ICMR-NIRT



Murugesan S
Technical Officer, Dept. of Virology & Biotechnology, ICMR-NIRT



Sathyamurthi P
Technical Officer, Dept. of Virology & Biotechnology, ICMR-NIRT



Dr. Amsaveni S



CENTRAL BIOREPOSITORY – PHASE I

The Central Biorepository was set up with support from the Department of Biotechnology (GOI), and started its operations in April 2017. Biospecimens were collected from two prospective observational cohorts of participants – (i) Newly diagnosed TB patients (including paediatric TB, extra-pulmonary TB and multi-multi-drug resistant TB – Cohort A) and (ii) Healthy Household Contacts (HHCs – Cohort B) of TB patients, at the Clinical Research Sites of the RePORT India Consortium and shipped to the Central Biorepository for long term storage.

The total number of biospecimens archived during Phase I of Common Protocol in the Biorepository was 127,752 vials of various kinds of specimens including plasma, serum, saliva, sputum *Mycobacterium tuberculosis* isolates, peripheral blood mononuclear cells (PBMC), DNA, RNA, QuantiFERON supernatants and urine from Cohort A and 96,046 vials from Cohort B. The sample inventory and chain of custody was managed using a cloud-based data management system (FreezerPro).

CENTRAL BIOREPOSITORY – PHASE II

With the progress of RePORT India into Phase II of its existence, the Central Biorepository expanded scope and capacity to meet the needs of the expanding activities of the Consortium. Sample collection is ongoing for Phase II.

ACHIEVEMENTS & DEVELOPMENT**Key Achievements**

- Established a fully operational Biorepository with over 220,000 biospecimens archived
- Successfully relocated the facility to Thiruvallur campus with enhanced capacity
- Implemented a robust quality management system for specimen integrity
- Integrated real-time temperature monitoring and cloud-based inventory tracking



Infrastructure Development

- Cryogenic storage including ultra-low deep freezers and liquid nitrogen tanks
- Advanced real-time temperature monitoring and security systems
- BSL laboratory with autoclave and effluent treatment facilities
- Record storage and inventory management systems

PERSONNEL TRAINING

- Study Protocol and Manual of Operating Procedures (MOP)
- Quality and safety of clinical trials and laboratory processes
- GCP, GCLP, and HSP certifications
- IATA (International Air Transport Association) training
- FreezerPro for specimen inventory management
- Wireless temperature monitoring system training

Training Imparted to RePORT India CRUs

- PBMC Isolation and Cryopreservation
- 3rd and 4th Generation QuantiFERON assays

FACILITIES

- Cryogenic equipment such as ultra-low deep freezers and liquid nitrogen storage systems
- Dry shipper
- Cryopod
- Vicell automated cell counter
- Real-time temperature monitoring units
- Fire safety alarms
- Oxygen monitors
- Access control
- CCTV surveillance
- Back-up generator
- BSL laboratory
- Autoclave
- Effluent treatment plant
- Record storage room
- Walk-in cold room
- Supplies stock room

Biorepository Facilities

Power Back Up System

Uninterrupted Power Supply

Capacity	20 KVA — 2 Nos
Location & No of Points Connected	
Reception	9
BSL 2 lab	17
AHU corridor	3
Biorepository 1 & 2	35 & 32

Automatic Diesel Genset

Capacity	625 KVA
Fuel tank capacity	100 L
Fuel burning per hour	70L/H half load 100 L/H full load
Time to start	15 seconds
Fuel stock	2 barrels at 200 L each
Mode	Auto

Safety & Security

Air Handling Unit

ID No	Servicing	CFM	TR
AHU-1	BSL-2 Lab	1900	7
AHU-2	Biorepository 1	2300	8
AHU-3	Biorepository 2	2300	8
AHU-4	Corridor	5300	15

Fire Alarm

Area	No of Alarms
Reception	2
Corridor-Front	1
Biorepository Room 1&2	2 (Each one)
Corridor-Back	1

CCTV Surveillance

Room	Camera No	HDMI No
Reception	1	1
Ground Floor Corridor	2	1
Biorepository 1	3&4	2
Biorepository 2	5&6	2
BSL-2	7	1
Ground Floor Autoclave Area	8	1
Ground Floor Service Lift	9	1

Access Control Systems

Location	No of Access Control
Ground Floor	Biorepository Room 1
	Biorepository Room 2
	Biorepository 2
	35 & 32
	Desktop, WiFi, TMS, LN2 freezers

Wireless Temperature Monitoring

Units Connected	Biorep Room 1	Biorep Room 2
-80c Freezers	11 Nos	-
LN2 Freezers	6 Nos	-
Room Temp & Humidity	1	1

JIPMER

Vision

To advance tuberculosis research through a collaborative and data-driven approach, fostering scientific discovery and improving public health outcomes in India and beyond.

Mission

- To strengthen multi-institutional partnerships for high-impact TB research.
- To facilitate data and biospecimen sharing to drive innovative discoveries.
- To support evidence-based interventions for TB prevention and treatment.
- To integrate cutting-edge methodologies in data management and analysis.

About the Institution & Campus

Jawaharlal Institute of Postgraduate Medical Education & Research (JIPMER) is a premier medical institution in India, established in 1823. It stands as a center of excellence in medical education, research, and patient care. The campus boasts state-of-the-art laboratories, an advanced medical research center, and a dedicated Data Coordination Unit that supports multi-site clinical studies. In 2019, JIPMER was designated as the Data Coordinating Center (DCC) for RePORT India Phase II, following SAS CHRD's role as the Data Management Center in Phase I.

Role of the Data Coordinating Center (DCC)

As the Data Coordinating Center, JIPMER plays a crucial role in ensuring data integrity, harmonization, and efficient study management across multiple sites. The DCC has been at the forefront of developing and implementing standardized data management practices, ensuring consistency, completeness, and accuracy across the consortium's studies.

Key Contributions of the DCC

- Standardizing case report forms (CRFs) and data dictionaries across sites.
- Implementing rigorous data validation checks using REDCap.
- Coordinating sample tracking across multiple clinical sites using FreezerPro.
- Conducting training programs for site teams on best practices in data entry, management, and compliance.
- Providing data-driven insights for study design and statistical analysis.



Dr. Sonali Sarkar, MBBS, MD
Professor and Principal Investigator



Personnel Training

- Conducted multiple training sessions on REDCap for multi-site data entry and validation.
- Organized workshops on advanced statistical methods for TB research.
- Hosted capacity-building programs for biostatisticians and data managers.

Key Achievements

- *Digital Transformation in Data Coordination:* Implementation of enhanced REDCap workflows and real-time monitoring to improve data accuracy and streamline multi-site collaboration.
- *Capacity Building:* Conducted training programs for clinical and data management teams to enhance research efficiency and compliance.
- *Expanding Research Horizons:* Strengthened collaborations with international consortia, fostering cross-border data sharing and multi-disciplinary research.
- *Harmonization of TB Research Data:* Successfully harmonized multi-site TB research data, ensuring standardization and consistency.
- *Robust Data Monitoring & Quality Control:* Established a robust data monitoring and quality control system using REDCap & automated QC checks.
- *Biomarker Evaluation Tools:* Contributed to the development of analytical tools for biomarker evaluation in TB.

Infrastructure Development

- Expanded the data management unit with high-speed servers and secure data storage.
- Upgraded FreezerPro for biorepository management across RePORT sites.
- Implemented cloud-based analytics for real-time monitoring of study progress.





JUNIOR INVESTIGATOR ABSTRACTS



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TITLE	INVESTIGATORS
Increased CD158b/KIR2DL+ and TGIT+ NK cells at baseline in HHCs who progress to ATB	Vara Lakshmi Mallidi , Anvesh Kumar Bogam, Venkata Sanjeev Kumar Neela, Padmaja Paidipally, Rajesh Radhakrishnan, Mohammad Soheb Ansari, Sindhu Joshi, Ramakrishna Vankayalapati, Vijaya Lakshmi Valluri, Kamakshi Prudhula Devalraju
MicroRNA-1246 regulates macrophage lipid metabolism and involved in innate resistance to <i>Mycobacterium tuberculosis</i> infection in household contacts of TB patients	Ashutosh Tripathi, Venkata Sanjeev Kumar Neela, Kamakshi Prudhula Devalraju, Anvesh Kumar Bogam, Tanmoy Mukherjee, Rajesh Kumar Radhakrishnan, Varalakshmi Mallidi, Abhinav Vankayalapati, Mohammad Soheb Ansari, Carlos Arana, Sindhu Joshi, Karan P Singh, Vijaya Lakshmi Valluri, Ramakrishna Vankayalapati, Deepak Tripathi
Integrative transcriptomic profile of household contacts of tuberculosis patients: Insights into TB disease progression	Evangeline Ann Daniel , Sathyamurthi Pattabiraman, Brindha Bhanu, Amsaveni Sivaprakasam, Mandar Paradkar, Vandana Kulkarni, Rajesh Karyakarte, Shri Vijay Bala Yogendra Shivakumar, Vidya Mave, Amita Gupta, Luke Elizabeth Hanna
Impact of anemia on pulmonary tuberculosis: A cross-sectional analysis of clinical and microbiological characteristics	Abilasha Narayanan , Anusuya Govindan, Anandhi Annasamy, Komala Ezhumalai, Senbagavalli Prakash Babu, Jerrold Ellner, Padmini Salgame, Prakash Babu Narasimhan, Sonali Sarkar
Comparison of Programmatic Truenat MTB Plus and Xpert Ultra in presumptive patients recruited for TB diagnostic studies	Reena Sekar , Kingsley Manoj Kumar S, Kinari Shah, Balamugesh Thangakunam, Reginald George Alex, DJ Christopher

Increased CD158b/KIR2DL+ and TGIT+ NK cells at baseline in HHCs who progress to ATB

Presenting Author: Vara Lakshmi Mallidi, Lab member
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Equal contribution.

Key Words: Mycobacterium tuberculosis, Latent TB, TB progressors, Biomarkers, NK cells

Primary Category: Basic Science

Background and Rationale: Tuberculosis (TB) remains a social and public health threat in almost all developing countries. Identification of the risk factors, tailored to reflect local disease epidemiology in high-burden countries, is key to controlling the global TB epidemic. We have previously showed that Mtb modulates host immune responses, during infection by affecting cell phenotypes. The lack of reliable biomarkers for progression to TB has hindered TB management and drug development. In household with active TB index case, following exposure to Mtb, almost 90% of immunocompetent adults establish an asymptomatic, latent TB infection (LTBI), which carries a 5–10% life-time risk of reactivation disease. Early detection is essential since progression of the disease occurs during the period of diagnostic delay. Understanding the basis for the increased susceptibility of HHCs to developing

TB is likely to lead to improved vaccines and immunodiagnostics. Several clinical studies have explored the potential association between peripheral blood NK cell counts and resistance or susceptibility to tuberculosis.

Methods: Healthy HHCs (N=600) were recruited and followed at regular intervals (0, 6, 12, 18 and 24 months) for 2 years for development of latent (LTBI) or active TB (ATB). After 2 years, depending on the outcome (so far N=92 met study outcomes), were categorised into TB progressors (N=9), non-converters (LTBI- remain LTBI-), non-progressors (LTBI+ remain LTBI+). Blood was collected, peripheral blood mononuclear cells (PBMCs) were isolated and flow cytometry was used to identify various immune cell populations, (NK, macrophage and T-cell subpopulations including T-regulatory cells). Remaining PBMC were cultured with ESAT-6 and CFP-10. The culture supernatants were collected to measure cytokine and chemokine levels by ELISA.

Continued: Increased CD158b/KIR2DL+ and TGIT+ NK cells at baseline in HHCs who progress to ATB

Results: HHCs who developed ATB on follow-up had significantly high CD158b/KIR2DL+ and TGIT+ NK cells at baseline compared to those who never developed Active or Latent TB and LTBI+ HHCs who remained LTBI+. Cytokine and chemokine levels in culture supernatants of ESAT-6 and CFP-10 cultured PBMC and plasma hormone levels will be determined to understand the physiological significance of CD158b/KIR2DL+ and TGIT+ NK cells in development of ATB. Data from additional donors will be included in discussion during the meeting.

Conclusions and Recommendations: Increased percentages of CD158b/KIR2DL+ and TGIT+ NK cells in PBMC of HHCs of TB patients can serve as biomarkers to identify, healthy HHCs those likely to develop ATB later time.

Funding: This study was supported by DBT-CRDF and NIH as a part of RePORT India consortium.

MicroRNA-1246 regulates macrophage lipid metabolism and involved in innate resistance to *Mycobacterium tuberculosis* infection in household contacts of TB patients

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Equal contribution

Continued: MicroRNA-1246 regulates macrophage lipid metabolism and involved in innate resistance to *Mycobacterium tuberculosis* infection in household contacts of TB patients

Affiliated RePORT CRU: Number 107, Immunology and Molecular Biology Department, Bhagwan Mahavir Medical Research Centre, Hyderabad, India and Saint Louis University, Saint Louis, MO, USA

Key Words: Tuberculosis, household contacts, microRNA, immune responses and metabolism

Primary Category: Basic Science

Background and Rationale: A significant proportion of household contacts (HHCs) remain resistant to tuberculosis (TB) despite prolonged exposure. This resistance is associated with several factors, including immune responses, metabolites, and genetic variations. However, the role of microRNAs (miRNAs) in the resistance to or development of latent or active TB is still not clear.

Methods: Household contacts (HHCs) of pulmonary TB patients in Hyderabad, India, were enrolled, HHCs with immunosuppressive conditions were excluded from the study. PBMCs and CD14⁺ macrophages were isolated for functional assays, RNA sequencing, and differential gene expression analysis were performed. Additional experiments included transfection of miRNA mimics/inhibitors, Seahorse XF metabolic assays, LC-MS/MS for protein quantification, and BODIPY staining for lipid analysis.

Results: We determined whether miRNAs regulate resistance to *Mycobacterium tuberculosis* (Mtb) infection in HHCs of TB patients. We recruited 460 healthy HHCs belonging to index cases with active pulmonary TB. Among them 293 (64.8%) remained IGRA-negative throughout a two-year follow-up with assessments conducted at four-month intervals. Transcriptome sequencing at baseline and follow-up and confirmation studies identified hsa-miR-1246 (downregulated) and hsa-miR-125b (upregulated) as potential candidates in the development of resistance in non-converters compared to converters and progressors. Mechanistic studies showed that hsa-miR-1246 regulates lipase activity in monocyte-derived macrophages (MDMs) by targeting proteins involved in acylglycerol metabolism, including alpha/beta hydrolase domain-containing protein 2 (ABHD2) controlling lipid metabolism and intracellular Mtb growth. We identified that inhibiting hsa-miR-1246 reduced Mtb growth within MDMs by modulating lipase activity via ABHD2 by increasing glycolytic activity and promoting a metabolic shift in macrophages conducive to pathogen clearance, suggesting its critical role in metabolic regulation and resistance to Mtb infection.

Conclusions & Recommendations: We found that microRNA-1246-in LTBI nonconverters regulates lipid metabolism of Mtb infected macrophages and resists Mtb infection. These findings highlight potential miRNA-based therapeutic strategies to enhance immunity against Mtb.

Integrative transcriptomic profile of household contacts of tuberculosis patients: Insights into TB disease progression

Presenting Author: Evangeline Ann Daniel, PhD Student
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Affiliated RePORT Team: C-TRIUMPH team

Key Words: Tuberculosis, progression, RNA sequencing, lncRNA, miRNA

Primary Category: Diagnostics & Laboratory

Background and Rationale: The identification of individuals with the greatest risk of progression to active tuberculosis (TB) disease from the huge reservoir of *Mycobacterium tuberculosis* (*Mtb*) infected individuals continues to remain an arduous ascent in the global effort to control TB. Whole blood transcriptomics can provide deeper insights into the host's immune response to *Mtb* infection and the progression to active disease. Hence, we aimed to elucidate the differential transcriptomic profile, including miRNA and lncRNA of Progressors and Non-Progressors.

Methods: Among the 1051 HHCs who were followed up for two years in the C-TRIUMPH cohort study, 8 HHCs who developed active TB (Progressors) and 10 HHCs who remained healthy (Non-Progressors) were included for the present analysis. Total RNA sequencing was performed in the Progressors at the time point closest to TB activation using Illumina Novaseq 6000. Significant differentially enriched genes (DEGs) were identified with p value < 0.05 and log₂Fold Change ≥ 1 or ≤ -1.

Pearson correlation analysis was performed for significant mRNA (p value < 0.05 & log₂FC > or < -1) and significant Known and Novel lncRNA (p value < 0.05 & log₂FC > or < -1) with a correlation threshold > 0.7. Functional enrichment analysis was performed by Gene ontology.

Results: Transcriptome analysis identified 410 differentially expressed genes (157 upregulated and 253 downregulated) between the Progressors and Non-progressors. lncRNA analysis revealed 1680 known and 113 novel significantly different lncRNAs between the Progressors and Non-Progressors. Functional enrichment analysis of the significantly dysregulated mRNAs and lncRNAs revealed upregulation of chemokine mediated signaling pathways and downregulation of interferon signaling pathways. Correlation of this data with our previously identified differentially expressed miRNAs revealed 1109 miRNA-mRNA pairs.

Conclusions: The present analysis provides further evidence to support the significant role of chemokine and interferon pathways in TB disease progression. Further, identification of biomarkers and biosignatures from this integrative data can pave way for the development of a predictive biosignature for TB disease progression.

Impact of anemia on pulmonary tuberculosis: A cross-sectional analysis of clinical and microbiological characteristics

Presenting Author: Abilasha Narayanan, Site Coordinator, JIPMER, RePORT India

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Key Words: Anaemia, Tuberculosis, Hematological Abnormalities, Socio-demographic Factors, Nutritional Status, Risk Factors

Primary Category: Epidemiology

Background: Anaemia is a common comorbidity among pulmonary tuberculosis (PTB) patients, potentially influencing disease outcomes. This study aims to evaluate the baseline demographic characteristics, radiological and microbiological profiles, and haematological parameters associated with anaemia in TB patients.

Methods: A cross-sectional analysis was conducted on 1,245 TB patients categorized into anaemic (n=865) and non-anaemic (n=380) groups. Baseline demographics, clinical, microbial characteristics, and laboratory parameters were compared using chi-square tests and t-tests. Logistic regression models identified factors independently associated with anaemia.

Results: Anaemia prevalence was 69.5%. It was higher among participants aged <20 years (84.2%), females (73.2%), illiterates (79.1%), unemployed individuals (78.6%), and those with income <3000 rupees (78.7%). Anaemia was associated with underweight status (77.3%), abnormal white blood cell counts (76.7%), abnormal platelet counts (84.1%), and abnormal lymphocyte levels (76.3%) (all p<0.001).

Radiological findings showed higher mean X-ray scores among anaemic patients (27.9 ± 13.9) compared to non-anaemic patients (21.8 ± 12.9) (p=0.002). Cavitation was more prevalent in anaemic patients (71.2%) than in non-anaemic patients (28.8%) (p=0.004). Regarding microbiological outcomes, smear conversion rates were higher in anaemic patients (67.3%) compared to non-anaemic patients (32.7%) (p=0.161), while unfavourable outcomes were more common among anaemic individuals (74.4%) Vs. non anaemic individuals (25.6%) (p=0.021).

Conclusions: Anaemia is highly prevalent among TB patients, especially in specific demographic groups, those with abnormal hematological parameters, and significant radiological findings. Routine screening and management of anaemia could improve TB outcomes.

Recommendations: Incorporating iron status assessments and addressing anemia through nutritional interventions could enhance TB management and recovery. Early intervention strategies may enhance treatment outcomes and reduce complications associated with anaemia.

Comparison of Programmatic Truenat MTB Plus and Xpert Ultra in presumptive patients recruited for TB diagnostic studies

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Key Words: Truenat MTB Plus; Xpert Ultra; Sensitivity; Specificity; Diagnosis

Primary Category: Diagnostics & Laboratory

Background: Molbio Truenat MTB Plus assay is used as a point of care test to diagnose TB in several parts of India. We conducted a study in a Secondary Care Centre (Chittoor Campus of CMC, Vellore) in Andhra Pradesh, India for TB diagnosis where we collected separate sputum samples for processing Xpert Ultra (1) and MGIT culture (2). In this centre, Truenat MTB Plus assay was performed as a standard of care. The primary objective was to assess Truenat MTB plus yield with culture (MGIT) and Xpert Ultra yield with culture (MGIT) and assess the differences in sensitivity and specificity.

Methods: We consecutively enrolled participants with presumptive TB at the Secondary Care Centre (Chittoor), from Oct 2023 to Nov 2024. We collected sputum sample for Xpert Ultra and Culture (MGIT) as part of an ongoing diagnostic research study. Truenat MTB Plus assay on sputum was performed as a standard of care. We assessed the overall diagnostic accuracy programmatic Truenat MTB Plus and Xpert Ultra in reference to Culture results (MGIT).

Results: Among 109 enrolled participants (median age 54, IQR 41-65, 34.9% female, 30.3% PLWD, 0.9% PLHIV), 15 participants (13.8%) were MGIT culture positive). The sensitivity of Truenat MTB Plus was 100% (95% CI 78.2-100), comparable to Xpert Ultra, with a sensitivity of 100% (95% CI 78.2-100). The specificity of Truenat MTB Plus was 94.7% (95% CI 88.0-99.3). Xpert had a slightly higher specificity of 97.9% (95% CI 92.5-99.7). The difference in specificity between Truenat MTB Plus and Xpert Ultra was 3.2% (95% CI -1.8-8.1, p=0.21) and not significant.

Discussion: Our findings demonstrate that Truenat MTB Plus has equivalent sensitivity and comparable specificity to Gene Xpert Ultra. The scale-up of Truenat MTB Plus in community health care and peripheral settings can assist in the quick diagnosis of TB patients.

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GRANTS & SUBSTUDIES



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RePORT International G CFAR Supplemental Funded Projects

TITLE	PARTNERS	CRDF #	START DATE	INVESTIGATORS
Predictors of Resistance Emergence Evaluation in MDR-TB Patients	Hinduja, Fiotech, Boston U, Rutgers U, Vanderbilt U	RiCC	2024	Arora PR, Ridolfi F, Y. Gao, C. R. Horsburgh, C. Rodrigues, V. C. Rolla, H. Safi, T. Sterling, and the Hinduja-RePORT Brazil team
Metabolites, inflammation, T2DM and tuberculosis patients	ICMR, Saint Louis U, DLSMHSI, U of Texas	RiCC	2024	Pavan Kumar N, Radhakrishnan RK, Yu C (RePORT Philippines), A. Aquino, K. Singh, R. Vankayalapati.
Evaluating the clinical utility of a novel RNA-based assay for predicting TB treatment outcomes and diagnosing paucibacillary TB	Weil Cornell, BJGMC, JHU, Makerere U, Oxford U	RiCC	2024	Zainabadi K, Joloba M, Karyakarte R, Nasinghe E, Paradkar M, Pradhan N, F. Basile, J. Ellner, A. Gupta, D. P. Kateete, M. H. Lee, V. Mave, R. Song and the BJMC team
Local Capacity Building to Develop Novel Drug- Resistant TB Testing and High-Throughput Multiplex Protein Measurement Programs in Pune, India	BJGMC	RiCC	2023	
RePORT India Consortium Strengthening Equipment Funding	BJGMC, Hinduja	RiCC	2023	Tornheim J, Udawadia Z, Ashavaid T, Rodrigues C, and the BJMC team
TB-RiCC Laboratory Enhancement and Capacity Building	JIPMER	RiCC	2023	
IFN γ -independent T cell-mediated protection in Mycobacterium tuberculosis infection	Rutgers, JIPMER, BJGMC, JHU	RiCC	2023	
Innovative Modelling for Predicting TB Treatment Outcomes in Global Cohorts	JHU, FIOTEC, Vanderbilt U, RePORT India, RePORT Brazil	RiCC	2022	Krishnan S, Robinson M, Andrade B, Sterling T, Gustavo, Gupta A, Gupte N, RePORT India, RePORT Brazil
Impact of Latent TB Infection and Trained Immunity on Susceptibility to SARS-CoV-2 Infection in India and the Philippines	Rutgers, JIPMER, U of Philippines Manila	RiCC	2021	Salgame P, Sarkar S, Marissa AM (RePORT Philippines)
Associative BRICS Research in COVID-19 and Tuberculosis (ABRICOT)	FIOTEC, Wits Health Consortium, NIRT-ICER	RiCC	2021	
Signature of Profiling and Staging the Progression of TB from Infection to Disease	JIPMER, BU	RiCC	2020	

RePORT International G CFAR Supplemental Funded Projects

Continued

TITLE	PARTNERS	CRDF #	START DATE	INVESTIGATORS
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
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
Pharmacokinetic Assessment of MDR-TB Drugs in the Treatment of TB Meningitis	JHU, PD Hinduja, Beijing Chest Hospital, BJG MC, Wits Health	65351	2020	Tornheim JA, Ashavaid T, Rodrigues C, Udwardia Z, Duan H, Sangle S, Varaiava E, Dooley K, Ignatius E, Mave V, Gupta A, Shivakumar SVBY, Chawla P, Patil S, Kulkarni V
Inflammasome Genetics and TB Treatment Outcomes	UPenn, JHU, UMass, BU, NIRT, MVDRC, BGJMC	65375	2020	Bisson G, Gupte A, Viswanathan V, Gupta A, Kornfeld H, Hanna L, Babu S, Andrade B, Dhanasekar an M
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
Determination of Efficacy of Xpert PCR Ultra And Transcriptional Signatures In The Diagnosis of Pleural Tuberculosis	CMC, Vellore G University of Cape Town, SA	64074	2018	Christopher DJ, Keertan D
Validation of Transcriptional Signature to Predict Active TB Disease among Advanced HIV Patients	RePORT Brazil, BMC, BJGMC, JHU, Rutgers	63158	2017	Mave V, Rolla V, Salgame P, Kadam D, Andrade B, Gupta A, Meshram S, Kulkarni V, Ellner J
Molecular Signatures of Tuberculosis- Diabetes Interaction (MSTDI) Study	JHU, UMass, BJGMC, NIRT, BU, 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
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
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

RePORT International G CFAR Supplemental Funded Projects

Continued

TITLE	PARTNERS	CRDF #	START DATE	INVESTIGATORS
MDR-TB and HIV at RePORT Sites India	BJGMC, NIRT, JIPMER, JHU, BMC	63076	2016	Horsburgh R, Padmapriyadarsini C, Mave V, Gupta A, Sarkar S
Validation and Fine Tuning of the Computer Aided Diagnosis of Pulmonary TB Model for the Indian Subcontinent	CMC	62922	2016	Christopher DJ, Thangakunam B, Lal B, Agrawal A
Extracranial Involvement as Detected by Positron Emission Tomography Scan in Patients with Tubercular Meningitis	CMC	62906	2016	Thangakunam B, Christopher DJ
Inflammatory Biomarkers as a Triage Test for Screening Symptomatic TB	JIPMER, Rutgers, BMC	63466	2016	Ellner J, Salgame P, Sarkar S, Pleskunas J
Characterization of Monocyte Responses in Pulmonary TB Patients with or without Type 2 Diabetes	NIRT-NIH – ICER, MVDRC	62911	2016	Kumar P
Effect of Malnutrition on Latent TB	Approved: JIPMER, Rutgers, BMC,	23719	2016	Hochberg NS, Negi VS, Mahalakshmy T, Johnson WE, Salgame P, Pleskunas J
Determining Barriers to TB Care	JIPMER, BMC/BU	64020	2016	Sabin L, Sarkar S, Hochberg NS, Fernandes P, Pleskunas J, Amsaveni
TH17 Cell Subsets as Potential Risk Markers of Latency and Active TB Infection in Household Contacts	BMMRC, SLU	62916	2016	Devalraju KP, Neela VSK, Valluri VL, Vankayalapati K
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

Grants Awarded

GRANT TITLE	PARTNERS	GRANT SOURCE	START DATE
Interleukin-6 signaling, lung injury and post-TB lung disease in TB/HIV	CMC, BJGMC, BU, JHU	NIH R01	2024
Nutritional Interventions to End Tuberculosis among persons with HIV in India (NUTRIENT-India)		NIH K01	2023
Baseline pRescription According to Direct from Sputum Sequencing and TArgeted drug Concentration Strategy	Hinduja, JHU, UCT, UCSD, Vanderbilt	NIH R01	2023
Multiplexed Detection of Cell- free M. Tuberculosis DNA and Its Drug-resistant Variants in Blood	Hinduja, JHU, Tulane	NIH R01	2023
InTGS: Whole Genome Sequencing of MTB Clinical Strains for Determining Drug Resistance and Strain lineage in India: A Structured Nationwide approach	JIPMER, NII, ICGB, CCMB, NIBMG, BMMRC, BJGMC, PGI, Hinduja, NIRT	DBT, India	2023
Learning Effect of Parasites and Reinforcing Diets on TB (TB-LEOPARD)	JIPMER, BU	Burroughs-Wellcome Fund	2022
Childhood 'Omics' and Mycobacterium tuberculosis- derived BLOsignatures (COMBO) for TB Diagnosis	UCSF, BJGMC	NIH R01	2021
A Nanopore Biosensor for Leveling MTB Antigens in Blood	Tulane, JHU, BJGMC	NIH R01	2021
Rapid Research for Diagnostics Development in TB Network	CMC Vellore, UCSF	NIH/NIAID R01	2021
Innate Immune Response of LTBI+HIV+ Children	BMMRC, SLU	NIH/NIAID R01	2021
Learning about Experience with Nutritional Supplementation in Tuberculosis (LENS): An Exploratory Study	JIPMER, BU	Boston University of India (Seed Grant)	2021
Understanding Mycobacterium tuberculosis Mediated Host Metabolomics in Pulmonary Tuberculosis: Correlation with Disease Severity and Treatment Course	JIPMER IISER, Pune	PEER Women in Science SEED Grants 2021: National Academies	2021
Hybrid Trial for Alcohol Reduction among People with TB and HIV in India (HATHI)	BJGMC, JHU, London School of Hygiene and Medicine, DY Patil	NIH NIAAA R01	2020

Grants Awarded *Continued*

GRANT TITLE	PARTNERS	GRANT SOURCE	START DATE
VITAL TB (Vitamins And Latency in Tuberculosis)	JIPMER, BU	U.S. Department of State's Partnership 2020 educational initiative	2020
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, SLU	R01	2020
Host and Microbiome Transcriptional Profiling in the Upper Airways for TB Susceptibility	JIPMER	CTSI Pilot Grant, BU, US	2020
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
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
Evaluation of Diagnostic Potential of Aptamer-based Assays for Pulmonary Tuberculosis: A Pilot Study	CMC	THSTI	2019
Tuberculosis: Learning the Impact of Nutrition (TB LION)	JIPMER, BMC, Rutgers, Tufts, NIRT	Warren Alpert Foundation	2018
Whole Genome Sequencing of Drug Resistant Tuberculosis in India: Genotype-Phenotype Correlation, Clinical Impact of Resistance, and Sequencing Directly from Sputum	Hinduja, JHU	NIH/NIAID K23	2018
Validating a Th17 Switch as a Novel Correlate of Protective Immunity to TB	NIRT, BJMC, IISc, Bangalore, JHU	DBT/ IISc	2018
Characterization of Genomics and Metabolomics among Individuals (TB-GWAS)	Emory, JHU, BJGMC, JIPMER, BMMRC, NIRT, PHRU, McGill	NIH/NIAID R01	2018
Prevalence of Latent Tuberculosis in Rheumatoid Arthritis and Ankylosing Spondylitis	CMC	Internal fluid research grant	2018

Grants Awarded *Continued*

GRANT TITLE	PARTNERS	GRANT SOURCE	START DATE
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
Validation of Indigenously Developed Technology (TruNat MTB) for Diagnosis of Extra-pulmonary Tuberculosis: Multi-centric Validation	CMC, Hinduja, NIRT, AIIMS	ICMR	2018
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 of India	2017-2022
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	2017
Transcriptomic and Metabolomic Analysis of Microbiologically Confirmed Pediatric Tuberculosis Patients and Uninfected Household Contacts	BJGMC, JHU	Ujala Foundation Wyncote Foundation BWI-CTU C-TRIUMPH	2017-2022
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
Association of Lipid Mediators of Inflammation with TB Treatment Outcomes	JHU, NIRT, BJGMC	CTRIUMPH and Gilead Foundation	2017
The Role of Innate Immunity in the Acquisition of Sterile Protection Against TB Infection	U Colorado, JHU, BJMC	NIH R21	2017
IFN- γ Independent Inhibition of MTB Growth in Human Macrophages	BMMRC, SLU	NIH/NIAID Ro1	2017

Grants Awarded *Continued*

GRANT TITLE	PARTNERS	GRANT SOURCE	START DATE
MDR-TB Free: Monitoring Adverse Effects, Utilizing Resources Optimally, Knowing Resistance Patterns, and Treatment Strategy (MDR TB – MUKT)	Hinduja, JHU	Hinduja	2017
The Role of Monocyte Subpopulation in HIV+LTB+ Individuals and Development of Active TB	BMMRC, SLU	NIH R21 Indo-US Vaccine Program, RePORT India Cohort	2016-2018
Measuring TB Drugs in Hair as a Tool to Monitor Adherence, Exposure and Response	BJGMC, NIRT, JHU	NIH/NIAID: R21	2016-2018
Role of Iron Deficiency in Resistance of Women of Child-Bearing Age to Tuberculosis	JIPMER, BMC	NIH	2016-2017
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
Impact of Immune Changes of HIV and Stages of Pregnancy on TB (PRACHITI)	BJGMC, NIRT, JHU	NIH/NICHD R01	2015-2020
Impact of Pregnancy on Tuberculosis	JIPMER, BMC	NIH/NIAID R01	2015-2018
Residual Respiratory Impairment Following Pulmonary Tuberculosis: The Lung Health Sub-Study	BJGMC, NIRT, JHU	UJALA/ Gilead Foundation/ RePORT India	2015-2017
D4GDI-mediated Immune Responses in LTBI+HIV+ Individuals	BMMRC, SLU	NIH R21 Indo-US Vaccine Program, RePORT India	2015-2017
Understanding of Tuberculosis Infection and Preventive Therapy Among Skin- Test Positive Household Contacts of Tuberculosis Cases	BJGMC, NIRT, JHU	NIH CFAR Fogarty D43	2015
T-regs Mediated Immune Responses in LTBI+HIV+ Individuals	BMMRC, SLU	SLU	2015
Compare Drug Levels in Newly Diagnosed or Relapsed PTB/ EPTB Following Daily ATT vs DOTS Regimen	CMC	Internal fluid research grant	2015
Impact of Personal Exposure to Black Carbon on Pulmonary Tuberculosis Severity	JIPMER BMC	Potts Memorial Foundation	2014-2018
Yield of TB using GeneXpert (Xpert MTB-Rif) by Induced Sputum Compared to Standard Sputum Samples	CMC	Internal fluid research grant	2014

Childhood 'Omics' and Mycobacterium tuberculosis-derived BIOSignatures (COMBO) for TB Diagnosis

Principal Investigators	Population	Funding
Adithya Cattamanchi (UCSF) Joel Ernst (UCSF) Devan Jagannath (UCSF) Aarti Kinikar (BJGMC) Vidya Mave (BJGMC-JHU CRS) Mandar Paradkar (BJGMC-JHU CRS)	BJGMC Pune site will contribute stored samples (plasma, urine) of eligible pediatric participants enrolled in the CTRIUMPH, RICC Pediatric, and TB Elispot studies.	NIAID

Design: We will utilize banked blood and urine specimens among children being evaluated for TB in India, Uganda, South Africa, The Gambia, and Peru. We will measure Mtb-specific proteins and host proteins, and metabolites in the discovery and initial validation set of banked samples from 150 children with Confirmed TB, 150 children with Unconfirmed TB, and 300 children with Unlikely TB per NIH consensus definitions with and without HIV infection.

Aims:

1. Quantify levels of known Mtb proteins using an Electrochemiluminescence (ECL)-based assay ultra-sensitive
2. Perform an untargeted, shotgun proteomic and metabolomic approach to identify host proteins and metabolites that can serve as biomarkers for detection of childhood TB
3. Derive and validate the diagnostic accuracy of Mtb and/or host biosignatures for childhood TB.
 - **Status:** Plasma metabolomic assay completed, analysis ongoing
 - Plasma and urine MTB protein assays- to be completed by mid-2025
 - Proteomic assays are under planning to be performed.

Markers of Lung Impairment in HIV-TB Coinfected Indian Adults

Principal Investigators	Sites	Population	Funding
Akshay Gupte (BU) Amita Gupta (JHU) Sanjay Gaikwad (BJGMC) Rajesh Karyakarte (BJGMC)	BJGMC	1. Adults (>18 years) with drug-susceptible pulmonary TB and HIV co-infection (HIV-TB group). 2. Adults with drug-susceptible pulmonary TB without HIV co-infection (TB group).	TREAT Asia NIAID/amfAR DBT

Design: A retrospective cohort study of already collected clinical samples and data from the CTRIUMPH study at BJGMC. BJGMC, Pune, India

Aims:

1. We will compare the degree of lung impairment between HIV-TB and TB participants at the completion of TB therapy. Lung impairment will be measured by pre-and post-bronchodilator spirometry. The primary outcome will be z-score standardized FEV1 using the Global Lung Initiative (GLI) reference equations. Secondary outcomes will include z-score standardized FVC and FEV1/FVC ratio. We will use linear regression to compare the degree of lung impairment in TB cases with and without HIV, adjusting for potential confounders. With 15 HIV-TB and 30 TB participants, we will have 80% power at 5% significance level to detect a 4.5 or higher percentile difference in lung function parameters between the two groups.
2. We will compare concentrations of inflammatory and metabolomic markers between HIV-TB and TB participants during TB therapy. Marker concentrations will be measured at individual time-points.

Status: Analysis is completed. Manuscript preparation underway.

Inflammasome Genetics and Tuberculosis Treatment Outcomes

Principal Investigators	Sites	Population	Funding
Gregory Bisson (UPenn)	BJGMC	Adults (>18 years) with drug-susceptible	RICC
Amita Gupta (JHU)	NIRT	pulmonary TB enrolled in the	
Akshay Gupte (BU) Luke	MVDRC	CTRIUMPH or EDOTS studies.	
Hanna (NIRT)			
Subash Babu (NIH-NIRT-ICER)			
Vijay Vishwanathan (MVDRC)			
Sanjay Gaikwad (BJGMC)			
Rajesh Karyakarte (BJGMC)			

Design: Retrospective case-cohort analysis of already collected clinical samples and data from the CTRIUMPH and EDOTS studies.

Aims:

1. To determine the association between single nucleotide polymorphisms (SNPs) in candidate genes related to inflammasomes and microbiologic treatment outcomes in adults being treated for drug-susceptible pulmonary TB.
2. To determine the association between SNPs in candidate genes related to inflammasomes and pulmonary involvement in adults who successfully complete treatment for a new diagnosis of drug-susceptible pulmonary TB.

Status: Analysis completed

Molecular Signatures of Tuberculosis-Diabetes Interaction (MSTDI) Study—Metabolomics

Principal Investigators	Sites	Population	Funding
Amita Gupta (JHU) Akshay	NIRT	1. TB with DM (TBDM)	RICC
Gupte (BU) Hardy Kornfeld	BJGMC	2. TB without DM (TB)	
(UMass)	MVDRC	3. DM without TB (DM)	
Rajesh Karyakarte (BJGMC)	RePORT Brazil	4. Healthy controls (HC)	
Padma Chandrasekaran (NIRT)			
Vidya Mave (BJGMC-JHU CRS)			
Bruno Andrade (RePORT Brazil)			

Design: We will conduct a retrospective cohort study using collected demographic and clinic data and archived whole blood samples in the CTRIUMPH study as well as a small cross-sectional study of MTB uninfected adults with DM.

Aims:

1. Compare baseline metabolomic signatures between newly diagnosed drug-sensitive PTB patients with and without DM.
2. Characterize and compare longitudinal change in metabolomic signatures in response to ATT between newly diagnosed drug-sensitive PTB patients with and without DM.

Status: Study completed

Publications:**A multi-center, prospective cohort study of whole blood gene expression in the tuberculosis-diabetes interaction.**

Queiroz ATL, Vinhaes CL, Fukutani ER, Gupte AN, Kumar NP, Fukutani KF, Arriaga MB, Sterling TR, Babu S, Gaikwad S, Karyakarte R, Mave V, Paradkar M, Viswanathan V, Gupta A, Andrade BB, Kornfeld H; RePORT Brazil; RePORT India Consortia. Sci Rep. 2023 May 12;13(1):7769. doi: 10.1038/s41598-023-34847-9. PMID: 37173394

Association of Altered Baseline Hematological Parameters with Adverse Tuberculosis Treatment Outcomes.

Nancy Pandiarajan A, Kumar NP, Moideen K, Thiruvengadam K, Hissar S, Sivakumar S, Bethunaickan R, Viswanathan V, Kornfeld H, Babu S. Pathogens. 2025 Feb 4;14(2):146. doi: 10.3390/pathogens14020146. PMID: 40005523

Molecular Signatures of Tuberculosis-Diabetes Interaction (MSTDI) Study—Transcriptomics

Principal Investigators	Sites	Population	Funding
Amita Gupta (JHU)	NIRT	1. TB with DM (TBDM)	RICC
Akshay Gupte (BU) Hardy	BJGMC	2. TB without DM (TB)	
Kornfeld (UMass)	MVDRC	3. DM without TB (DM)	
Rajesh Karyakarte (BJGMC)	RePORT Brazil	4. Healthy controls (HC)	
Padmapriyadarsini Chandrasekaran (NIRT)			
Vidya Mave (BJGMC-JHU CRS)			
Bruno Andrade (RePORT Brazil)			

Design: We will conduct a retrospective cohort study using collected demographic and clinic data and archived whole blood samples in the RePORT India and RePORT Brazil study.

Aims:

1. Compare baseline whole blood RNA-seq transcriptional signatures between newly diagnosed drug-sensitive PTB patients with and without DM in Pune and Chennai, India and Salvador, Brazil.
2. Characterize and compare longitudinal change in transcriptional signatures in response to A TT between newly diagnosed drug-sensitive PTB patients with and without DM in Chennai, India.

Status: Study completed

Immune Responses & Effect of Disulfiram on MTB Infected PBMCs: Disulfiram as a Potential Host Directed Therapy

Principal Investigators	Sites	Population	Funding
Amit Singhal (Singapore Immunology Network, Agency for Science, Technology and Research [A*STAR])	NIRT	1. Adult PTB patients on TB treatment with an AUDIT score 8 (n = Up to 20)	DBT, NIH
Ramandeep Singh (NCR Biotech Science Cluster)	BJGMC	2. Adult PTB patients on TB treatment with an AUDIT score < 8 (n = Up to 40)	
Rajesh Karyakarte (BJGMC)		3. Adult healthy contacts (n=Up to 20)	
Amita Gupta (JHU)			
Padmapriyadarsini Chandrasekaran (NIRT)			
Vidya Mave (BJGMC-JHU CRS)			

Design: We will conduct a cross-sectional study using already collected CTRIUMPh and RePORT India common protocol data (baseline demographic, clinical) and archived whole blood PBMC samples from the baseline visit to assess those with and without harmful use of alcohol as assessed by AUDIT scores 2::8. immunophenotyping will be performed by flow cytometry. Additional plasma cytokine and chemokine will also be considered.

Aims:

1. To assess immune responses among adult PTB patients with harmful alcohol use defined by an AUDIT score ≥ 8 compared to those with AUDIT scores < 8 at the time of treatment initiation.
2. Aim 2: To assess the effects of disulfiram on Mtb growth in PBMCs of alcoholic and nonalcoholic individuals

Status: Study discontinued

Evaluation of a Urinary Biomarker Assay for Diagnosis and Test of Cure for Tuberculosis**Principal Investigators**

Jeffrey Tornheim (JHU) Sanjay
Gaikwad (BJGMC) Rajesh
Karyakarte (BJGMC) Aarti
Kinikar (BJGMC)
Vidya Mave (BJGMC-JHU CRS)

Population

Stored samples

Funding

NIH CFAR

Design: We will conduct a case-control diagnostic study nested within the CTRIUMPh cohort study using stored urine samples to identify positive results by the urine FujiLAM, conventional LAM, and the LAM and ESAT-6 nanocage assays. Samples have been collected from patients at multiple time points during treatment, and we will evaluate samples at enrollment (start of treatment), 2 months into treatment, and at the end of treatment (6 months).

Aims:

1. To assess the ability of the FujiLAM kit and a urine lipoarabinomannan glycan (LAM) nanocage assay and a urine ESAT-6 nanocage assay to diagnose tuberculosis (TB) among Indian adults and children with HIV and CD4 counts >100 as well as among age-matched Indian TB patients without HIV,
2. To compare the TB treatment response as measured by urine LAM and ESAT-6 nanocage assays to TB treatment response as measured by sputum conversion, radiographic improvement, and clinical improvement among Indian TB patients with HIV and CD4 counts > 100 as well as among age-matched Indian TB patients without HIV.
3. (Exploratory): To assess the ability of FujiLAM kits and urine LAM and ESAT-6 nanocage assays to diagnose pediatric TB in Indian children with confirmed and unconfirmed TB.

Status: Study completed

Biomarkers for Tuberculosis Diagnosis and Treatment Response**Principal Investigator**

Jyothi Rengarajan (Emory)

Sites

NIRT
BJGMC
JHU
Emory

Population

Stored samples of participants
enrolled in the Active TB cohort and
Household contact cohort in the
CTRIUMPh study

Funding

RePORT India

Design: Cross-sectional longitudinal study

Aims:

1. To evaluate biomarker performance on PBMCs from confirmed pulmonary TB and difficult-to-diagnose cases such as sputum smear-negative and HIV-infected individuals, extrapulmonary and pediatric TB patients.
2. To assess the ability of our biomarkers to monitor treatment response by selecting PBMCs from a subset of adult ATB patients, obtained at Time 0 (pre-treatment) and 1, 2, 6, and 12 after treatment initiation.
3. To use comprehensive immune profiling by mass cytometry (CyTOF) and multiparameter flow cytometry on a subset of ATB and control samples, to generate antigen-specific signatures of Adult TB, with the goal of discovering new markers that could further increase the sensitivity of our candidate biomarkers, particularly for difficult-to diagnose TB cases.

Status: Study discontinued due to the non-viability of PBMCs

A Nanopore Biosensor for Leveling MTB Antigens in Blood

Principal Investigators	Sites	Population	Funding
Tony Ye Hu (Tulane U) Robert C Bollinger (JHU) Amita Gupta (JHU) Rajesh Karyakarte (BJGMC)	BJGMC Tulane U JHU	The purpose of the CTRIUMPH study was to evaluate the risk factors for TB among adults and children < 15 in India. Three cohorts were established: 1. Active TB cohort included adults with newly diagnosed active pulmonary TB (PTB) and children with TB 2. Household contacts cohort enrolling household members of active TB cases Stored plasma samples from participants enrolled in these three cohorts at the Pune site will be utilized for the proposed study for assessment and the performance of the portable prototype system of the protein-based nanopore technology to quantify Mtb target peptides. These CTRIUMPH samples, as well as their linked clinical and microbiological data, will be analyzed to evaluate the performance of the peptide detection assay.	NIH R01

Design: This ROI will employ components of our current platform in a study to develop and optimize a robust and portable protein nanopore-based platform (QuantiPep) that meets WHO guidelines for new TB diagnostics and which can sensitively detect Mtb antigens in adult and pediatric blood samples.

Shifting the assay from a mass spectrometry- to a nanopore-based system will allow rapid, sensitive and cost-effective TB detection and management in leaner clinical environments worldwide. Single channel recording technology is sensitive, specific, fast and affordable alternative to mass spectrometry. Nanopore ion currents are very sensitive to target molecule interactions as they occupy and translocate through the pore, and such interactions can generate signatures

(current-time relationships) that are characteristic for a given target.

Aims:

1. Develop a sensitive and specific QuantiPep TB assay suitable for resource-limited settings;
2. Validate Mtb antigen-derived peptides for TB diagnosis in a well-characterized cohort of adults and children with serially collected clinical, radiological and bacteriological data.
3. Evaluate how serum levels of Mtb antigens change in adult PTB cases in during anti-TB therapy.

Status: Nanopore assays are ongoing, two Indian lab scholars to visit Tulane in April 2025 for training.

T-Cell Biomarkers and T-Regulatory Responses to Pediatric TB

Principal Investigators	Sites	Population	Funding
Jyothi Rengarajan (Emory) Vidya Mave (BJGMC-JHU CRS) Anju Kagal (BJGMC) Aarti Kinikar (BJGMC)	BJGMC	Stored samples of participants enrolled in the CTRIUMPh Pediatric Active TB cohort and RICC Pediatric study.	RICC

Design: We will use cryopreserved PBMC samples from CTRIUMPH cohorts: pediatric unconfirmed TB, confirmed TB, latent TB and no TB controls. We will also be leveraging the data and specimens from the RePORT International Coordinating Centre (RICC) Pediatric Diagnostic Cohort study at BJGMC, Pune and analyze PBMCs isolated from pediatric TB suspects.

Aims

1. Validate host T cell biomarkers for diagnosis of pediatric TB
2. Investigate the phenotype and functions of T-regulatory cells in pediatric TB

Status: Plasma cytokine testing has been completed, data analysis ongoing

Identification of Biomarkers that Can Predict Progression from Latent TB Infection to Active TB Disease

Principal Investigators	Sites	Population	Funding
Subash Babu (NIH-NIRT-ICER) Rajesh Karyakarte (BJGMC) Vidya Mave (BJGMC-JHU CRS) Luke Hanna (NIRT) Padmapriyadarsini Chandrasekaran (NIRT) Amita Gupta (JHU)	NIRT BJGMC NIH-NIRT-ICER	Adult and child household contacts of adult PTB cases from India enrolled in CTRIUMPh study: 1. HHCs of adult PTB cases, who progressed to active TB disease 2. HHCs of adult PTB cases, who did not progress to active TB disease	ICMR DBT NIH

Design: Case-control analysis of stored specimens and associated data between progressors and non- progressors

Aims:

1. To identify soluble cytokine/chemokine biomarkers in antigen-stimulated QFT supernatants that can predict risk of progression to active TB disease

Publication: Daniel EA, Thiruvengadam K, Rajamanickam A, Chandrasekaran P, Pattabiraman S, Bhanu B, Sivaprakasam A, Paradkar M, Kulkarni V, Karyakarte R, Shivakumar SVBY, Mave V, Gupta A, Babu S, Hanna LE. QuantiFERON Supernatant-Based Host Biomarkers Predicting Progression to Active Tuberculosis Disease Among Household Contacts of Tuberculosis Patients. Clin Infect Dis. 2023 May 24;76(10):1802-1813. doi: 10.1093/cid/ciac979. PMID: 36582115.

2. To identify predictive miRNA biomarkers in QFT supernatants for risk of progression to active infectious TB

Publication: Daniel EA, Thiruvengadam K, Chandrasekaran P, Hilda N, Umadhankar P, Prashanthi P, Selvachithiram M, Pattabiraman S, Bhanu B, Sivaprakasam A, Paradkar M, Kulkarni V, Karyakarte R, Shivakumar SVBY, Mave V, Gupta A, Hanna LE. Discovery of a blood-based miRNA signature that can predict onset of active tuberculosis among household contacts of TB patients. Front. Tuberc. 2024 Oct 29; 2:1. doi:10.3389/ftubr.2024.1415346.

3. To identify small metabolite biomarkers in QFT supernatants for predicting risk of progression to active TB disease

Publication: Daniel EA, Upadhyay S, Selvachithiram M, Pattabiraman S, Bhanu B, Sivaprakasam A, Kulkarni V, Karyakarte R, Gaikwad S, Paradkar M, Yogendra Shivakumar SVB, Mave V, Gupta A, Prasad K, Hanna LE. Predictive metabolite signatures for risk of progression to active TB from QuantiFERON supernatants of household contacts of TB patients. Emerg Microbes Infect. 2025 Dec;14(1):2437242. doi: 10.1080/22221751.2024.2437242. Epub 2024 Dec 22. PMID: 39628384.

4. To analyze the plasma biomarker profile of HHCs who progressed to active TB and see if the profile reflected the pattern seen in QFT supernatants

Publication: Rajamanickam A, Ann Daniel E, Dasan B, Thiruvengadam K, Chandrasekaran P, Gaikwad S, Pattabiraman S, Bhanu B, Sivaprakasam A, Kulkarni V, Karyakarte R, Paradkar M, Shivakumar SVBY, Mave V, Gupta A, Hanna LE, Babu S. Plasma Immune Biomarkers Predictive of Progression to Active Tuberculosis in Household Contacts of TB Patients. J Infect Dis. 2024 Jul 19;jiae365. doi: 10.1093/infdis/jiae365. Epub ahead of print. PMID: 39028003.

Status: Study completed; four papers published; preparation of additional manuscripts underway

Host RNA Expression for Diagnosis & Monitoring of Pediatric TB in Africa & India RICC Pediatric Transcriptomic Study

Principal Investigators	Sites	Population	Funding
Lesley Workman (U of Cape Town) Aarti Kinikar (BJGMC) Mandar Paradkar (BJGMC-JHU CRS) Syed Hissar (NIRT)	Cape Town BJGMC NIRT	Baseline samples from 365 South African children will be tested as part of the existing Levin biomarker validation study and are not budgeted here. Follow up samples from a subset of 200 South African children will be included as part of the proposed study.	RICC

Design: This study involves the collaboration of two RePORT consortia, South Africa and India, both high burden TB and TB-HIV settings with well-established pediatric cohorts of children with TB disease, together with the Imperial College group leading the current NIH-supported pediatric TB biomarker validation study.

Aims:

1. Primary Objectives: To derive and validate a global RNA expression signature for the diagnosis of pulmonary TB, and extra-pulmonary TB in children; and to identify longitudinal changes in RNA expression with TB treatment in children who have microbiologically confirmed or clinically diagnosed TB, using bio-banked samples from the South Africa and Indian cohorts and clinical information from the TB RePORT Common Protocol (CP) and India parent protocol databases.
2. Secondary Objectives: To establish a biorepository of samples that can be used for future pediatric TB diagnostic and pathogenesis studies.

Status: Assays completed, final data analysis ongoing at the Imperial College, London

Residual Respiratory Impairment Following Pulmonary Tuberculosis: The Lung Health Sub-Study

Principal Investigators	Sites	Population	Funding
Rahul Lokhande (BJGMC) Shashikala Sangle (BJGMC) Sriram Selvaraju (NIRT) Akshay Gupte (BU) Amita Gupta (JHU)	BJGMC NIRT	1. Active TB cohort comprising 400 new adult pulmonary TB (PTB) cases. 2. Reference cohort comprising 400 adults without TB. 3. Cohort of 200 adults with chronic obstructive pulmonary disease (COPD) Each study site will enroll approximately 50% of the total sample size. COPD controls will be enrolled at BJGMC only.	NIAID

Design: Prospective cohort study nested within the CTRIUMPH study.

Aims:

1. To characterize trends in respiratory impairment among new adult PTB cases undergoing anti-tuberculous treatment (ATT) in India.
2. To identify host factors measured during the first 2 months of ATT initiation that are associated with respiratory impairment at ATT completion among new adult PTB cases in India.
3. To explore the impact of TB disease; alone and in combination with smoking exposure, indoor air pollution (IAP) exposure, HIV infection and diabetes mellitus (DM); on respiratory impairment up to 42 months following ATT completion among successfully treated adult PTB cases in India.
4. Characterize the chronicity and progression of lung impairment, and its responsiveness to bronchodilator therapy, in successfully treated PTB cases

Status: Study completed; analysis underway for two additional manuscripts

Characterization of Genomics and Metabolomics among Individuals Highly Exposed, but Resistant to Mtb Infection (TB-GWAS)

Investigators	Sites	Population	Funding
Neel Gandhi (Emory)	BJGMC	Household contacts of adult	NIH R01
Yan Sun (Emory)	JIPMER	pulmonary TB cases from	
Sanjay Gaikwad (BJGMC)	BMMRC	parent protocols study, RePORT	
Rajesh Karyakarte (BJGMC)		India Common Protocol phase I	
Amita Gupta (JHU)		at all sites; and Prospective TB	
Vidya Mave (BJGMC-JHU CRS)		GWAS study enrollments at	
Neil Martinson (Perinatal HIV		BJGMC, Pune site.	
Research Unit, SA)			
Timothy Sterling (Vanderbilt, US)			
Bruno Andrade (Fiotec, Brazil)			

Aims:

1. To characterize a phenotype for resistance to Mtb infection using TST and IGRA results among household contacts recently exposed to TB.
2. To determine genetic predictors for resistance to Mtb infection.
3. To identify metabolomic markers associated with resistance to Mtb infection.

Status: Data collection and laboratory analyses completed. Manuscript and abstract preparation underway.

Abstracts:

Gyorffy MF, Gandhi NR, Hui Q, Andrade B, Martinson N, Paradkar M, Prakash S, Devalraju KP, Figueiredo MC, Cordeiro-Santos M, Mofokeng NJ, Willis F, Sterling T, Gupta A, Sun YV on behalf of the TB GWAS collaboration. Genome-Wide Meta-Analysis Identifies Genetic Associations with Resistance to Mtb Infection. [poster presentation at 2025 Conference on Retroviruses and Opportunistic Infections, San Francisco 2025]

Proteomic Discovery of Protein-based TB Recurrence and Death Signatures (IIT-M Proteomics Study)

Principal Investigators	Funding
Sanjeeva Srivastava (IIT-Bombay)	DBT
Sonia Krishnan (JHU)	NIH
Amita Gupta (JHU)	Phase 2
Mandar Paradkar (BJGMC-JHU	
CRS)	
Sanjay Gaikwad (BJGMC)	
Rajesh Kayakarte (BJGMC)	
Vandana Kulkarni (BJGMC-JHU CRS)	

Aims: To identify markers of TB recurrence/death by mass spectrometry

Status: Specimen processing completed; abstract submitted to the Journal of the American Society for Mass Spectrometry

The Role of Innate Immunity in the Acquisition of Sterile Protection Against TB Infection

Principal Investigators

Adriana Weinberg (University of Colorado)
Vandana Kulkarni (BJGMC-JHU CRS)
Rajesh Kayakarte (BJGMC)

Funding

NIH R21

Design: To identify potential targets for new TB vaccines by characterizing the immune responses that distinguish individuals with sterilizing protection against TB (TB-resisters), defined by presence of TB-specific immune responses and absence of latent infection, from individuals with latent TB infection (LTBI-participants)

Status: Study closed; paper published

Epidemiologic Factors Associated with TB Treatment Outcomes across RePORT International Consortia

Principal Investigators

Bruno Andrade (RePORT Brazil)
Timothy Sterling (RePORT Brazil)
Mark Hatherill (RePORT South Africa)
Thomas Scriba (RePORT South Africa)
Amita Gupta (RePORT India)

Sonali Sarkar (RePORT India)
Retna Mustika Indah (RePORT Indonesia)
Muhammad Karyana (RePORT Indonesia)
Yuhong Liu (RePORT China)
Jingtao Gao (RePORT China)

Marrissa Alejandria (RePORT Philippines)
Ray (Sang Nae) Cho (RePORT Philippines)

Funding

RICC

Design: Analysis of data collected from a prospective multi-site cohort study to determine the Impact of key non-communicable and communicable diseases on tuberculosis treatment outcomes and recurrence using data from multiple RePORT International consortia

Aims:

1. To create a harmonized analytical dataset from multiple RePORT International consortium sites
2. To determine the Impact of non-communicable diseases, including prediabetes and diabetes mellitus, and communicable diseases, including HIV, on tuberculosis treatment outcomes and recurrence, both globally and regionally

Status: Analysis completed manuscript preparation underway

Validation of Transcriptional Signature to Predict Active TB Disease among Advanced HIV Patients

Principal Investigators

Vandana Kulkarni (BJGMC-JHU CRS)

Funding

RICC

Design: The 1:1 case-control study to assess the performance of the 15 gene signature to detect TB among patients with advanced HIV. The cases would be advanced HIV patients (CD4 <100 cells/ul) with confirmed active TB and controls would be advanced HIV patients without any clinical and microbiologic evidence for active TB. The study was performed at BJGMC, Pune, India, Rio de Janeiro and Manaus at Brazil.

Study Exploratory Objectives: To assess and compare changes in the T cell activation of HLA-DR+ and CD38+ T cell subsets, cytokine profiles of inflammatory markers and co-relate blood transcriptional and cytokine signatures of TB among advanced HIV patients with or without TB.

1. To conduct testing and validation of the 15-gene signature to predict active TB disease among advanced HIV patients with CD4 <100 cells/ul.
2. To assess and compare the cytokine/chemokine signature that may be predictive for active TB among advanced TB-HIV and HIV patients in India and Brazil.

Status: Study completed; paper published

Impact of Latent TB Infection and Trained Immunity on Susceptibility to SARS-CoV- 2 Infection in India and the Philippines

Principal Investigators	Sites	Population	Funding
Padmini Salgame Sonali Sarkar Alejandria Marcelo Marissa	JIPMER University of Philippines	HHCs of pulmonary TB patients from RePORT India Phase I studies; Index COVID cases and their HHCs (Philippines)	RICC

Design: About 300 household contacts of pulmonary TB patients enrolled through RePORT Phase 1 studies will be re-consented and stratified into 4 groups based on the presence of LTBI +/- and SARSCoV +/- . About 300 SARS-CoV-2 positive patients identified from the hospital database (index cases) and an additional 250 of their household contacts will be enrolled in Philippines. For each of the 4 groups, 20 subjects will be selected and the trained immunity of their monocytes and NK cells will be examined.

Aims:

1. Examine whether there is a correlation between LTBI and SARS-CoV-2 IgG seroconversion and/or COVID-19 disease severity
 - In India, determine the seroprevalence of COVID-19 in healthy household contacts of prior active PTB cases stratified according to the presence of LTBI
 - In the Philippines, determine the prevalence of LTBI in patients with confirmed COVID-19 infection and in their household contacts; and the association of LTBI with disease severity
2. Examine in a subset if enhanced trained immunity in LTBI positively correlates with protection from SARS-CoV-2 infection

Status: Enrollment and follow up completed. Study closeout activities are ongoing; sample processing yet to start.

Therapeutic Outcomes with Second Line Drug Exposures in a Cohort of Patients with Drug Resistant TB: A Pharmacokinetic-Pharmacodynamic Assessment

Principal Investigators	Sites	Population	Funding
Tester F. Ashavaid (Hinduja) Camilla S. Rodrigues (Hinduja) Neil Martinson (PHRU, SA) Ebbrahim Variava (PHRU, SA)	Hinduja (India) PHRU (South Africa)	Cohort A: Adults and adolescents ≥15 years of age with MDR-TB (n=200)	SA MRC DBT

Design: The study is designed to study the pharmacokinetic (PK) and pharmacodynamics (PD) profiles of second line TB drugs and develop PK-PD models to help understand efficacy of these drugs.

Aims:

1. To determine the pharmacokinetic parameters of second-line agents in South African and Indian patients receiving DR-TB treatment regimens with particular attention to moxifloxacin, linezolid, clofazimine, bedaquiline and SLI (Kanamycin, Amikacin)
2. To assess the MIC of these drugs using Thermoscientific Fisher Sensititre panels.
3. To characterize the population pharmacokinetics of these drugs in the study population and determine factors associated with low drug exposures
4. To study the association between drug exposures of second-line TB drugs and therapeutic outcomes in a pharmacokinetic-pharmacodynamic analysis among patients with DR-TB

Status: Data analysis ongoing

Manuscripts in progress:

- Evaluation of cycloserine dose regimens in multidrug-resistant tuberculosis participants from India, presented at the Union World Conference on Lung Health, Bali, Indonesia, 11-Nov-24
- Population pharmacokinetics of moxifloxacin in Indian patients with multidrug-resistance tuberculosis, ACBICON Chandigarh, India, December, 2024

MDR-TB Free: Monitoring Adverse Effects, Utilizing Resources Optimally, Knowing Resistance Patterns, and Treatment Strategy (MDR TB MUKT)

Principal Investigators	Sites	Population	Funding
Zarir F. Udwadia (Hinduja) Camilla S. Rodrigues (Hinduja) Tester F. Ashavaid (Hinduja) Amita Gupta (JHU) Jeffrey A Tornheim (JHU)	Hinduja	1. Cohort A: Adults and adolescents ≥ 15 years of age with MDR-TB (n=200). 2. Cohort B: Adult and child household contacts of MDR-TB Cohort A participants with pulmonary TB (n=60).	Hinduja Foundation RePORT India NIH: K23

Design: This study comprises two prospective observational cohorts. Cohort A will enroll adults and adolescents ≥ 15 years with active multidrug resistant tuberculosis (MDR-TB). Cohort B will enroll adult & child household contacts of participants in Cohort A pulmonary MDR-TB cases.

Aims: To establish well-characterized prospective cohorts of active MDR-TB cases and their household contacts with associated biorepositories.

Cohort A Primary Objectives: To document participant outcomes including early treatment response, MDR-TB treatment-associated adverse events, mortality, and loss to follow-up.

Cohort B Primary Objectives: To assess rates of prevalent and incident TB infection and disease in household contacts of MDR-TB cases.

Cohort A Secondary Objectives

1. To evaluate the impact of comorbid diseases including diabetes mellitus, prediabetes, HIV, COPD, smoking status, alcoholism, depression, quality of life, and malnutrition on treatment outcomes and TB treatment-associated adverse events.
2. To assess the genotype-phenotype correlation among resistant TB isolates through MIC-based phenotypic drug susceptibility testing and next generation sequencing of TB isolates, including assessment of strain evolution, drug susceptibility pattern changes during treatment, and impact of strain on treatment outcomes.
3. To derive pharmacokinetic parameters of second-line agents in participants receiving multidrug treatment regimens with particular attention to linezolid, clofazimine, high-dose moxifloxacin, aminoglycosides, and any new drugs that become available including bedaquiline and delamanid.
4. To assess host biomarkers of treatment response and correlates of progression from exposure to TB disease using multiomics approaches (e.g. transcriptomics, metabolomics, cellular markers, and immunity- and inflammation-associated soluble biomarkers).
5. To assess microbial markers of treatment response including smear and culture conversion, quantitative burden, and the time to conversion.
6. To assess standard and novel imaging approaches to monitor treatment responses.
7. To assess the impact of TB on the quality of life and mental health of subjects with MDR-TB, and in turn their impact on treatment adherence and outcomes.
8. To assess host immune responses to and inflammation following TB exposure and TB treatment and correlate these responses with clinical outcomes.
9. To ascertain true outcomes and self-reported barriers to treatment retention of MDR-TB participants lost to follow-up (≥ 2 consecutive months of missed visits) during treatment through prospective phone follow-up and/or home visits.

Cohort B Secondary Objectives

1. To determine the feasibility of enrolling household contacts of index adult MDR TB cases.
2. To explore the proportion of contacts with prevalent TB disease and infection, what proportion develop new TB disease and infection during follow-up, and what are prevalent comorbidities (diabetes mellitus, prediabetes, HIV, COPD, smoking status, alcoholism, depression, quality of life, and malnutrition) among the household contacts.
3. To contribute samples to a global repository for the study of biomarkers of incident TB and progression from exposure to TB disease using multiomics approaches (e.g. transcriptomics, metabolomics, cellular markers, and immunity- and inflammation-associated soluble biomarkers).

Status: Analysis nearly completed; manuscript preparation underway

Dynamics and Immune Mechanisms of QFT Response in Close Contacts of TB Cases

Principal Investigators	Site	Population	Funding
Padmini Salgame (Rutgers)	JIPMER	HHCs of TB patients	NIH
Sonali Sarkar (JIPMER)	BJGMC		
Vidya Mave (BJGMC)			

Design: Establish a prospective observational cohort of 1000 household contacts (HHC) of TB patients at JIPMER and BJMC. The proposed cohort will be classified after 12 months of follow-up into four groups: sustained QFT negatives, sustained QFT positives, QFN converters and QFN reverters.

Objectives:

1. Determine the clinical implications of dynamic changes in the QFT response in 12 months following close contact with a TB patient.
2. Examine if dynamic changes in the QFT response are associated with activation of phenotypically and functionally distinct subsets of T cells.
3. Examine if the dynamic changes in the QFT response are associated with altered macrophage anti-mycobacterial effector responses.

Status: Enrollment and follow-up completed

Analysis of Host Biomarkers Associated with Adverse TB Treatment Outcomes Across RePORT International Sites

Principal Investigators			Funding
Sheetal Verma (Rutgers)	Beatriz Barreto-Duarte (Oswaldo Cruz Foundation, Brazil)	Erlina Burhan (INA RESPOND, Persahabatan Hospital)	RiCC
Senbagavalli Prakash Babu (JIPMER)	Simon Mendelsohn (South African Tuberculosis Vaccine Initiative)	Sri Ram Pentakota (Rutgers)	
Artur Queiroz (Oswaldo Cruz Foundation, Brazil)	John Carlo Malabad (University of Philippines-Manila)	Dr. Arthur Vanvalkenburg (Rutgers)	
Mariana Araújo-Pereira (Oswaldo Cruz Foundation, Brazil)			

Design: Host biomarkers will be assessed in nested case-control cohorts using archived Paxgene RNA and plasma samples from Common protocols that were collected at baseline and treatment month 2 and 6; Participants with microbiological treatment failure or recurrence will be matched 1:2 with controls with lasting cure. Samples from EOT will assess the risk of recurrence after cure. Testing at baseline addresses response prediction prior to ATT initiation. Month-2 evaluates response kinetics, that may provide insights into mechanisms of treatment failure when analyzed in the context of host and microbial parameters. Testing at month-6 is an approach to confirm cure and predict recurrence at ATT completion.

Aims:

1. To validate a small panel of host blood RNA signatures that predict the outcome of tuberculosis treatment using the Fluidigm (Standard Biotoools™) platform.
2. To develop a parsimonious and generalizable signature of failure from a large panel of existing signatures using the digital NanoString platform.
3. To validate host blood protein signatures that predict the outcome of tuberculosis treatment using Luminex platform and derive a reduced proteome signature.
4. To develop a novel "cure" signature using RNA-seq as a discovery-based approach.

Status: Analysis in progress

Rapid Research in Diagnostics Development for TB Network (R2D2 TB Network) Study

Principal Investigators	Sites	Population	Funding
D.J. Christopher (India)	CMC Vellore, India	Adult outpatients (age ≥ 18 years) with cough ≥ 2 weeks' duration, a commonly accepted criterion for identifying patients with presumed pulmonary TB	NIH
Adithya Cattamanchi (USA)	Hanoi Lung Hospital, Vietnam		
Payam Nahid (USA)	De La Salle Medical and Health Sciences Institute, Philippines		
Claudia Denking (Germany)	Stellenbosch University, SA		
	Makerere University College of Health Sciences, Uganda		

Design: For the novel TB triage and diagnostic tests, we will conduct large-scale evaluation of design-locked tests in a cohort of adults with presumed TB, with nested feasibility/pilot studies of early and late prototype tests. The large-scale evaluation is a prospective cross-sectional study of 3,000 participants (600/clinical study site).

Objectives:

1. To conduct pilot studies of the diagnostic accuracy and usability of early and late prototypes of novel TB tests in settings of intended use to inform their further development.
2. To conduct large-scale validation studies of the diagnostic accuracy and usability of design-locked novel TB tests to inform policy development.

Our study hypotheses are:

1. Early and late prototypes of novel TB tests will meet pre-specified decision thresholds for advancement to the next phase of assessment.
2. Design-locked novel TB tests will meet updated WHO target product profile (TPP) requirements for minimum diagnostic accuracy.

Status: Enrollment ongoing.

Predictors of Resistance Emergence Evaluation in Multidrug Resistant-Tuberculosis Patients on Treatment (PREEMPT)

Principal Investigators	Sites	Population	Funding
Zarir F. Udwadia (Hinduja)	NIRT (India)	Adult PTB MDR patients on TB treatment (N=400 for India and 200 for Brazil)	NIH: R01
Camilla S. Rodrigues (Hinduja)	BJGMC (India)		
Tester F. Ashavaid (Hinduja)	JIPMER (India)		
C. Robert Horsburgh (BU)	Hinduja (India)		
	NEGRIMS (India)		
	YRJ CARE (India)		
	INI – FIOCRUZ (Brazil)		
	UFRJ (Brazil)		

Design: In this observational cohort study, we propose to study the contribution of potential causes to resistance and develop the knowledge base required to stop resistance from developing by analyzing AUC and sputum samples.

Aims:

1. Determine whether low serum antimycobacterial drug concentrations are associated with the clinical emergence of drug resistance in MDR-TB patients.
2. Determine whether HIV seropositivity is a risk factor for low serum drug concentrations.
3. Determine the contribution of increased DNA mutation to clinical emergence of drug resistance in patient isolates.
4. Determine the earliest time at which mutations responsible for drug resistance can be detected during treatment

Status: Enrollment completed, minimal follow-up ongoing. Laboratory analyses and PK analysis underway.

Whole Genome Sequencing of Drug Resistant Tuberculosis in India: Genotype-Phenotype Correlation, Clinical Impact of Resistance, and Sequencing Directly from Sputum (K23)

Principal Investigators	Sites	Population	Funding
Camilla S. Rodrigues (Hinduja) Jeffery A. Tornheim (JHU)	Hinduja	Cohort A (MDR-TB MUKT): Adults and adolescents ≥ 15 years of age with MDR-TB (n=200)	NIH: K23

Design: The K23 analysis will correlate mutations identified by whole genome sequencing with both MGIT and MIC drug susceptibility test results, correlate those results with plasma drug levels and participant outcomes, and compare the results obtained by sequencing the isolates without culture to those obtained by sequencing MGIT cultures and solid cultures.

Aims

1. Characterize MIC distribution for mutations identified on WGS in Indian MDR-TB strains and compare the frequency and predictive value of WGS-derived mutations in Mtb isolates from Indian MDRTB patients with those from South African MDR-TB patients in the ReSeqTB Data Platform.
2. Assess the impact of partial resistance (identified by WGS and MIC-testing) and drug exposures (using PK-PD analysis) on patient outcomes in a cohort of MDR-TB patients.
3. Assess a new direct-from-sputum method for WGS compared to culture-based WGS for DST.

Status: Sample processing completed; data analysis ongoing

Publication: Diagnostic performance of a direct-from-sputum next generation sequencing method for prediction of phenotypic resistance to second-line tuberculosis drugs, Union World Conference on Lung Health, Bali, Indonesia, 11-Nov-24

Abdominal and Thoracic Ultrasound for the Diagnosis of Pulmonary and Extra-pulmonary Tuberculosis. Assessing the Accuracy of Point-of-care Ultrasound for the Diagnosis and Therapy Monitoring in Patients with Presumed Tuberculosis in India and Germany

Principal Investigators	Sites	Population
D.J. Christopher (India) Claudia M. Denking (Germany)	CMC Vellore, India Heidelberg University, University Clinics Cologne University Clinics Frankfurt, Germany	Patients aged 18 years or older presenting with: clinical constellation compatible with Pulmonary (PTB) and extra-pulmonary TB (EPTB)

Design: A prospective, multicentre study (Germany, India), we will enroll patients with presumed active TB of any anatomic site and in both in- and outpatient settings.

Objectives:

- To assess the accuracy of the FASH-protocol for diagnosing TB in extra-pulmonary sites (i.e. abdominal lymph nodes, splenic micro-abscesses, pleural or pericardial effusions, liver micro-abscesses) using a microbiological reference standard (MRS), an extended microbiological (eMRS) and composite reference standard (CRS) in presumptive adult TB-patients in Germany and separately in India
- To assess the accuracy of lung ultrasound for the diagnosis of pulmonary tuberculosis (unilateral large pleural effusion, especially with stranding, subpleural nodules (SUN) pattern, consolidation with an additional sign of TB (SUN, abdominal nodes, splenic lesions, pericardial effusions)) using a microbiological (MRS), extended microbiological (eMRS) and composite reference standard (CRS) in presumptive adult TB-patients in Germany and separately in India

Status: Enrollment completed.

Manuscript in process: Lung and abdominal ultrasound accuracy for tuberculosis: an Indian prospective cohort study

Pharmacokinetic Assessment of MDR-TB Drugs in the Treatment of TB Meningitis (MDR-TBM PK)

Principal Investigators	Sites	Population	Funding
Jeffrey A Tornheim (JHU)	BJGMC	Adult MDR TBM patients on	CRDF Global
Tester F. Ashavaid (Hinduja)	Hinduja	TB treatment (N=70 all sites)	
Hongfei Duan (Beijing Chest Hospital)	International Sites	- (Hinduja site n=20)	
Ebrahim Variava (Perinatal HIV Research Unit)	Johns Hopkins		
Rohidas Tanku Borse (BJGMC)	Beijing Chest Hospital PHRU		
	Wits Health		

Design: Patient suspected of TBM will be screened for the eligibility of enrolment in the study. Eligible participants will be consented, enrolled and followed up for a 6-month period after enrollment with a total of 8 clinical encounters each. On enrolment, a baseline lumbar puncture (LP) will be performed to confirm the diagnosis of TBM. If suspected patients have already undergone an LP, the sample will be retrieved from the labs and stored for biorepository. This LP will be a part of standard of care (SOC). For the PK studies, participants will be followed up for Week 1 & Week 4 with repeat LP. These LP may be as a part of SOC or for research use only for PK studies.

Aims:

1. Penetration coefficient of each drug into the CSF
2. Relationship between PK parameters, survival, and functional status.

Status: Sample processing ongoing, Analysis ongoing

Manuscript in process: On Cycloserine PK, Moxifloxacin PK, LZD PK

Baseline pRescription According to Direct from Sputum Sequencing and Targeted drug Concentration Strategy (BRASS TACS)

Principal Investigators	Site	Population	Funding
Tester F. Ashavaid (Hinduja)	Hinduja	Adult with Pulmonary RR/MDR-TB	NIH: R01
Camilla S. Rodrigues (Hinduja)		(n=210)	
Zarir F. Udwadia (Hinduja)			
Jeffrey A. Tornheim (JHU)			

Design: This study is an observational study of a combined treatment strategy informed by NGS, TDM, and MIC testing. The study will enroll adults starting treatment at Hinduja Hospital for RR/MDR-TB of the lungs. All data will be provided to clinicians to help personalize therapy. Outcome and side effect data will be compared to data from historical controls with MDR-TB enrolled in previous RePORT-India associated cohort studies at Hinduja Hospital using propensity score matching by disease severity and resistance to assess the impact of the BRASS TACS treatment strategy to outcomes among similar patients treated without this strategy.

Aims:

1. To determine the proportion of patients with MDR-TB in Mumbai, India with resistance-associated mutations that would prevent treatment with moxifloxacin, linezolid, bedaquiline, clofazimine, or cycloserine using culture-free NGS.
2. To identify the proportion of cohort participants with MDR-TB that achieve model-derived steady-state plasma levels meeting efficacy and toxicity targets.
3. To assess the time to final regimen, frequency of treatment-associated side effects, time to culture conversion, and final outcome of cohort participants who complete culture-free NGS and TDM.

Status: 8 participants enrolled; enrollment ongoing

Identification of *M. tuberculosis* and Prediction of Drug-resistance among Adults with Pulmonary Tuberculosis Using a Novel Urine Collection and Target Concentration Device, Followed by Cartridge-based Nucleic Acid Amplification Testing (Urigami and CBNAAT Study)

Principal Investigators	Site	Population	Funding
Tester F. Ashavaid (Hinduja) Camilla S. Rodrigues (Hinduja) Jeffrey A. Tornheim (JHU)	Hinduja	1. Adult PTB MDR patients on TB treatment (N=400 for India and 200 for Brazil) 2. Adult healthy contacts (n=Up to 20)	CFAR NIH: R21

Design: We will transfer the novel urine capture and affinity bait method developed at the Liotta Lab in the USA to the PD Hinduja National Hospital and Medical Research Centre in Mumbai, India where it will be used to assess the baseline and 6-month urine samples collected from newly diagnosed adults with drug susceptible pulmonary tuberculosis, as well as the de-identified baseline and 6-month urine samples collected from participants in the MDR-TB MUKT cohort with pulmonary MDR-TB and fluoroquinolone resistance stored in the MDR-TB MUKT biorepository. Specificity will be assessed by repeating the assay among de-identified samples collected from household contacts of pulmonary TB patients stored in the MDR-TB MUKT biorepository.

Aims:

1. To assess the diagnostic accuracy of the combination of a collapsible urine collection device with hydrogel nanocage affinity baits for *Mtb* cfDNA and the Xpert MTB/RIF and Xpert Ultra for the detection of pulmonary *Mtb* and rifampin resistance from freshly collected urine.
2. To assess the accuracy of this combination method to identify resistance to isoniazid, fluoroquinolones, and second-line injectable drugs using the Xpert XDR cartridge on de-identified samples in a well-characterized biorepository.
3. To implement this novel concentration technology in a high burden setting by transferring technology developed in a US laboratory to the Indian context. To achieve an analytical sensitivity for genomic DNA of 10 pg/mL in urine matrix.

Status: Study stopped due to lack of funding

CRISPR - Multiplexed detection of cell-free *M. tuberculosis* DNA and its drug-resistant variants in blood

Principal Investigators	Site	Population	Funding
Prerna Arora (Hinduja) Jeffrey A Tornheim (JHU) Tony Hu (Tulane)	Hinduja Tulane JHU	Adults with drug resistant and drug susceptible disease and their household contacts	NIH R01

Design: A diagnostic accuracy and treatment response study nested within MDR-TB MUKT and BRASS TaCS to evaluate a novel assay to detect cell-free *Mtb* DNA fragments in the blood of people with active tuberculosis, to evaluate the ability of the same assay to detect markers of drug-resistance, and to assess the response to successful treatment using biorepository specimens.

Aims:

1. To optimize our CRISPR-TBD POC assay to analyze *Mtb*-cfDNA in blood samples.
2. To evaluate the performance of the CRISPR-TBD assay for TB diagnosis and treatment evaluation.
3. To conduct an in-field validation of the multiplex CRISPR-TBD POC assay in an Indian clinical laboratory whose population faces a high burden of drug resistant TB

Status: Laboratory analysis ongoing

InTGS: Whole Genome Sequencing of MTB Clinical Strains for Determining Drug Resistance and Strain Lineage in India: A Structured Nationwide Approach

Principal Investigators	Site	Population	Funding
Dr. Sonali Sarkar (JIPMER)	JIPMER, NII,	Cohort A participants of parent	DBT
Dr. Vinay Kumar Nandicoori (CCMB)	ICGEB,	protocol from JIPMER, CMC,	
Dr. G. Aneeshkumar Arimbasseri (NII)	CCMB,	NIRT and BJGMC	
Dr. Arindam Maitra (NIBMG)	NIBMG,	Microbiologically confirmed TB	
Dr. Camilla Rodrigues (Hinduja)	BMMRC,	patients from participating sites	
Dr. S. Siva Kumar (NIRT)	BJGMC, PGI,		
	Hinduja, NIRT		

Design: We propose to use both retrospective and prospective approaches for sample collection. Retrospective approach will use samples collected under the Regional Prospective Observational Research in Tuberculosis (RePORT) India studies or samples (sputum/extra pulmonary specimens) from studies involving TB positive patients (smear/CBNAAT/TrueNat) from participating institutions. Prospective samples (MTB positive sputum/extra-pulmonary specimens), will be obtained from selected Intermediate Reference Laboratories (IRL) culture drug susceptibility testing (C-DST) centers and in-patient and out-patient departments of participating hospitals/institutions

Aims:

1. To perform WGS of 32,200 clinical strains from active TB patients and to develop a centralized biorepository of clinical MTB strains in India.
2. To map genetic diversity of pulmonary and extrapulmonary isolates of MTB from newly reported active TB cases in India and the associated treatment outcomes.
3. Association of mutations of MTBC to phenotypic drug resistance patterns.
4. To combine epidemiological data with WGS results to extract actionable public health data-driven information

Status: 8098 WGS analysis processed; enrollment ongoing.

Understanding Mycobacterium tuberculosis Mediated Host Metabolomics in Pulmonary Tuberculosis: Correlation with Disease Severity and Treatment Course

Principal Investigators	Sites	Population
Senbagavalli Prakash Babu	JIPMER	Adult participants enrolled in the Active TB cohort
Sonali Sarkar	IISER	(Cohort A) and Household contact (Cohort B) of common protocol phase I

Design: We will use plasma samples collected from common protocol cohorts to measure the metabolomic markers; active pulmonary TB (n=20) grouped as per disease severity (mild and severe) and their household contacts (n=10). For cohort A participants, samples will be analyzed at baseline, Month 1 and End of treatment; for cohort B at baseline

Aims

1. To study the differences in MTB influenced host metabolomics in mild and severe disease groups.
2. To study the dynamic changes of host metabolites at baseline, during and at the end of the standard anti-TB treatment regimen.
3. To examine whether there is a correlation between host metabolomics with disease severity and course of standard anti-TB treatment.

Status: Study completed; manuscript under review

Innate immune response of LTBI+HIV+ children**Principal Investigators**

Ramakrishna Vankayalapati

Funding

NIH R01

Description: Mycobacterium tuberculosis (Mtb) infects one-third of the world's population and causes almost 1.3 million deaths per year, including 100,000 children. Approximately 90% of infected persons have latent tuberculosis infection (LTBI), have protective immunity and remain well, but 10% develop primary tuberculosis (TB) soon after infection or reactivation TB many years later. TB is the leading cause of death in HIV-infected persons and more than half a million coinfecting people die annually. Children are more susceptible to TB infection, due to an immature immune system. HIV infection in children markedly increases susceptibility to TB. To develop adequate prophylaxis or therapy, it is important to understand immune responses to Mtb. Identification of HIV+ children with LTBI who are at greatly increased risk for development of TB would allow treating only high-risk children, facilitating completion of therapy for LTBI and preventing future development of TB. To identify these children, it is important to pinpoint the nature of the defective immune responses that permit development of active TB in HIV+LTBI+ pediatric patients. This proposal will identify a novel memory-like NK cell subpopulation mediated mechanisms that regulate immune responses and pinpoint the nature of the defective responses that permit development of active TB in HIV-LTBI+ and HIV+LTBI+ children. These studies will lay the groundwork for strategies to develop novel anti-tuberculosis vaccines that stimulate strong NK cell mediated immunity in HIV+ and HIV-children with LTBI, and reduce development of TB

Status: Study ongoing; preparation of four 4 manuscripts underway

Identifying TB Treatment Response Biomarkers Using qRT-PCR Signature for TB Treatment Response and TB NanoString for Tx**Principal Investigators**

Hardy Kornfeld (UMass)

Padmini Salgame (Rutgers)

Funding

RICC

Design: To validate five signatures (RESPONSE5, ACS6, RISK4, Khatri 3-gene, and Maertzdorf4-gene) as blood biomarkers in predicting TB treatment response to favorable and unfavorable treatment outcomes in the RePORT cohorts

Aims: To develop a promising blood biomarker for identifying response to TB treatment among active TB cases

Status: Study on hold because initial funding used up by the nanoString study

Aim 1: Diagnostics: evaluate novel diagnostics & biomarkers of diverse states of MTB infection

Plasma Triage Test

Aim: To evaluate the performance of a promising plasma-based triage test for TB diagnosis in the Dx cohort in collaboration with Dr. Gerhard Walzl and Leiden University Medical Centre.

Proposed Manuscript: Comparison of plasma triage test accuracy between TB suspects with and without TB

Status: Potential study for future

TB NanoString Transcriptomics

Aim: To utilize NanoString technology to measure mRNA expression levels of TB-associated gene signatures, aiming to derive a parsimonious TB signature for distinguishing incipient, subclinical, and active TB disease.

1. Diagnosis of Incident TB Infection (TBI)

Aim: To evaluate the ability of TB NanoString and plasma cytokine profiles to distinguish recent TB infection (incident TBI) from stable IGRA-positive and IGRA-negative individuals. The goal is to improve risk stratification for disease progression by identifying sensitive and specific biomarkers of recent infection.

Proposed Manuscript: Diagnostic accuracy of NanoString for PTB in adults and children.

Status: Potential study for future

2. Diagnosis of Subclinical TB

Aim: To identify transcriptional and cytokine biomarkers capable of distinguishing incipient and subclinical TB, particularly in high-risk populations such as household contacts (HHC) of XDR-TB cases. This study will utilize NanoString RNA expression profiling and plasma cytokine analysis to enhance early detection and disease monitoring.

- **Proposed Manuscript:** Identification of recent TBI using NanoString and cytokine profiles.

Status: Enrolled 78 household contacts of adult PTB patients with pulmonary RR/pre-XDR/XDR TB into our Phase II HHC study using nanoString.

- **Proposed Manuscript:** Detection of subclinical TB using transcriptional signatures

Status: Manuscript preparation underway.

Aim 1: Diagnostics: evaluate novel diagnostics & biomarkers of diverse states of MTB infection *Continued*

Plasma Cytokines (Luminex)

Aim: To assess the association between plasma cytokine signatures, particularly those linked to lung damage and fibrosis, and TB infection and disease using the Biorad Luminex system.

- **Proposed Manuscript:** Optimized cytokine signatures for diagnosing PTB and EPTB in adults and children
Status: Samples available. Assays not performed yet
- **Proposed Manuscript:** Use of plasma cytokines for identifying incipient and subclinical TB
Status: Samples available. Assays not performed yet

Urinary LAM

Aim: To evaluate the effectiveness of novel monoclonal antibody-based detection methods for quantifying ManLAM in urine, improving sensitivity and specificity for TB diagnosis compared to current commercial assays.

- **Proposed Manuscript:** Diagnostic accuracy of the new urine LAM assay compared to FujiLAM and XpertULTRA
Status: Potential study for future
- **Proposed Manuscript:** Utility of urine LAM in TB diagnosis among HIV-infected and uninfected individuals
Status: Potential study for future

Urinary Biomarker Assay for TB

Status: Study completed. Assay was negative

Computer-Aided Diagnosis (CAD)

Aim: To leverage artificial intelligence-driven CAD systems to analyze digitized chest radiographs within the RePORT India consortium, improving the accuracy and efficiency of early TB detection.

- **Proposed Manuscript, Adult:** Artificial Intelligence in Tuberculosis Diagnosis: Enhancing Accuracy and Speed with Computer-Aided Diagnosis Systems; Deep Learning Models for Tuberculosis Diagnosis: A Study on the Application of AI to Digitized Chest Radiographs
Status: In the process of procuring the AI software
- **Proposed Manuscript, Pediatric:** Artificial Intelligence in Tuberculosis Diagnosis: Enhancing Accuracy and Speed with Computer-Aided Diagnosis Systems; Deep Learning Models for Tuberculosis Diagnosis: A Study on the Application of AI to Digitized Chest Radiographs
Status: Enrolling patients

Aim 2: Markers of treatment response

2A: Identify TB treatment response biomarkers

TB NanoString for Treatment Response

Aim: To optimize and test a concise NanoString panel for TB diagnosis in an Indian population and evaluate its performance in monitoring treatment response.

Proposed Manuscript: Validation of NanoString Platform for TB Treatment Response Biomarkers in India

Status: Analysis completed

DR-TB RNA Treatment Response Signatures

Aim: To assess the utility of RNA signatures in monitoring treatment response in drug-resistant TB (MDR-TB, pre-XDR-TB, and XDR-TB) and compare their performance across different resistance profiles and treatment time points.

Phase II, Aim 2a Biomarker Samples Tested						
Month	M00	M02	M06	M12	End of Tx	Total
nanoString	80	13	77	20	71	261
RNAseq	34	12	31	10	25	112
K/T Ratio, hsCRP, ADA	74	73	72		69	288
Cytokines	50	50	50		50	200

Proposed Manuscript: Early Detection of Treatment Response in Drug-Resistant TB Using RNA Signatures

Status: Manuscript preparation underway

Plasma Cytokine for Treatment Response

Aim: To evaluate plasma cytokine signatures as potential biomarkers for TB treatment response, using multiplex analysis to assess their association with treatment outcomes.

- Proposed Manuscript:** Plasma Cytokine Signatures as Predictors of TB Treatment Success
Status: Samples collected and assays need to be performed. Due to funding concerns study is on hold
- Proposed Manuscript:** Correlation Between Plasma Cytokine Levels and TB Treatment Outcomes in an Indian Cohort
Status: Samples collected and assays need to be performed. Due to funding concerns study is on hold

Aim 2: Markers of treatment response

2A: Identify TB treatment response biomarkers *Continued*

Proteomic Discovery of Protein-based TB Recurrence and Death Signatures

Aim: To identify protein biomarkers associated with TB recurrence and mortality through high-sensitivity proteomic analysis using mass spectrometry.

- **Proposed Manuscript:** Proteomic Markers of TB Recurrence and Mortality
Status: Analysis ongoing
- **Proposed Manuscript:** Mass Spectrometry-Based Discovery of TB Recurrence Biomarkers
Status: Analysis ongoing

Comorbidities and Their Impact on Treatment Response

Aim: To assess the influence of undernutrition, diabetes, smoking, and alcohol use on TB treatment outcomes and biomarker performance and explore the feasibility of integrating

Proposed Manuscript: Nutritional and Comorbidity Factors Affecting TB Treatment Outcomes in India

Status: Analysis ongoing

Clinical Treatment Response Prediction

Aim: To develop and evaluate predictive models for TB treatment response that integrate clinical data, RNA signatures, and biomarker-based risk scores, ensuring affordability and feasibility for implementation in Indian clinical settings

Proposed Manuscript: Prediction of Individual Unfavorable TB Treatment Outcomes in Brazil and India Using Machine Learning

Status: Abstract published in The Union World Conference on Lung Health 2024

Aim 2: Markers of treatment response

2B: Investigate host-related mechanisms of treatment failure

Investigate Host-Related Mechanisms of Treatment Failure

- 1. Investigate Host-Related Mechanisms of Treatment Failure:** To assess how undernutrition and diabetes mellitus (DM) influence TB treatment outcomes, particularly their impact on drug pharmacokinetics (PK) and pharmacodynamics (PD). This study will investigate whether these comorbidities contribute to lower drug concentrations, leading to treatment failure, recurrence, and drug resistance.
Status: Analysis underway
 - **Aim:** Comparison of drug concentrations across different patient groups
Proposed Manuscript: PK Variability and Drug Concentrations in TB Patients with DM and Undernutrition
Status: Analysis ongoing
 - **Aim:** Relationship between body composition changes and treatment outcomes
Proposed Manuscript: Nutritional Status and its Influence on TB Treatment Efficacy and Outcomes
Status: Analysis ongoing
 - **Aim:** To establish preliminary links between TB drug concentrations and clinical outcomes among patients with DM and/or undernutrition
Status: Analysis ongoing
 - To evaluate potential toxicity associated with increased drug concentrations in patients with these comorbidities
 - **Proposed Manuscript:** Evaluating Toxicity and Drug Levels in TB Patients with Comorbid Diabetes and Undernutrition
 - **Status:** Manuscript outline under preparation (Part of the RePORT India 2025 Writing Workshop)
- 2. Influence of gut pathogens and microbiome on drug PK and treatment success**
 - **Aim:** To determine whether DM and undernutrition significantly alter TB drug pharmacokinetics, necessitating therapeutic drug monitoring or dose adjustments to improve treatment outcomes. Additionally, this study will explore the role of enteropathogens in drug absorption and treatment efficacy, offering insights into potential microbiome-based interventions for TB patients.
Proposed Manuscript: Prevalence of Intestinal Parasitic Co infections among TB Patients in India
Status: Sample shipment underway

Aim 2: Markers of treatment response

2c: Investigate pathogen-related mechanisms & predictors of recurrence

Investigate Pathogen-related Mechanisms & Predictors of Recurrence

- Aim:** Perform sub-breakpoint MIC testing for INH, RIF and PZA in pre-treatment sputum cultures
Proposed Manuscript: Sub-breakpoint MICs of INH, RIF, and PZA in Predicting TB Recurrence
Status: Potential study for future
- Aim:** Measure SCVs in pre-treatment sputum samples and identify the responsible mutations
Status: Potential study for future
- Aim:** Determine which SCVs have altered MICs or a drug-persistence phenotype and measure the rate of reversion to LCs
Proposed Manuscript: Genetic Mutations and Phenotypic Variations of SCVs in TB Persistence
Status: Potential study for future
- Aim:** Study the relationship between type and number of SCVs and sub-breakpoint MICs to INH, RIF, and PZA
Proposed Manuscript: Relationship Between Small Colony Variant Proportions and Sub-breakpoint MICs in TB
Status: Potential study for future

Aim 3: Investigating the impact of lung injury on TB treatment outcomes

Association Between Lung Injury and Treatment Outcomes

Aim: To measure the association between clinical, functional, and imaging markers of lung injury and unfavorable TB treatment outcomes in newly diagnosed drug-susceptible PTB cases in India.

Proposed Manuscript: Association between Lung Injury Markers and Treatment Response in PTB Cases

Status: Preliminary analysis ongoing

Identification of Plasma and Sputum Inflammatory Markers

Aim: To identify inflammatory markers in plasma and sputum associated with lung injury in PTB cases.

Proposed Manuscript: Inflammatory Markers of Lung Injury in PTB Cases

Status: Preliminary analysis ongoing

Aim 3: Investigating the impact of lung injury on TB treatment outcomes

Continued

Characterization of Lung Injury Phenotypes

- **Aim:** To categorize lung injury phenotypes and their prevalence in successfully treated PTB cases in India
Proposed Manuscript: Characterization of Lung Injury Phenotypes During and After PTB Treatment
Status: Preliminary analysis ongoing
- **Aim:** To build on Phase 1 findings, which demonstrated that microbiologically cured PTB patients often exhibit significant lung function impairment. This study will expand the investigation into inflammatory markers, lung function, and imaging to predict treatment outcomes and long-term respiratory health.
Proposed Manuscript: Risk-factors of Lung Injury among Adult PTB Patients in India
Status: Preliminary analysis ongoing

Pulmonary Function and Exercise Testing

Aim: To assess lung function impairment using spirometry, 6-minute walk tests (6MWT), and additional lung function assessments (TLC and DLCO) in a subset of participants.

Lung Imaging

Aim: To evaluate lung injury through chest X-ray (CXR), high-resolution CT (HR-CT), and PET-CT scans at multiple time points to assess structural and inflammatory changes in response to TB therapy.

- **Proposed Manuscript:** Evaluation of PET-CT Imaging in Monitoring TB Treatment Response
Status: Ongoing
- **Proposed Manuscript:** Quantitative imaging of TB-associated lung injury
Status: Preliminary analysis ongoing

Respiratory Health Status

Aim: To measure respiratory health outcomes using validated patient-reported assessments (SGRQ, CAT, MMRC) to track quality of life and treatment response.

Status: Preliminary analysis ongoing

Cytokine Testing

Aim: To measure inflammatory cytokine levels in plasma and sputum samples to assess their role in lung injury and treatment response.

Proposed Manuscript: Cytokine Signatures and TB Treatment Outcomes

Status: Preliminary analysis ongoing

Aim 3: Investigating the impact of lung injury on TB treatment outcomes *Continued*

Sputum Storage for Mtb mRNA

Aim: To store induced sputum samples for future studies correlating residual lung inflammation on PET-CT with Mtb mRNA transcription and TB recurrence.

Treatment Outcomes

Aim: To define unfavorable TB treatment outcomes, including failure, recurrence, death, and emerging drug resistance, aligning with Aim 2 methodologies.

Proposed Manuscript: Impact of Lung Injury on TB Recurrence and Mortality

Status: Preliminary analysis ongoing

Aim 4A: Examine host antimicrobial pathways in inducing their IR phenotype in HHC

Examine Host Antimicrobial Pathways in Inducing the IR Phenotype in HHCs

Aim: To test whether the IR phenotype is characterized by enhanced antimicrobial and IL-17 immune pathways, leading to effective innate resistance against Mtb infection.

Proposed Manuscripts:

- Differential Activation of Innate Immune Pathways in TB-Exposed Individuals
- Role of IL-36 and PGE2 in Mediating TB Resistance: Detailed examination of the IL-36 and PGE2 pathways in macrophage-mediated Mtb control.
- Antigen-Specific Th17 Responses in TB Resistance: Analysis of Th17 cell responses and their contribution to the IR phenotype
- Cytokine Balance and TB Resistance: Analysis of the balance between IL-36, PGE2, IL-1, and type I IFN in TB resistance

Status: Potential studies for future

Anticipated Results

Aim: To identify increased IL-36 and PGE2 levels in IR individuals, demonstrating their role in Mtb growth restriction. Additional experiments will confirm the mechanistic interplay between cytokines in macrophage apoptosis and infection control.

Proposed Manuscript: Functional Analysis of IL-36 in Macrophage-Mediated Mtb Control: Detailed study of IL-36's role in macrophage responses to Mtb infection.

Status: Potential studies for future

Aim 4A: Examine host antimicrobial pathways in inducing their IR phenotype in HHC *Continued*

Other Investigations

Aim: To examine potential roles of non-conventional T cells (MAIT cells), NK cells, and microRNAs (miRNAs) in contributing to the IR phenotype.

Proposed Manuscript: Non-conventional T cells: Non-Conventional T Cell Contributions to TB Resistance: Examination of the roles of CD8+ MAIT cells and NK cells in the IR phenotype.

Proposed Manuscripts: microRNAs (miRNAs)

- MicroRNA Profiles Associated with TB Resistance: Identification of miRNAs specific to IR and IS phenotypes and their roles in infection resistance
- Enhanced Antimicrobial Pathways in TB-Resistant Individuals: Identification and validation of key genes and pathways

Status: Potential studies for future

Aim 4B: Test if IR & plasma differ in modulating macrophage-mediated restriction of Mtb growth & evaluate ab repertoires of plasma from the IR and IS cohorts

Investigate Functional Differences in Antibodies from IR and IS Cohorts

Aim: To test whether IR and IS individuals have functionally distinct immunoglobulin (Ig) repertoires that mediate differential resistance to Mtb infection.

Proposed Manuscripts:

- Functional Differences in Antibodies from TB-Resistant and Susceptible Individuals: Analysis of Ig-mediated macrophage responses and antibody specificity.
- Antibody Repertoires in TB-Resistant and Susceptible Individuals: Comparison of antigen-specific antibody responses in IR and IS cohorts.

Status: Potential studies for future

Macrophage-Mediated Mtb Growth Restriction

Aim: To compare plasma from IR and IS individuals for its ability to enhance Mtb killing in macrophages and promote phagolysosomal fusion and autophagy.

Status: Potential study for future

NK Cell Activation & Antibody-Dependent Cellular Cytotoxicity (ADCC)

Aim: To evaluate whether IR plasma enhances NK cell-mediated cytotoxicity against Mtb-infected monocytes using granzyme B cytotoxicity assays.

Status: Potential study for future

Aim 4B: Test if IR & plasma differ in modulating macrophage-mediated restriction of Mtb growth & evaluate AB repertoires of plasma from the IR and IS cohorts *Continued*

Immunoreactivity to Mtb Protein and Glycan Arrays

Aim: To assess differential antibody responses to Mtb protein and carbohydrate antigens in IR and IS plasma samples using microarray technology.

Status: Potential study for future

Anticipated Results

Aim: To demonstrate that IR plasma enhances Mtb killing in macrophages, identify the antigen-specificity of protective antibodies, and establish mechanistic pathways of Fc-mediated effector functions.

Status: Study on hold

Aim 5: Progression to disease: identify immunologic markers of persons at highest risk of progression of latent TB infection to TB

Progression to Disease: Identifying Immunologic Markers of Persons at Highest Risk of Progression from Latent TB Infection to Active TB

Aim: To identify immunologic biomarkers that predict which individuals with latent TB infection (LTBI) are at the highest risk of progressing to active TB disease. This will enable targeted preventive therapy, optimizing public health interventions in TB-endemic settings.

Aim 5A: Stored samples: validation of PREDICT29 in progressors & non-progressors from RePORT

Validation of PREDICT29 Biomarker in Progressors & Non-Progressors

Aim: To validate PREDICT29, a novel blood biomarker signature, in RePORT India cohorts for its ability to stratify individuals at risk of TB progression.

Aim: To validate PREDICT29 in Indian cohorts as a predictive biomarker for TB progression.

Status:

- 100% (N=123) eligible samples shipped in December 2022
- Sample testing completed
- Data analysis ongoing

Aim 5B: Immune & hormone studies in freshly collected samples

Immune & Hormone Studies in Freshly Collected Samples

Aim: To explore immunologic and hormonal factors associated with TB progression, including thyroid hormone (T4) levels, NK and T-regulatory cell profiles, and cytokine responses in PBMCs from TB progressors and non-progressors.

Proposed Manuscript: Identify Immune Biomarkers in children who never develop TB infection or disease using flowcytometry, hormone analysis, RNA sequencing data.

Status: Manuscript preparation underway.

NK Cell Function

Aim: To quantify cytokine production, receptor expression, and cytotoxic activity of NK cells in fresh PBMCs to assess their role in TB progression.

Status: Potential study for future

Monocyte/Macrophage Phenotypes

Aim: To determine whether differential monocyte/macrophage responses contribute to TB progression.

Status: Potential study for future

CD4+ and CD8+ T Cell Function

Aim: To analyze memory and effector T cell phenotypes, including Th1, Th2, and Th17 subsets, and their role in TB progression.

Status: Potential study for future

Aim 5B: Immune & hormone studies in freshly collected samples

Continued

T-Regulatory Cell Function

Aim: To evaluate the suppressive function of CD4⁺CD25⁺FoxP3⁺ Tregs and their association with TB progression.

Status: Potential study for future

Signaling Pathways & MicroRNA Regulation

Aim: To identify signaling molecules and microRNAs that regulate immune responses in TB progressors versus non-progressors.

Proposed Manuscript: Gene Expression and MicroRNA Profiles in TB Progression: Use RNA sequencing to study gene expression and microRNA profiles.

Status: Manuscript preparation underway.

Developing an ELISA-Based Kit for TB Progression Prediction

Aim: To develop a multiplex ELISA kit for detecting early immunologic markers of TB progression, similar to QuantiFERON-TB Gold Plus.

Proposed Manuscript: Development and Validation of a Diagnostic Kit for Early TB Risk Detection: Analyze the cytokine and chemokine production capacity of these cells.

Status: Samples being analyzed

Describing Index Cases to Identify Geographic Differences in TB Disease

Proposed Manuscript: Geographic Variations in TB Disease Presentation and Severity Across RePORT Study Sites

Status: Yet to be started

Measuring Characteristics Associated with TB Disease Severity, Including Radiographic and Microbiologic Data

Proposed Manuscript: Clinical and Socio-Demographic Determinants of TB Disease Severity

Status: Yet to be started

Predictors of Poor TB Treatment Outcomes

Proposed Manuscript: Identifying Predictors of Poor TB Treatment Outcomes in the Context of Comorbidities and Healthcare Settings

Status: Ongoing

Measuring Population Attributable Risk of Different Comorbidities on TB Treatment Outcomes

Proposed Manuscript: Quantifying the Impact of Comorbidities on TB Treatment Outcomes: A Population Attributable Risk Analysis (Phase II compared with Phase I)

Status: Yet to be started

Studying Gender-related Differences in TB Disease Presentation and Outcomes

Proposed Manuscript: Gender Disparities in TB Disease Presentation and Outcomes

Status: Ongoing

Developing and Validating an Epidemiological Risk-score for Predicting TB Disease

Proposed Manuscript: Creating and Validating an Epidemiological Risk-Score for Predicting TB Disease

Status: Concept in preparation

Assessing the Impact of Baseline Nutritional Status and Changes Over Time on Treatment Outcomes and Drug PK

Proposed Manuscript: Nutritional Status and Its Impact on TB Treatment Outcomes and Drug Pharmacokinetics

Status: Manuscript outline under preparation (Part of the RePORT India 2025 Writing Workshop)

Validating the Diagnostic Algorithm for Pediatric TB Suspects

Proposed Manuscript: Validating a Diagnostic Algorithm for Pediatric TB Suspects

Status: Enrolling participant

Describing Causes of Death and Associated Risk Factors in TB Patients During and After Therapy

Proposed Manuscript: Mortality in TB Patients: Causes and Risk Factors During and Post-Therapy

Status: Study ongoing

Describing the Treatment Seeking Behavior and Pathways to TB Diagnosis and Treatment

Proposed Manuscript: Treatment Seeking Behavior and Pathways to TB Diagnosis and Treatment Among TB Patients

Status: Manuscript outline under preparation (Part of the RePORT India 2025 Writing Workshop)

Assessing the Burden of TB Disease and Infection at the Household Level

Proposed Manuscript: Household Clustering of TB Disease and Infection: An Assessment of Community Burden

Status: Ongoing

Identifying Characteristics Associated with Prevalent and Incident TB Disease in Households

Proposed Manuscript: Household Characteristics Linked to Prevalent and Incident TB Disease

Status: Ongoing

Identifying Characteristics Associated with TST/QFT Discordance

Proposed Manuscript: Factors Contributing to TST/QFT Discordance in Household TB Contacts

Status: Manuscript outline under preparation (Part of the RePORT India 2025 Writing Workshop)

Using Clinical and Epidemiologic Data with Basic Science Research to Identify Factors Associated with TB Resistance and Progression

Proposed Manuscript: Integrating Clinical and Epidemiologic Data with Basic Science to Understand TB Resistance and Progression

Status: Study on hold

Longitudinal Dynamics of Respiratory Symptoms etc with Radiographic Findings

Status: Concept in preparation

Validating and Recalibrating the Timika CXR Score for Predicting Response to TB Therapy

Proposed Manuscript: Validation and Calibration of the Timika CXR Score in Predicting TB Therapy Response

Status: Analysis ongoing

Describing index cases to identify geographic differences in TB disease

Proposed Manuscript: Geographic Variations in TB Disease Presentation and Severity Across RePORT Study Sites.

Status: Yet to be started

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CONCEPT SHEETS



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Resistance to TB Genome-wide Association Study (GWAS)

Lead Investigators: Neel Gandhi, Yan Sun

Institution: Emory University

Submission Date: 8/24/2017

Funding: NIH R01 Awarded

Status: Open - DBT NOC Pending

EC Approval Status: Fully Approved | Initial: 9/25/2017 | Additional Sites: 10/4/2019

CP Data Access: NOC Approved

Action Items: Dec 2020: DBT NOC pending (including additional sites) | Dec 2020: DBT approved TBGWAS NOC

Updates: See DBT NOC Tracker

Collaboration for NIH IMPAc-TB Contract Application: Immune Responses Associated with Progression to TB

Lead Investigator: Jyothi Rengarajan

Institution: Emory University

Submission Date: 6/20/2018

Funding: NIH Award not funded

Status: Closed

EC Approval Status: Approved (contingent on funding)

UCSF Proposal for NIH IMPAcTB BAA - Identifying Key Immune Responses Needed for Protection against Mtb and for the Development of TB Vaccines

Lead Investigators: Joel Ernst, Adithya Cattamanchi, Payam Nahid

Institution: University of California, San Francisco

Submission Date: 6/26/2018

Funding: NIH Award not funded

Status: Closed

EC Approval Status: Approved (contingent on funding)

RePORT Xpert TB Host Response RUO

Lead Investigator: Robert W. Kwiatkowski

Institution: CEPHEID

Submission Date: 3/5/2019

Funding: Self-funded

Status: Closed- No longer pursuing

EC Approval Status: Initial Review Complete, Awaiting Revised CS

Action Items: RePORT India PIs involved to revise concept sheet and submit for EC/WG review (March) | EC/WG to review revised concept sheet (March/April)

Updates: Sept 2020: Concept sheet submission in progress, specimen availability confirmation and final number of samples based on sample availability across sites to be finalized.

Impact of Nutrition on TB Outcomes (INTO study)

Lead Investigators: Natasha S Hochberg, Padma Chandrasekaran

Institutions: Boston Medical Center and NIRT

Submission Date: 5/14/2019

Funding: N/A (Analysis only)

Status: Open - Analysis Ongoing

EC Approval Status: Fully Approved (4/8/2020)

CP Data Access: Requested: 6/13/2020 | Granted: 7/15/2020

Action Items: Dec 2020: Drs Ponnuraja, Sinha, Hochberg to complete data analysis.

Updates:

- Dec 2020: Analysis Ongoing
- Sept 2020: PP Data granted. They have their analytical plan sketched out with Dr. Padma, Dr. Ponnuraja, Nikhil, Natasha, and Dr. Pranay.
- They are awaiting some missing variables from the SAS team and can then begin data analysis.
- April 2020: DBT has approved Concept sheet inclusive of Indian participants on 8th April. Access for data granted by all participating PIs from Phase I.
- July 2020: Access to CP data has been sent to SAS CHRD on 13th June 2020. SAS has shared the data with the team on 15th July. Awaiting PP data confirmation by the team.
- Oct 2020: SAS sent data elements.
- Nov 2020: Response from SAS: They checked the list of variables for the concept sheet#6 and these diabetes variables were not mentioned in the list, if the team wants data of these diabetes variables, they need to update the concept sheet#6 and get it approved from DBT and EC.
- Dec 2020: Dr. Pranay is currently working on the variables in the PP data. They will make the request for additional variables in the CP dataset just in case they need something more than just the diabetes variables.
- Dec 2020: Dr. Sonali has requested DBT to authorise SAS to release the data as requested by the team (diabetes element). Awaiting response from SAS.

Immune Responses and Effect of Disulfiram on MTB Infected PBMCs as a Potential Host Directed Therapy

Lead Investigators: Amit Singhal, Ramandeep Singh

Institutions: THSTI

Submission Date: 9/26/2019

Funding: Self-funded

Status: Open - Shipment Pending

EC Approval Status: Fully Approved (2/25/2020)

CP Sample Access: Awaiting THSTI investigators to complete & sign Sample Request Form & MTA

Action Items: Dec 2020: THSTI signature on Sample Request Form and MTA

Updates:

- Sept 2020: Concept sheet approved by EC in Feb 2020. Revised protocol with CP samples included approved at BJMC IRB in March 2020, awaiting approval from NIRT and THSTI. Final MTA between THSTI and NIRT Central repository to be signed. Will initiate sample shipments after IRB approvals and MTA signed.
- Dec 2020: NIRT IEC submission for 19th December 2020 in Progress, IRB approval for revised version of the protocol at THSTI unknown (awaiting response from THSTI), NIRT CR will sign the MTA after THSTI completes their signatures. Samples are identified and the CR is aware of the sample list. Once the MTA process completes, sample should be ready to be shipped.

Description of Radiological Involvement and Correlation with Disease Severity Variables & Outcomes

Lead Investigators: DJ Christopher, Bala Thangakunam

Institution: CMC Vellore

Submission Date: 3/24/2021

Funding: CP existing budget will be used

Status: Complete

EC Approval Status: Fully Approved (10-06-21)

Factors Associated with Favorable and Unfavorable Treatment Outcomes among Pulmonary Tuberculosis Patients in South India

Lead Investigators: Senbagavalli Prakash Babu, Sonali Sarkar

Institutions: JIPMER

Submission Date: 5/27/2021

Funding: Funds from the Common Protocol budget will be used to support these efforts

EC Approval Status: Fully Approved

Action Items: Review was waived at the request of Clinical Epi WG Co-Chairs

Understanding Mycobacterium tuberculosis Mediated Host Metabolomics in Pulmonary Tuberculosis: Correlation with Disease Severity and Treatment Course

Lead Investigators: Senbagavalli Prakash Babu, Sonali Sarkar

Institutions: JIPMER

Submission Date: 9/9/2021

Funding: Partnerships For Enhanced Engagement in Research (PEER) Women in Science SEED Grants 202

EC Approval Status: Fully Approved

Innovative Modelling for Predicting TB Treatment Outcomes in Global Cohorts

Lead Investigator: Sonya Krishnan

Institutions: JHU

Funding: NIH/CRDF - TB RICG Grant

Status: Open - DBT NOC Pending

EC Approval Status: Fully Approved

Population Attributable Fractions for TB Disease and Unfavorable TB Treatment Outcomes among TB Cases and their Household Contacts in RePORT India

Lead Investigators: Akshay Gupte, Sonali Sarkar, Natasha Hochberg, Nikhil Gupte, Pranay Sinha

Institutions: JHU, JIPMER, Boston University, BJMC-JHU

Funding: Not related to an existing grant; No RePORT funds will be used

Status: Open - DBT NOC Pending

EC Approval Status: Fully Approved

Psychological Distress Among TB Patients and their Household Contacts

Lead Investigator: Nishi Suryavanshi

Institution: BJGMC

Analysis of Host Biomarkers Associated with Adverse TB Treatment Outcomes across RePORT International Sites

Lead Investigator: Padmini Salgame

Institution: Rutgers

Validation of Differentially Expressed Monocyte Genes_NIRT

Lead Investigator: Uma Devi

Institution: NIRT

Status: Approved - LOS given

Updates: Awaiting approval for LOS to begin shipment process

Whole Genome Sequencing of MTB Clinical Strains for Determining Drug Resistance and Strain Lineage in India: A Structured Nationwide Approach

Lead Investigator: Sonali Sarkar

Institution: JIPMER

Submission Date: 1/18/2024

Funding: Part of an already approved grant with the involvement of only Indian funding

Status: Approved

EC Approval Status: Part of an already approved grant with the involvement of only Indian funding

Updates: Awaiting approval for LOS to begin shipment process

Metabolites, Inflammation, Type 2 Diabetes Mellitus and Tuberculosis Patients

Lead Investigator: N. Pavan Kumar

Institution: NIRT

Submission Date: 11/4/2024

Funding: RICC Cross Consortium

Status: Approved - LOS given

Updates: Will first receive the Paxgene and Plasma samples and begin the work. Once the validation process is completed, they will then receive the PBMC vials to continue with the next steps

Impact of Alcohol Consumption on Tuberculosis Severity, Treatment Response, and Outcomes: A Longitudinal Analysis of AUDIT-C Categories

Lead Investigator: Spurthi Kodali

Institutions: JHU

Submission Date: 2/15/2025

Funding: Common Protocol Budget

Status: Awaiting Operational Review

EC Approval Status: Approved

Action Items: Review was waived at the request of Clinical Epi WG Co-Chairs

Neutrophil-to-lymphocyte Ratio and Post-tuberculosis Pulmonary Function

Lead Investigator: Jacqueline Dinh

Institution: Boston University

Submission Date: 2/14/2025

Funding: BUMC Fellowship Program

Status: Awaiting Operational Review

EC Approval Status: Approved

The Burden of Anemia in Tuberculosis Progression

Lead Investigator: Sonali Sarkar

Institution: JIPMER

Submission Date: 6/3/2025

Funding: Internal Funding

Status: Awaiting Operational Review

EC Approval Status: Fully Approved

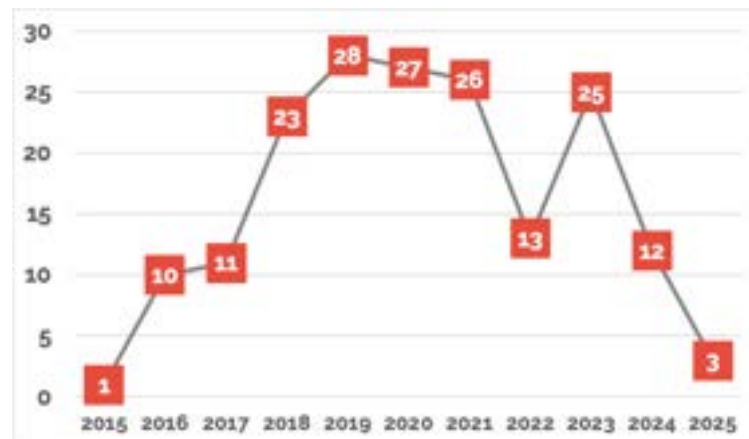
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PUBLICATIONS



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Publications for all years are accessible on RePORT India's website

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2025

Nancy Pandiarajan A, Kumar NP, Moideen K, Thiruvengadam K, Hissar S, Sivakumar S, Bethunaickan R, Viswanathan V, Kornfeld H, Babu S. **Association of Altered Baseline Hematological Parameters with Adverse Tuberculosis Treatment Outcomes.** Pathogens. 2025 Feb 4;14(2):146. doi: 10.3390/pathogens14020146. PMID: 40005523.

Dasan B, Munisankar S, Kumar NP, Moideen K, Pandiarajan AN, Nott S, Viswanathan V, Shanmugam S, Hissar S, Thiruvengadam K, Kornfeld H, Babu S. **Coexistent anemia modulates systemic inflammation and exacerbates disease severity and adverse treatment outcomes in tuberculosis.** Front Tuberc. 2025 Jan 13;2:1462654. doi: 10.3389/ftubr.2024.1462654

Nogueira BMF, Rangel F, Andrade AMS, Daniel EA, Figueiredo MC, Staats C, Rolla VC, Kritski AL, Cordeiro-Santos M, Gupta A, Hanna LE, Sterling TR, Araújo-Pereira M, Andrade BB; RePORT Brazil and RePORT India Consortia. **Predictive Markers of Incident Tuberculosis in Close Contacts in Brazil and India.** J Infect Dis. 2025 Jan 7;jiae642. doi: 10.1093/infdis/jiae642. PMID: 39763217

2024

Richterman A, Sinha P, Ivers LC, Gross R, Rantleru T, Tamuhla N, Bisson GP. **Food Insecurity and Undernutrition Are Associated With Distinct Immunologic Profiles in People With Tuberculosis and Advanced HIV Starting Antiretroviral Therapy.** J Acquir Immune Defic Syndr. 2024 Apr 15;95(5):494-504. doi: 10.1097/QAI.0000000000003386. PMID: 38346410; PMCID: PMC10947883.

Sinha P, Guerrant RL. **The Costly Vicious Cycle of Infections and Malnutrition.** J Infect Dis. 2024 Jun 14;229(6):1611-1613. doi: 10.1093/infdis/jiad513. PMID: 37972258; PMCID: PMC11175688.

Rajamanickam A, Kothandaraman SP, Kumar NP, Viswanathan V, Shanmugam S, Hissar S, Nott S, Kornfeld H, Babu S. **Cytokine and chemokine profiles in pulmonary tuberculosis with pre-diabetes.** Front Immunol. 2024 Aug 29;15:1447161. doi: 10.3389/fimmu.2024.1447161. PMID: 39267759; PMCID: PMC11390597.

2024 Continued

Rajamanickam A, Ann Daniel E, Dasan B, Thiruvengadam K, Chandrasekaran P, Gaikwad S, Pattabiraman S, Bhanu B, Sivaprakasam A, Kulkarni V, Karyakarte R, Paradkar M, Shivakumar SVBY, Mave V, Gupta A, Hanna LE, Babu S. **Plasma Immune Biomarkers Predictive of Progression to Active Tuberculosis in Household Contacts of TB Patients.** J Infect Dis. 2024 Jul 19;jiae365. doi: 10.1093/infdis/jiae365. Epub ahead of print. PMID: 39028003.

Daniel EA, Upadhyay S, Selvachithiram M, Pattabiraman S, Bhanu B, Sivaprakasam A, Kulkarni V, Karyakarte R, Gaikwad S, Paradkar M, Yogendra Shivakumar SVB, Mave V, Gupta A, Prasad K, Hanna LE. **Predictive metabolite signatures for risk of progression to active TB from QuantiFERON supernatants of household contacts of TB patients.** Emerg Microbes Infect. 2025 Dec;14(1):2437242. doi: 10.1080/22221751.2024.2437242. Epub 2024 Dec 22. PMID: 39628384; PMCID: PMC11703509.

Daniel EA, Thiruvengadam K, Chandrasekaran P, Hilda N, Umashankar P, Prashanthi P, Selvachithiram M, Pattabiraman S, Bhanu B, Sivaprakasam A, Paradkar M. **Discovery of a blood-based miRNA signature that can predict onset of active tuberculosis among household contacts of TB patients.** Front Tuberc. 2024 Oct 28;vol2. <https://doi.org/10.3389/ftubr.2024.1415346>

Sinha P, Ezhumalai K, Du X, Ponnuraja C, Dauphinais MR, Gupte N, Sarkar S, Gupta A, Gaikwad S, Thangakunam B, Paradkar M, Christopher DJ, Mave V, Viswanathan V, Ellner JJ, Kornfeld H, Horsburgh CR Jr, Padmapriyadarsini C, Gupte A. **Undernourished Household Contacts Are at Increased Risk of Tuberculosis (TB) Disease, but not TB Infection-a Multicenter Prospective Cohort Analysis.** Clin Infect Dis. 2024 Jul 19;79(1):233-236. doi: 10.1093/cid/ciae149. PMID: 38652286; PMCID: PMC11259213.

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Pandiarajan AN, Kumar NP, Selvaraj N, Ahamed SF, Viswanathan V, Thiruvengadam K, Hissar S, Shanmugam S, Bethunaickan R, Nott S, Kornfeld H, Babu S. **Distinct TB-antigen stimulated cytokine profiles as predictive biomarkers for unfavorable treatment outcomes in pulmonary tuberculosis.** Front Immunol. 2024 Jun 3;15:1392256. doi: 10.3389/fimmu.2024.1392256. PMID: 38887283; PMCID: PMC11180841.

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2024 Continued

Prakash Babu S, Ezhumalai K, Raghupathy K, Karoly M, Chinnakali P, Gupte N, Paradkar M, Devarajan A, Dhanasekaran M, Thiruvengadam K, Dauphinais MR, Gupte AN, Shivakumar SB, Thangakunam B, Christopher DJ, Viswanathan V, Mave V, Gaikwad S, Kinikar A, Kornfeld H, Horsburgh CR, Chandrasekaran P, Hochberg NS, Salgame P, Gupta A, Roy G, Ellner J, Sinha P, Sarkar S. **Factors Associated With Unfavorable Treatment Outcomes Among Persons With Pulmonary Tuberculosis: A Multicentric Prospective Cohort Study From India.** Clin Infect Dis. 2024 Oct 15;79(4):1034-1038. doi: 10.1093/cid/ciae367. PMID: 38991034; PMCID: PMC11478802.

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Tabackman A, Gupte A, Babu SP, Du X, Paradkar M, Ponnuraja C, Cox S, Gupte N, Tornheim J, Dauphinais M, Gupta A, Christopher DJ, Kornfeld H, Mave V, Viswanathan V, Ellner JJ, White L, Padmapriyadarsini C, Sinha P*, Sarkar S*. **Impact of premorbid nutritional status on tuberculosis severity in India: a multicenter prospective cohort analysis.** The International Journal of Tuberculosis and Lung Disease. 2025 (accepted, in press).

Carwile MR, Jain K, Dauphinais MR, Narasimhan PB, Maloomian K, Manju R, Cintron C, McQuaid CF, Locks LM, Sabin LL, Lakshminarayanan S*, and Sinha P*. **Food insecurity in South Indian households with TB during COVID-19 lockdowns and the impact of nutritional interventions: a qualitative study.** Plos Global Public Health. 2025 (accepted, in press).

Sinha P, Bhargava M, Carwile ME, Dauphinais MR, Tisile P, Cintron C, Locks LM, Hauser J, Oliver M, Heysell SK, Mehta S, Finkelstein JL, Koura KG, Cegielski JP, Houben R, McQuaid CF, Bhargava A. **Impact of premorbid nutritional status on tuberculosis severity in India: a multicenter prospective cohort analysis.** Lancet Global Health. 2025. (accepted, in press).

Submitted Manuscripts

Spotting the Silent Threat: Early Detection of Subclinical Tuberculosis in High-Risk Individuals. First Author: Luke Elizabeth Hanna

Incidence of asymptomatic tuberculosis recurrence among cured pulmonary tuberculosis patients in India. First Author: Mandar Paradkar

Evaluation of cycloserine dose regimens in an Indian cohort with multidrug-resistant tuberculosis: a population pharmacokinetic analysis. First Author: Juan Galvan

Creating-A-Hope: Most Preferred Psycho-Social Intervention among Adolescents and Young Adults with Multidrug-Resistant Tuberculosis to Improve Treatment Outcomes in Pune, India. First Author: Gauri Dhumal

Contribution of Key Comorbidities to Unfavorable Tuberculosis Treatment Outcomes among Adults with Drug-sensitive Pulmonary Tuberculosis in India: a Prospective Cohort Analysis. First Author: Pranay Sinha

Programmatic Management of Tuberculosis Prevention Treatment in India

Paradkar M, Padmapriyadarsini C, Jain D, Shivakumar SVBY, Thiruvengadam 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, S R, Suryavanshi N, B M S, Cox SR, Selvaraju S, Gupte N, Mave V, Gupta A, Bollinger RC; CTRIUMPH-RePORT India Study Team. **Tuberculosis preventive treatment should be considered for all household contacts of pulmonary tuberculosis patients in India.** PLoS One. 2020 Jul 29;15(7):e0236743. doi: 10.1371/journal.pone.0236743. Erratum in: PLoS One. 2020 Dec 31;15(12):e0244914. doi: 10.1371/journal.pone.0244914. PMID: 32726367; PMCID: PMC7390377.

- **Guidelines for Programmatic Management of Tuberculosis Preventive Treatment in India, NTEP, July 2021**

Strengthening Nutritional Support for TB Care

Sinha P, Lakshminarayanan SL, Cintron C, Narasimhan PB, Locks LM, Kulatilaka N, Maloomian K, Prakash Babu S, Carwile ME, Liu AF, Horsburgh CR, Acuna-Villaorduna C, Linas BP, Hochberg NS. **Nutritional Supplementation Would Be Cost-Effective for Reducing Tuberculosis Incidence and Mortality in India: The Ration Optimization to Impede Tuberculosis (ROTI-TB) Model.** Clin Infect Dis. 2022 Sep 10;75(4):577-585. doi: 10.1093/cid/ciab1033. PMID: 34910141; PMCID: PMC9464065.

- **The Hindu**, Published October 07, 2024: "Government doubles monthly nutrition support for tuberculosis patients to ₹1,000. All household contacts of TB patients will be covered under the Pradhan Mantri TB Mukht Bharat Abhiyaan and will be eligible to receive social support from the Ni-kshay Mitra initiative.
- **The Indian Express**, Published October 08, 2024: "Monthly nutrition support for TB patients doubled to Rs 1000: India has set 2025 as its target year for TB elimination, five years ahead of the target set by SDG."

TB Patients Must also Be Screened for Prediabetes in India

Viswanathan V, Devarajan A, Kumpatla S, Dhanasekaran M, Babu S, Kornfeld H. **Effect of prediabetes on tuberculosis treatment outcomes: A study from South India.** Diabetes Metab Syndr. 2023 Jul;17(7):102801. doi: 10.1016/j.dsx.2023.102801. Epub 2023 Jun 8. PMID: 37354752; PMCID: PMC10528008.

- **The Hindu**, Published October 02, 2023: "Currently pre-diabetic TB population falls through the cracks of National TB Elimination Programme and are not easily picked up for focussed care."

Biomarkers to Predict Advance of TB in Household Contacts of Patients

Rajamanickam A, Ann Daniel E, Dasan B, Thiruvengadam K, Chandrasekaran P, Gaikwad S, Pattabiraman S, Bhanu B, Sivaprakasam A, Kulkarni V, Karyakarte R, Paradkar M, Shivakumar SVBY, Mave V, Gupta A, Hanna LE, Babu S. **Plasma Immune Biomarkers Predictive of Progression to Active Tuberculosis in Household Contacts of TB Patients.** J Infect Dis. 2024 Jul 19;jiae365. doi: 10.1093/infdis/jiae365. Epub ahead of print. PMID: 39028003.

- **The Indian Express**, Published October 5, 2023: "Biomarkers to predict advance of TB in household contacts of patients an important find"

RePCORT

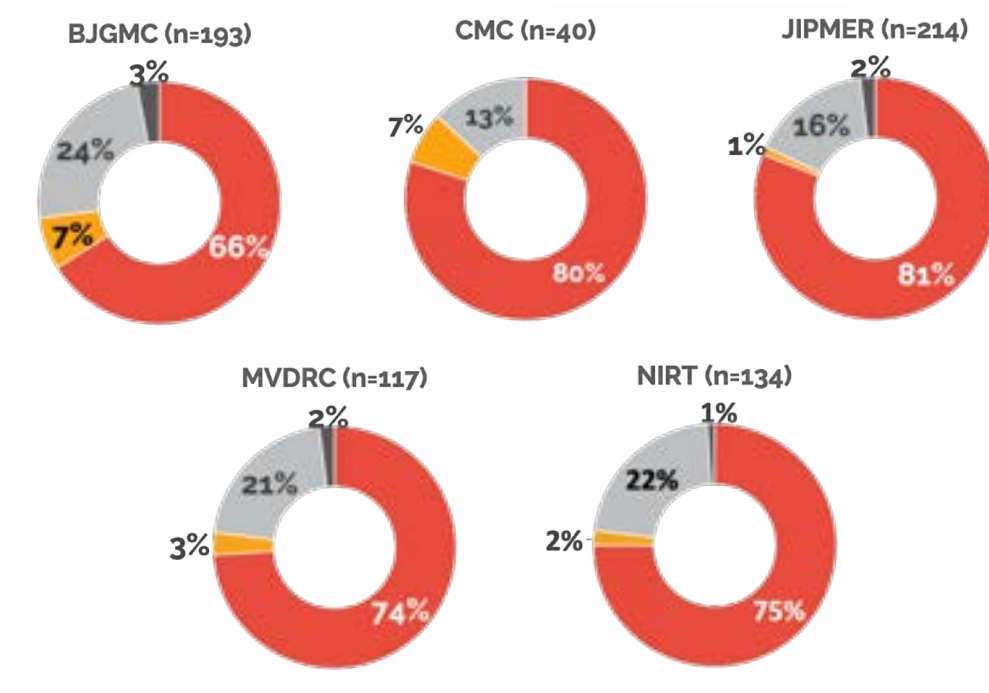
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DATA

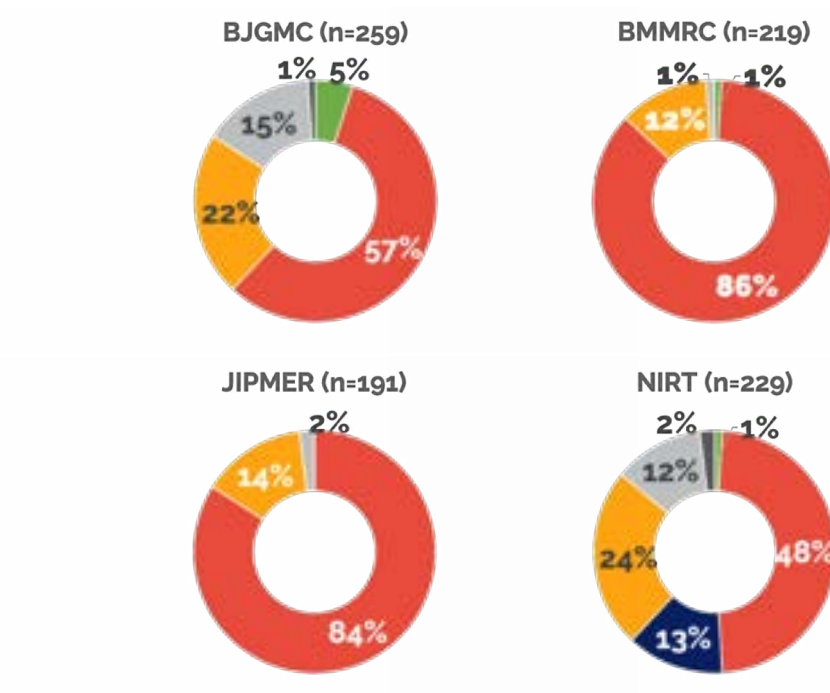
10 YEARS OF
TB RESEARCH

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Phase 1: Common Protocol Cohort A: Accrual



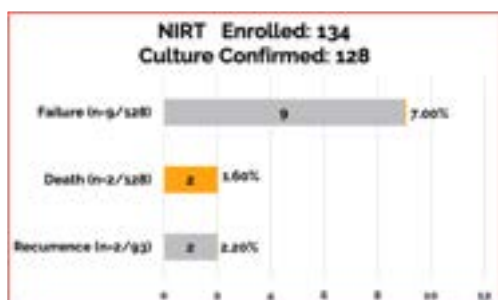
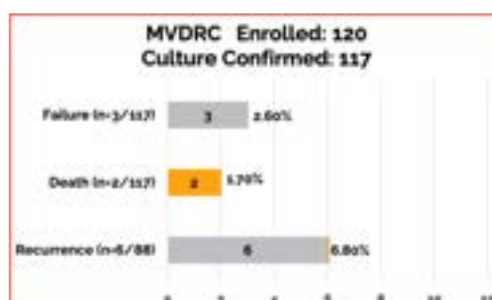
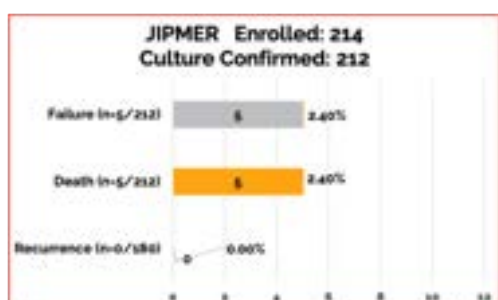
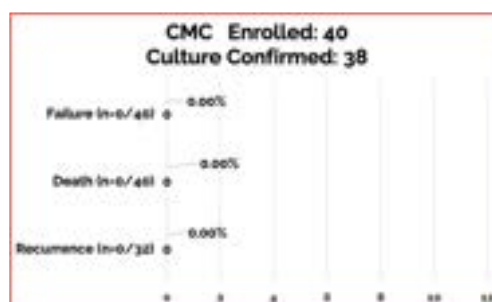
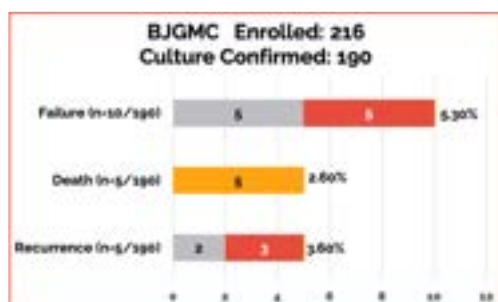
Phase 1: Common Protocol Cohort B: Accrual



Enrolled | Completed Follow Up | On Active Follow Up

Lost to Follow Up | Prematurely Discontinued | Death

Phase 1: Cohort A Treatment Outcomes



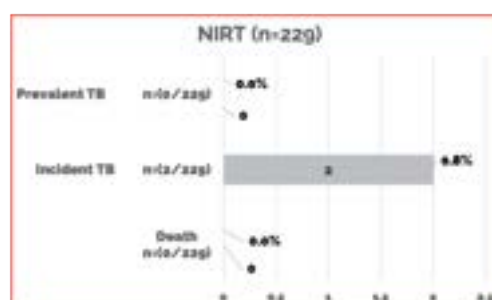
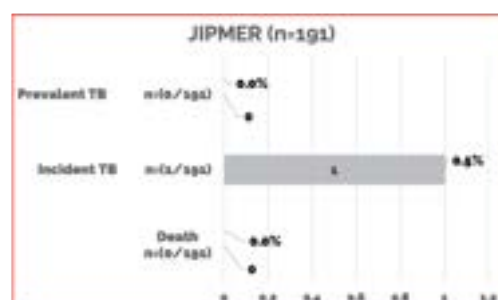
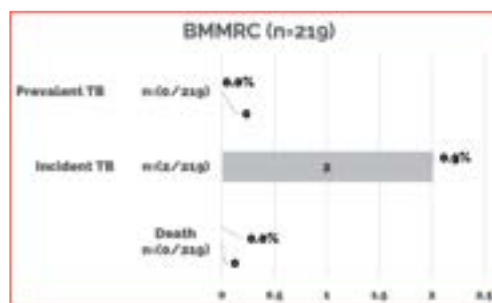
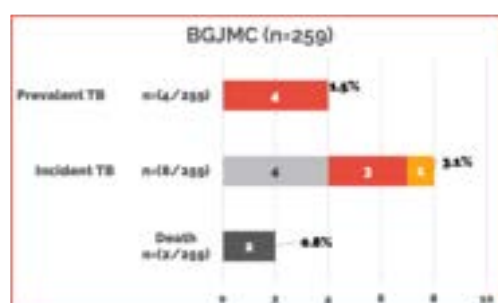
Bacteriological

Clinical

Total

Death

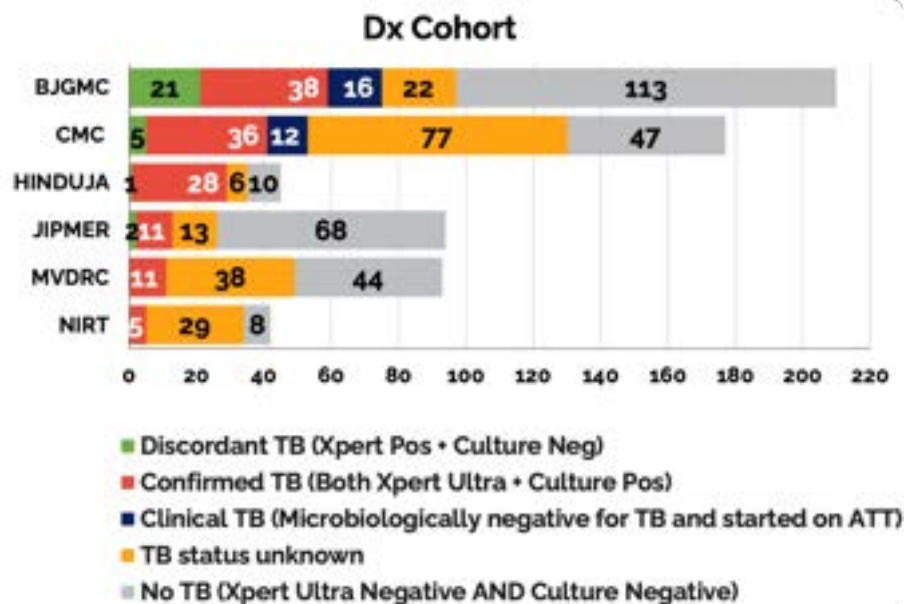
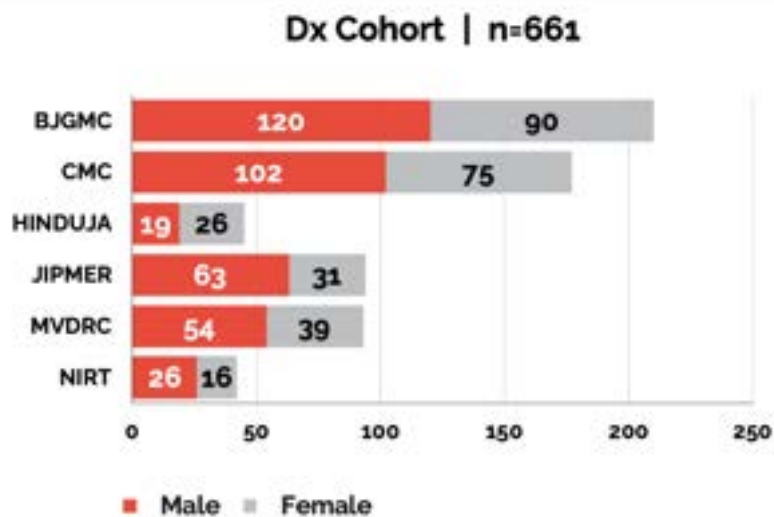
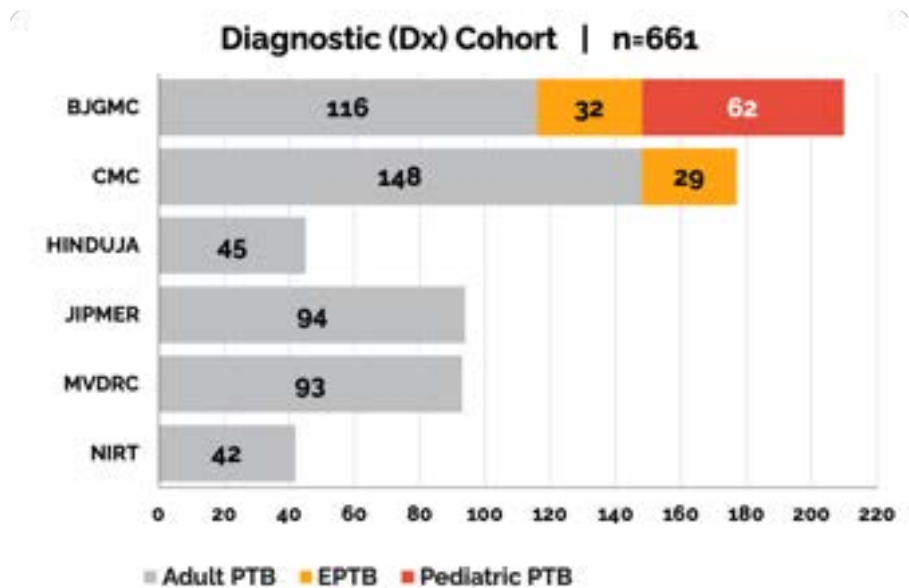
Phase 1: Cohort B Study Outcomes



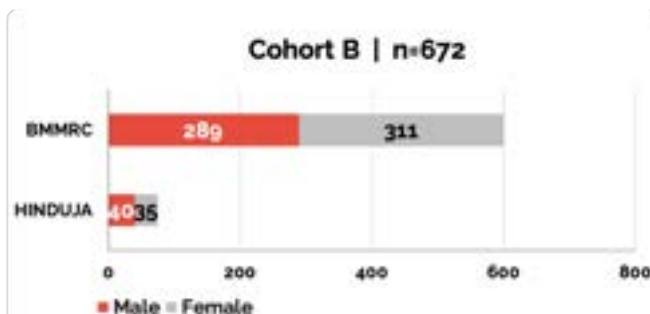
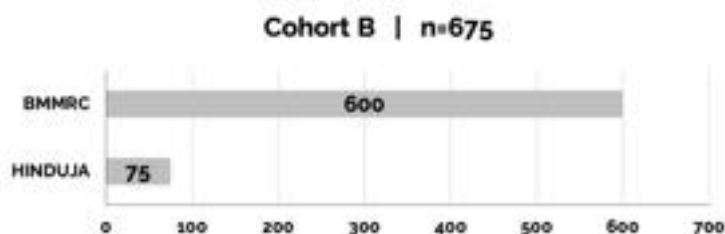
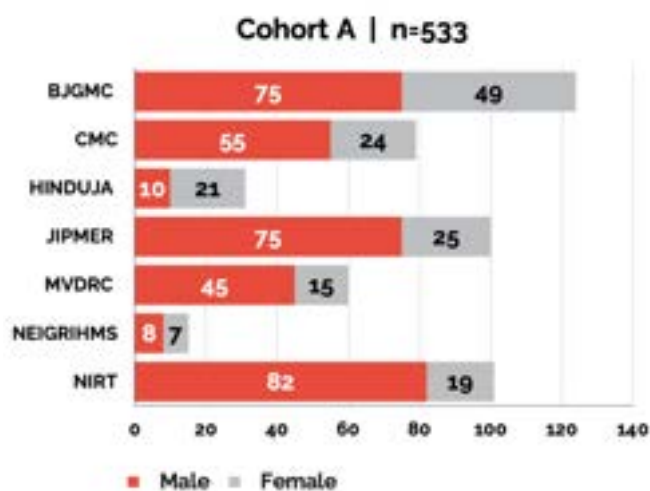
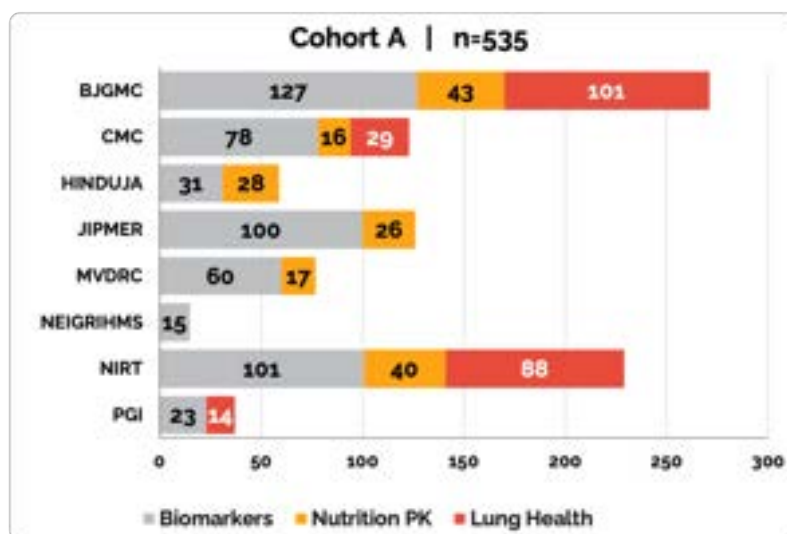
Outcomes

Participants

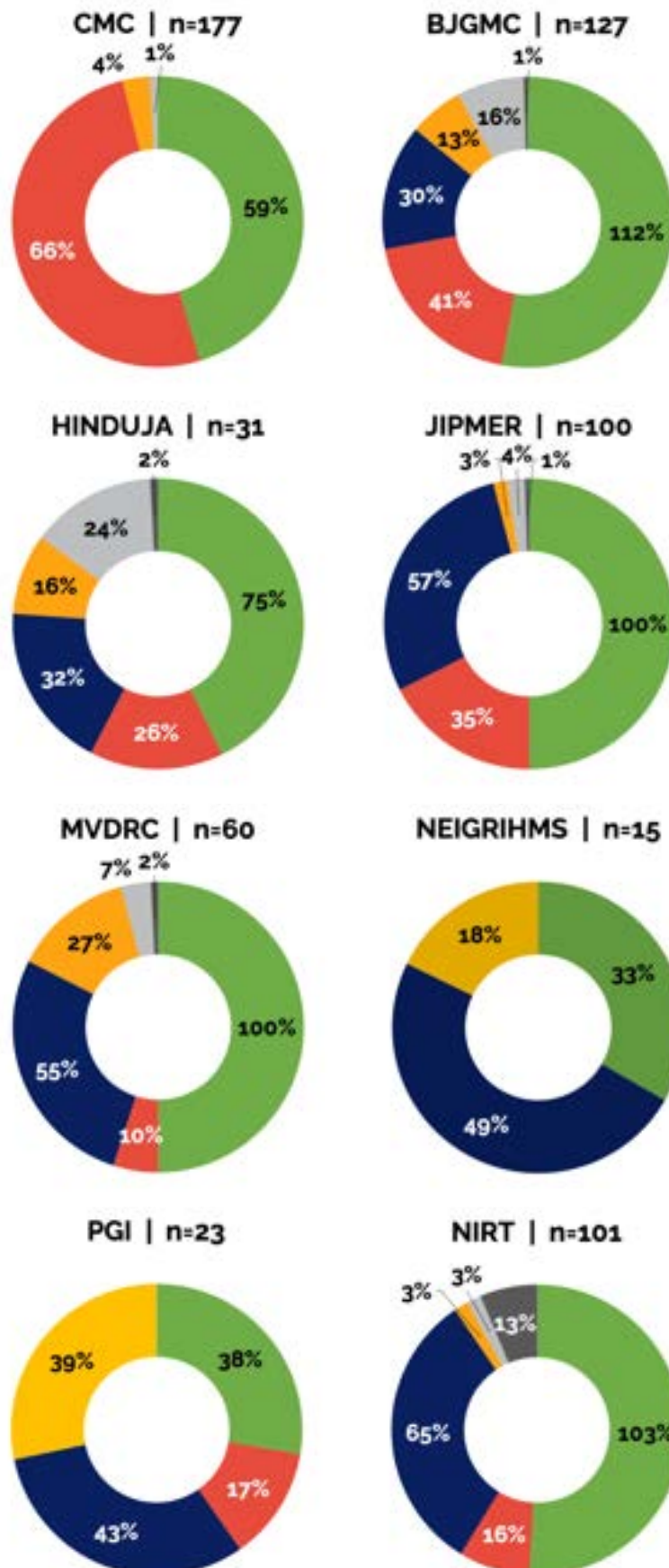
Diagnostic Cohort Enrollment & Outcomes



Enrollment



Cohort A Accrual Status



Enrolled

Completed Follow Up

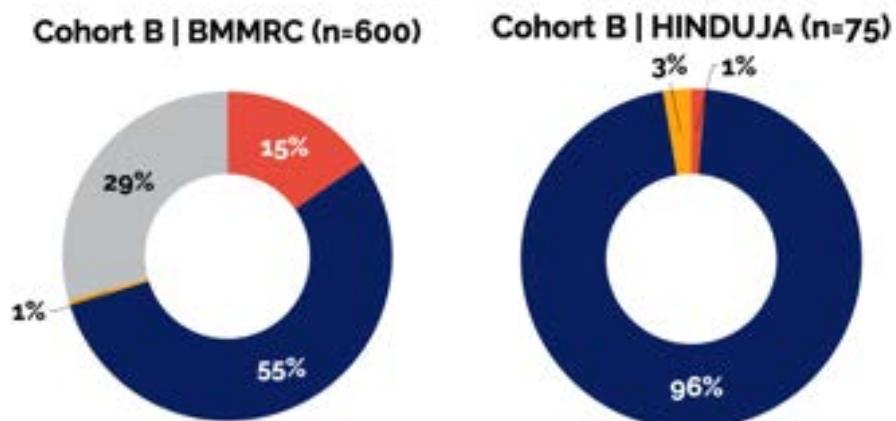
On Active Follow Up

Lost to Follow Up

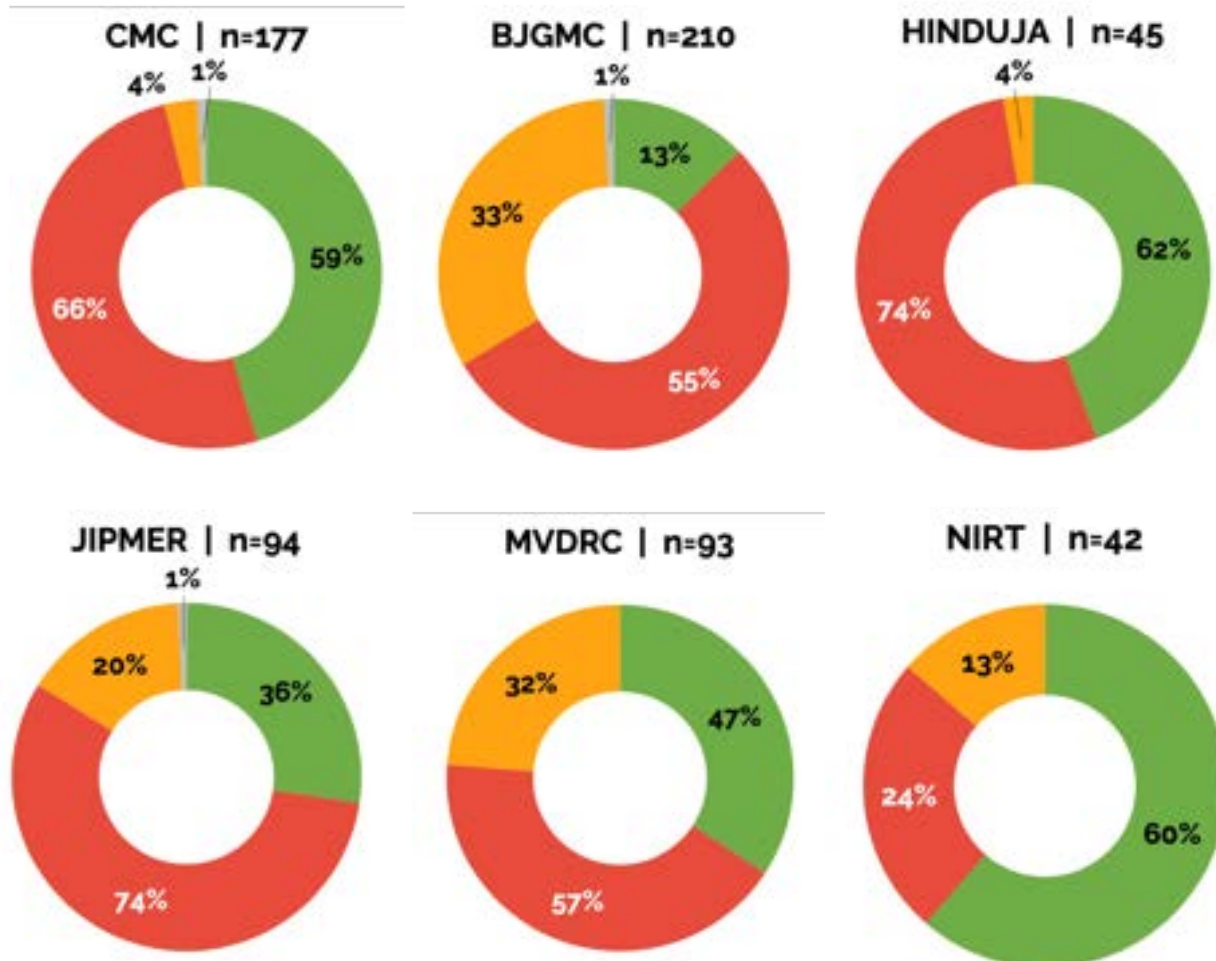
Prematurely
Discontinued

Death

Cohort B Accrual Status



Diagnostic Cohort Accrual Status

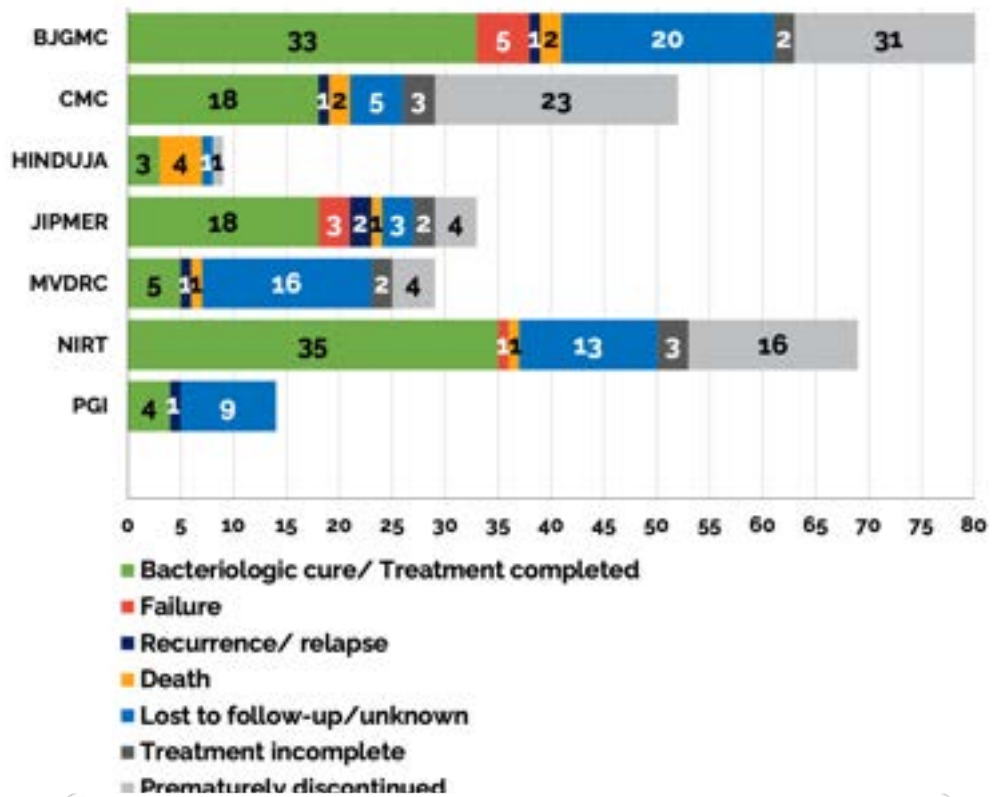


Enrolled | Completed Follow Up | On Active Follow Up

Lost to Follow Up | Prematurely Discontinued | Death

Outcomes

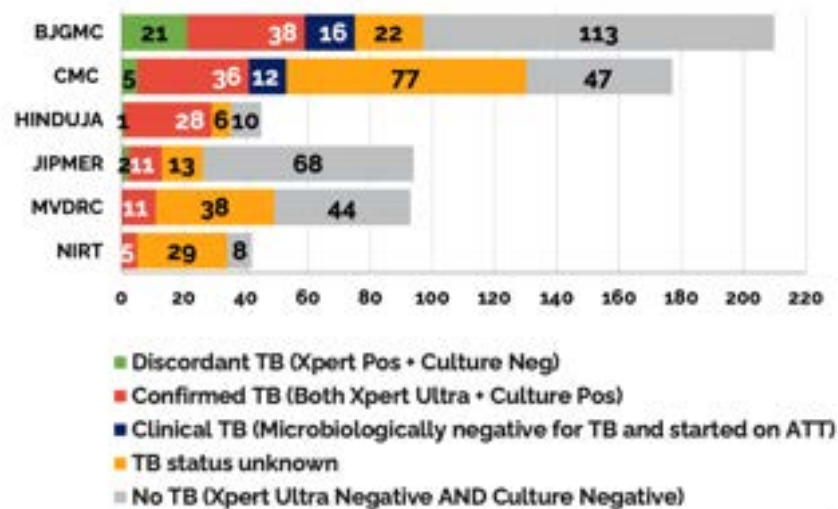
Cohort A



Cohort B



Dx Cohort



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RePCORT

INDIA

FUNDING

10 YEARS OF
TB RESEARCH

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Funding in USD

India Institutions: CRDF Funding	\$2,688,143
US Institutions: CRDF Funding	\$7,068,191
India Institutions: DBT Funding	\$2,565,507
Total	\$12,321,841

Funding in INR

India Institutions: CRDF Funding	₹22,84,92,155
US Institutions: CRDF Funding	₹60,07,96,269
India Institutions: DBT Funding	₹21,80,68,073
Total	₹1,04,73,56,497

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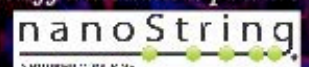
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References: 1. Nijhawan, A., et al. (2016) Cost analysis of tuberculin skin test and the QuantiFERON-TB Gold In-tube test for tuberculosis screening in a correctional setting in Dallas, Texas, USA. *BMC Infect. Dis.* 16, 564.

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