ISTM 2026

CENMIG

THE 3rd INTERNATIONAL SYMPOSIUM ON TUBERCULOSIS AND MYCOBACTERIA: A MULTIDISCIPLINARY APPROACH

ISTM 2026

2 - 4 FEBRUARY 2026
Arnoma Grand Hotel Bangkok, Thailand

272 Rama VI Road, Ratchathewi
Bangkok, Thailand 10400

Email : ISTM2026@gmail.com
TEL : (+66)2-201-5548

The 3rd International Symposium on Tuberculosis and Mycobacteria: A Multidisciplinary Approach

2-4 February 2026

Arnoma Grand Hotel Bangkok, Thailand

Organized by

Emeritus Professor Pornchai Matangkasombut
Center of Microbial Genomics (CENMIG),
Department of Microbiology,
Faculty of Science, Mahidol University

and

Professor Igor Mokrousov
Saint Petersburg's Pasteur Institute

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Welcome Address from Igor Mokrousov

As co-chair of ISTM2026, I would like to take a few moments to briefly recollect the history of this event. In September 2014, a Symposium on Tuberculosis and Mycobacteriosis was held in St. Petersburg. It was organized by scientists from the St. Petersburg Pasteur Institute and the Research Institute of Phthisiopulmonology. It was a one-day event with Russian participation in general. However, 6 experts from Germany, Great Britain, France, Sweden, and Japan also took part in it, making it a unique event of this kind in Russia.

Four years later, under the umbrella of the 110th anniversary conference of St. Petersburg Pasteur Institute, the 2nd Symposium on Tuberculosis and Mycobacteria took place. It was already a full-size, two-day meeting focused on molecular aspects in the field of mycobacteriology. The international component increased significantly. The participants represented 23 countries: mostly Europe (Russia and 15 EU countries) but also the USA, Japan, Thailand, and South Africa. The Best Poster Awards were given to Margaretha de Vos (Stellenbosch University, South Africa) and Irina Linge (Central Tuberculosis Institute, Russia). The 2nd symposium became a multidisciplinary event at the intersection of population and systems biology, genome bioinformatics, fundamental and personalized medicine.

I had the honor and pleasure to co-organize and chair both meetings in St. Petersburg in 2014 and 2018. I anticipated to make the next one in 3-4 years. This did not happen due to unfortunate and unforeseen challenges. Which is why I was most sincerely grateful to Professor Prasit Palittapongarnpim and the Mahidol University for the kind offer to make the 3rd symposium in Bangkok. During the last year, the team of Professor Prasit Palittapongarnpim accomplished a hard and tremendous organizational job. I am convinced that the 3rd symposium ISTM2026 will be a great success.

As before, the target audience is all those interested in the latest achievements in this field and seeking to acquire new knowledge, exchange ideas, and network for future cooperation. Oral and poster sessions will take place within a single space with enough time for lectures and free communication. This time, we will have a more visible and diverse participation from Asia that will hopefully contribute to establishing new collaboration links. Participation of researchers from different fields will highlight the multidisciplinary nature of this symposium.

I expect the fantastic spirit of scientific curiosity would stimulate our interaction throughout both intense sessions and relaxing long breaks, as well as beyond the scientific program. Indeed, the advantages of a moderate-scale event include the unrestricted opportunity for learning, talking, and meeting all persons of interest, be they world-level experts, PhD students, or postdocs.

Welcome to Bangkok, and let's enjoy the hospitality of Krung Thep – “City of Angels” and three days of the amazing science.

Igor Mokrousov, PhD, DSc
Head, Lab. of Molecular Epidemiology and Evolutionary Genetics,
St. Petersburg Pasteur Institute,
St. Petersburg, Russia

Welcome Address from Prasit Palittapongarnpim

It is our great honor and pleasure to collaborate with Professor Igor Mokrousov in organizing this important symposium. ISTM2026 brings together a distinguished group of dedicated tuberculosis researchers from around the world to share and discuss state-of-the-art knowledge, technologies, and perspectives.

Tuberculosis remains the leading cause of death among infectious diseases worldwide. This is despite more than a century of intensive research and development, reflected in several hundred thousand scientific publications. Although the End TB Strategy has achieved progress in certain areas, its ambitious targets may unfortunately not be fully realized by 2035. Importantly, the strategy rightly identifies research and innovation as a central pillar. This has driven the application of advanced technologies—ranging from genomics to artificial intelligence—leading to the generation of vast amounts of data, knowledge, and tools for tuberculosis control.

To effectively translate this growing body of information and technology into meaningful impact, communication and collaboration among scientists are of paramount importance. ISTM2026 has therefore been established as a platform to facilitate such exchange, with a strong emphasis on the participation of researchers from low- and middle-income countries. We also place special importance on engaging the next generation of scientists by offering a limited number of scholarships for students to present their work, fostering cross-generational dialogue and collaboration.

Mahidol University is named after Prince Mahidol Adulyadej (1892–1929), also known as the Prince of Songkla and the grandfather of His Majesty the King of Thailand. During his relatively short career as a medical doctor, Prince Mahidol was a strong advocate for tuberculosis control. He authored an influential pamphlet on tuberculosis and helped organize what later became the Anti-Tuberculosis Association of Thailand. In this spirit, Mahidol University has continuously upheld a strong commitment to tuberculosis research and control.

We therefore hope that this symposium will serve as a catalyst for collaboration across disciplines and inspire new partnerships to address the complex challenges of tuberculosis and mycobacterial diseases. We sincerely thank all invited speakers from 13 countries who will generously share their latest findings. We also extend our appreciation to participants from an additional 11 countries for presenting their valuable work, and to all attendees for their active engagement.
Our heartfelt gratitude also goes to our generous sponsors and to everyone who has contributed in various ways to making this symposium possible.

Beyond the academic program, we hope that you will enjoy the opportunity to explore the surroundings of the symposium venue in the heart of Bangkok, as well as other fascinating destinations in Thailand.

Once again, welcome to ISTM2026, and we wish you a productive and inspiring symposium.

Professor Prasit Palittapongarnpim,
M.D., Fellow of the Royal College of Pediatrician, Thailand
Emeritus Professor Pornchai Matangkasombut Center for Microbial Genomics,
Department of Microbiology, Faculty of Science,
Mahidol University, Rama 6 Road, Bangkok, Thailand

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Program

2 February 2026 (Arnoma Grand Hotel)

8:50	9:00	**Opening Remarks by Assoc. Prof. Prasit Suwannalert, Dean, Faculty of Science, Mahidol University**
9:00	9:10	**Opening Remarks by Prof Igor Mokrousov, Saint Petersburg's Pasteur Institute**
		Session chaired by Igor Mokrousov and Prasit Palittapongarnpim
9:10	9:40	**Keynote – Taane G. Clark** (London School of Hygiene and Tropical Medicine, UK) *What can 'omics tell us about tuberculosis?*
9:40	10:00	**Christophe Sola** (Université Paris-Saclay, Saint-Aubin, France) *Reconstructing a global evolutionary history of tuberculosis: what are the still unanswered questions ??*
10:00	10:20	**Kiatichai Faksri** (Faculty of Medicine, Khonkaen University, TH) *Application of Genomics and OMICS Approaches for the Diagnosis and Control of* Mycobacterium *and Related Pathogens*
10:20	10:50	**Coffee Break**
		Session chaired by Christophe Sola
10:50	11:10	**Amador Goodridge** (INDICASAT-AIP, City of Knowledge), Panama) *Endemic transmission of* Mycobacterium tuberculosis *Sublineage L2.2.M3 within Panama*
11:10	11:35	**Igor Mokrousov** (Saint Petersburg Pasteur Institute, Russia) *Genomic insight into* Mycobacterium tuberculosis *adaptation to external stress in the in vivo and in vitro models*
11:35	12:35	**Presentations sponsored by Qiagen** **Speaker 1: Vanitha Palaeya** (QIAGEN, Malaysia) *Transforming TB Genomic Surveillance and Resistance Profiling with QIAseq xHYB* Mycobacterium tuberculosis *Panel* **Speaker 2: Zirwatul Adilah Bt Aziz,** (National Public Health Surveillance Laboratory, Malaysia) *Culture-Free Whole Genome Sequencing: The NPHL Experience with QIAseq xHYB* Mycobacterium tuberculosis *Workflow*
12:35	13:30	**Lunch**
13:30	14:30	**Poster Session 1: Presentation of posters with odd numbers**
		Session chaired by Kiatichai Faksri
14:30	14:50	**Danila Zimenkov** (Engelhardt Institute of Molecular Biology, Russian Academy of Sciences, Moscow, Russia) *The hidden diversity of* Mycobacterium
14:50	15:10	**Nawamin Pinpathomrat** (Faculty of Medicine, Prince of Songkla University, Songkla, TH) *TB vaccine platforms and delivering system*
15:10	15:40	**Coffee Break**
15:40	16:55	**Oral Presentations chaired by Sayera Banu** **Oren Tzfadia** (Institute for Tropical Medicine, Belgium) *A next-generation Mycobacterial knowledge base* **Mohammad Khaja Mafij Uddin** (icddr,b, Bangladesh) *Genomic insights into drug resistance and transmission dynamics of multidrug-resistant tuberculosis strains in Bangladesh*

		Dyshelly Nurkartika Pascapurnama (Universitas Padjadjaran, Indonesia) *Proportion of pathogenic non-tuberculous mycobacteria identified by partial-gene sequencing among presumptive tuberculosis patients in Indonesia* **John Carlo Macasaddug Malabad** (Department of Science and Technology, Philippines) *A molecular epidemiologic analysis of drug-resistant* Mycobacterium tuberculosis *isolates derived from the Third Philippines TB Drug Resistance Survey 2018 and community-based study* **Pundharika Piboonsiri** (Medical Life Sciences Institute, Department of Medical Sciences, MOPH, Thailand) *Whole genome sequencing of* Mycobacterium tuberculosis *reveals emerging bedaquiline resistance variants in Thailand* **Motunrayo Badejo** (Stellenbosch University, South Africa) *Superparamagnetic iron oxide nanoparticles perturb mycobacterial homeostasis and unveil gene expression signatures of antimicrobial action*

3 February 2026 (Arnoma Grand Hotel)

		Session chaired by Katsushi Tokunaga
9:00	9:30	**Keynote – Qian Gao** (Shanghai Medical College of Fudan University, China) *Molecular epidemiology of* Mycobacterium tuberculosis *in China*
9:30	10.00	**Keynote – Katsushi Tokunaga** (National Center for Global Health and Medicine, Tokyo, Japan) *Genomic approach to infectious diseases*
10.00	10:20	**Surakameth Mahasirimongkol** (Assistant Permanent Secretary, MOPH, TH) *Precision Control of TB: The future of ending TB by 2030.*
10:20	10:50	**Coffee Break**
		Session chaired by Richard Anthony
10:50	11:10	**Taisei Mushiroda** (RIKEN Center for Integrative Medical Sciences, Japan) *Toward Patient-Centered, Stratified Tuberculosis Treatment Through Pharmacogenomics*
11:10	11:30	**Margarita Shleeva** (Federal Research Centre "Fundamentals of Biotechnology" of the Russian Academy of Sciences, Russia) *A novel biochemical reaction in mycobacteria: coproporphyrin III tetramethyl ester synthesis and its adaptation significance*
11:30	11:50	**Egor Shitikov** (Lopukhin Federal Research and Clinical Center of Physical-Chemical Medicine, Moscow, Russia) *Mycobacteriophages: From Laboratory Research to Practical Applications in Medicine*
11:50	13:00	**Lunch**
13:00	14:00	**Poster Session 2: Presentation of posters with even numbers**
		Session chaired by Amador Goodridge
14:00	14:20	**Marisa Ponpuak** (Department of Microbiology, Faculty of Science, Mahidol University, TH) *Monocyte transcriptional responses to* Mycobacterium tuberculosis *associated with natural resistance to tuberculosis infection*
14:20	14:40	**Alexander Apt** (Central Institute of Tuberculosis, Moscow, Russia) *Tuberculosis infection control by the MHC-II in mice and the sequence of innate/adaptive immune responses to infection*
14:40	15:00	**Tomasz Jagielski** (University of Warsaw, Poland) *A water tale – new insights into the ecology of nontuberculous-mycobacteria*
15:00	15:20	**David Couvin** (Institut Pasteur de la Guadeloupe, France) *SITVIT++: Next-Generation* Mycobacterium tuberculosis *databases and biobanks for genomic surveillance, drug resistance monitoring, and predictive intelligence*

15:20	15:50	**Break**
15:50	17:00	**Oral Presentations chaired by Marisa Ponpuak** **Noppadon Nuntawong** (National Electronics and Computer Technology (NECTEC), Thailand) *Engineering a robust SERS-based POC system for tuberculosis screening* **Saradee Warit** (National Center for Genetic Engineering and Biotechnology (BIOTEC) Thailand) *Advancing tuberculosis diagnosis in macaques: A One Health approach* **Narisa Mohthong** (Prince of Songkla University, Thailand) *Investigating immune profiles in healthy and latent tuberculosis-infected participants.* **Yoopie Setiawan** (Universitas Katolik Parahyangan, Indonesia) *The interferon-gamma response to Latin American Mediterranean and modern Beijing sub-lineages of* Mycobacterium tuberculosis *in drug-sensitive and resistant tuberculosis* **Pyae Sone Oo** (Prince of Songkla University, Thailand) *Differential immune responses to novel and established* Mycobacterium tuberculosis *antigens among tuberculosis patients in Southern Thailand*

4 February 2026 (Arnoma Grand Hotel)

		Session chaired by Qian Gao
9:00	9:30	**Keynote – Urvashi Singh** (All Indian Institute of Medical Sciences, Delhi and Head of National TB program, India) Mycobacterium tuberculosis *genomics and transmission tracing in India*
9:30	9:50	**Virasakdi Chongsuvivatwong** (Faculty of Medicine, Prince of Songkla University, Songkla, TH) *Geno-spatio-temporal analysis, interpretation and implications on Infectious diseases*
9:50	10:10	**Richard Anthony** (National Institute for Public Health and the Environment, Netherland) *Micro-evolution in clustered cases of tuberculosis a useful signal or noise?*
10:10	10:40	**Coffee Break**
		Session chaired by Igor Mokrousov
10:40	11.00	**Sayera Banu** (Head, Programme on Emerging Infections, Infectious Diseases Division, icddr, Bangladesh) *Targeted next-generation sequencing for detection of drug-resistant tuberculosis: Challenges and insights from high burden settings in Bangladesh*
11:00	11:30	**Pakorn Aiewsakun** (Center for Microbial Genomics, Faculty of Science, Mahidol University, TH) *Whole genome sequence analysis to detect* Mycobacterium tuberculosis *transmission cluster*
11:30	12:00	**Robin Warren (**Stellenbosch University, South Africa) *The genesis and transmission of drug-resistant TB.*
12:00	13:00	**Lunch**
13:00	14:00	**Oral Presentation chaired by Violeta Valcheva** **Tania Jim** (National University of Singapore, Singapore) *The use of a novel conjugated oligoelectrolyte molecule to potentiate antibiotic efficacy against Non-Tuberculous Mycobacteria* **Kishan Kumar Parida** (National Institute of Pharmaceutical Education and Research, India) *Structure based identification and validation of Benzothiazole derivatives as potent DprE1 inhibitors against* Mycobacterium tuberculosis **Hleziphi Violah Mpundu** (Stellenbosch University, South Africa) *Targeting drug-tolerant tuberculosis through repurposing of approved drugs* **Arnab Roy** (National Institute of Pharmaceutical Education and Research, India) *Overcoming metabolic redundancy in* Mycobacterium tuberculosis *via dual inhibition of terminal oxidases*

		Session chaired by Egor Shitikov
14:00	14:20	**Mi Kaixia** (Institute of Microbiology, Chinese Academy of Sciences, China) *Elucidating the dual role of mycobacterial MfpA in fluoroquinolone resistance and virulence regulation*
14:20	14:40	**Violeta Valcheva** (Department of Infectious Microbiology, Stephan Angeloff Institute of Microbiology, ulgarian Academy of Sciences, Bulgaria) *Development and pharmacological evaluation of novel hydrazide - hydrazone derivatives as potential antituberculosis drug candidates*
14:40	15:00	**Oleg Ogarkov** (Scientific Center for Family Health and Human Reproduction Problems, Irkutsk, Russia) *The formation of a polybacterial community in caseous necrosis: a common and adverse consequence of tuberculosis*
15:00	15:20	**Prasit Palittapongarnpim** (Center for Microbial Genomics, Faculty of Science, Mahidol University, TH) *Structural variations of the pe/ppe gene family*
15:20	15:30	**Awarding and Closing ceremony**
1530	1630	**Coffee Break**

Brief biography

Symposium co-chair

Igor Mokrousov
St. Petersburg Pasteur Institute
Saint Petersburg, Russia

Dr. Igor Mokrousov, Ph.D., D.Sc., is the Head of the Laboratory of Molecular Epidemiology and Evolutionary Genetics at the St. Petersburg Pasteur Institute (Russia). His research focuses on phylogenomics, evolution, drug resistance of *Mycobacterium tuberculosis*, its co-adaptation with humans, and experimental evolution both in vitro and in vivo. Dr. Mokrousov has co-authored more than 190 peer-reviewed articles (H-index: 42; >6,000 citations), including papers in Clinical Microbiology Reviews, The Lancet Infectious Diseases, Nature Genetics, and book chapters published by Cambridge, Oxford, Elsevier, and Springer. He received the Scientific Prize from the International Union Against Tuberculosis and Lung Disease (2004), a Marie Curie Fellowship (2007), and several Honor Awards from the Russian Health Service. He currently serves as a Senior Editor for Infection, Genetics and Evolution and BMC Microbiology.

Brief biography

Symposium co-chair

Prasit Palittapongarnpim
CENMIG, Department of Microbiology, Faculty of Science, Mahidol University
Bangkok, Thailand

Prof. Prasit Palittapongarnpim received his M.D. with First Class Honors from Mahidol University, a Certificate of Proficiency in Pediatrics from Chiang Mai University, Thailand, and postdoctoral training at the University of Alberta, Canada. He also earned B.Sc. degrees in both Medical Sciences and Mathematics. His main scientific interests are in the molecular biology and genomics of *Mycobacterium tuberculosis* as well as antimicrobial resistance (AMR). He founded and leads the Pornchai Matangkasombut Center for Microbial Genomics at Mahidol University. He has regularly published research on tuberculosis genomics and AMR and was recognized as a top 1% researcher at Mahidol University in both 2022 and 2023. He has also worked on antituberculous drug discovery and has been involved in several networks related to emerging disease preparedness and research integrity. Dr. Prasit serves as an editorial board member and reviewer for several journals and funding agencies both in Thailand and internationally. He has also served multiple times as a temporary advisor to the World Health Organization (WHO). To date, he has published more than 130 papers, mostly on tuberculosis. He held various administrative positions in Thailand including Vice President of Mahidol University and Executive Vice President of the National Science and Technology Development Agency. He currently serves as a university council member and a steering committee member for several institutes.

Brief biography

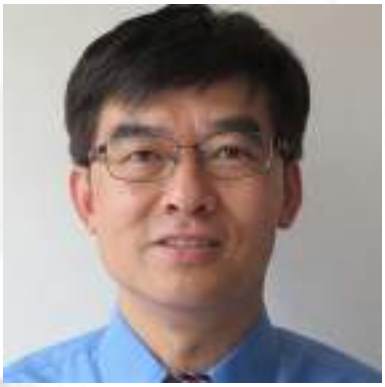
Keynote speaker

Taane G. Clark
London School of Hygiene and Tropical Medicine
London, United Kingdom

Taane Clark is a Professor of Genomics and Global Health, and a genomic epidemiologist specialising in population-genetic and statistical approaches to investigate the transmission and drug resistance of infectious diseases. His research in tuberculosis genomics has contributed significantly to the field, including the development of widely adopted strain barcodes for *Mycobacterium tuberculosis*, the application of genome-wide association studies and AI-driven methods to identify drug resistance mutations, and the creation of genotypic profiling tools such as TB-Profiler. He has also pioneered genome-to-genome analyses to uncover genetic interactions between the host and the mycobacterial pathogen. Professor Clark has authored over 350 peer-reviewed publications and has led efforts to strengthen global capacity in 'omics research, including the organisation of more than 40 data analysis workshops in London and across multiple international settings.

Brief biography

Keynote speaker



Qian Gao
Shanghai Medical College, Fudan University
Shanghai, China

Dr. Gao received his bachelor's degree from Southwest Agricultural University, China, and earned his Ph.D. in molecular bacteriology from the University of Southern California. He began his research in tuberculosis (TB) in 2000 during a postdoctoral fellowship at Stanford University School of Medicine. Dr. Gao's research focuses on the molecular epidemiology of *Mycobacterium tuberculosis* (M.tb.), with a specific emphasis on transmission dynamics in China; the genetic diversity and pathogenic mechanisms of Beijing genotype strains of M.tb.; and the micro-evolution of drug resistance in this pathogen. His program integrates national and international collaborations, combining research studies with training activities across China. Over the past decade, his team has conducted a prospective, population-based molecular epidemiological study of TB in China, revealing ongoing transmission of TB, particularly multidrug-resistant TB (MDR-TB), within communities. These findings highlight the urgent need for strategies aimed at interrupting transmission, including novel approaches for rapid diagnosis and control. Dr. Gao believes these efforts are critical for the eventual elimination of TB in China.He has collaborated extensively with public health professionals and researchers in China since 2004.

Brief biography

Keynote speaker

Katsushi Tokunaga
National Center for Global Health and Medicine
Tokyo, Japan

Katsushi Tokunaga is the Director of the Genome Medical Science Project at the National Institute of Global Health and Medicine (NIGHM), Director of the Central Biobank at the National Center Biobank Network (NCBN), and Professor Emeritus at The University of Tokyo. His research interests focus on genomic studies of immune-related complex diseases, including infectious diseases—particularly HLA-disease associations—as well as human genome diversity and personalized medicine. In recent years, he has led the National Center Biobank Network and large-scale whole genome sequencing projects targeting rare and complex diseases. He is a member of the Science Council of Japan and a Councilor of the International HLA and Immunogenetics Workshop. He has also served as a board member of the Japan Society of Human Genetics and as President of the Japanese Society for Histocompatibility and Immunogenetics. Additionally, he has held editorial roles as Editor-in-Chief of the Journal of Human Genetics, advisory editor for several academic journals, and founding editor of Human Genome Variation. He has published 767 peer-reviewed original articles in English, with works appearing in Nature, Science, The New England Journal of Medicine, The Lancet, Nature Genetics, and Nature Medicine.

Brief biography

Keynote speaker

Urvashi Singh
All Indian Institute of Medical Sciences, Delhi and Head of National TB Program
New Delhi, India

Dr. Urvashi B Singh's research interests include adult and pediatric tuberculosis, Drug resistant TB, TB treatment and novel regimens, TB epidemiology, TB diagnostics, novel biomarkers, HIV-associated TB, Non-tubercular mycobacteria and *Mycobacterium avium*-paratuberculosis, in multiple domains including epidemiology, pathogenesis, spread of MDR-TB, novel rapid detection method, molecular typing and WGS. Her pioneering work for detecting viable TB bacteria in treatment failure patients therapeutic drug monitoring have direct policy relevance. She publishes more than 150 articles and hold several patents in different stages of translation. She holds several academic posts including a Member, National TB Expert Group, National TB Elimination Program, GoI; Member, Subject Expert Committees, CDSCO (DCGI), GoI; Member, Diagnostic Committee, India TB Research Consortium, ICMR; Member, Operational Research Committee, National TB Elimination Program, GoI; Member, Project Review Committees of DBT, ICMR, TDB, GoI; Member, ICMR Task Force on Genital Tuberculosis; Member Editorial Board, Associate Editor, Frontiers in Medicine, Frontiers in Public Health and Frontiers in Microbiology; Scientific Collaborations with Several International and National Institutes; Reviewer for International and National Journals.

Brief biography

Invited speaker

Pakorn Aiewsakun
CENMIG, Department of Microbiology, Faculty of Science, Mahidol University
Bangkok, Thailand

Dr. Pakorn Aiewsakun received a B.Sc. in Biological Sciences and an M.Sc. in Bioinformatics and Theoretical Systems Biology from Imperial College London, and subsequently earned a D.Phil. in Zoology from Oxford University. During his doctoral study, his research focused on endogenous viruses, exploring viral genomic fossils in the genomes of animals, to connect recent and ancient viral evolution. His key findings included the time-dependent rate phenomenon, demonstrating that both DNA and RNA viruses evolve rapidly in the short term but remain highly conserved over longer periods. Following his doctoral studies, Dr. Pakorn Aiewsakun continued at Oxford University as a postdoctoral researcher, developing a sequence-based framework for family-level virus classification called GARViTy. Since joining Mahidol University in late 2017, he has been a pioneering force in microbial genomics research as a founder of the Pornchai Matangkasombut Center for Microbial Genomics (CENMIG). He also leads many research projects in bacterial and virus genomics and has organised many hands-on bioinformatics workshops to disseminate knowledge and technical skills. In his spare time, he enjoys competitive ballroom dancing.

Brief biography

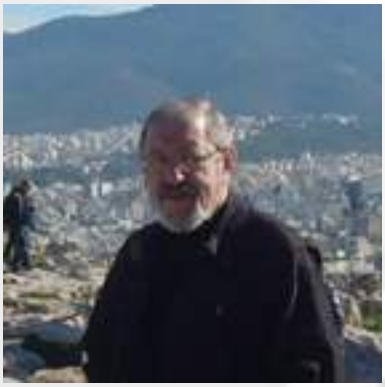
Invited speaker

Richard M. Anthony
National Institute for Public Health and the Environment (RIVM)
Bilthoven, The Netherlands

Dr. Richard M. Anthony is a microbiologist specializing in tuberculosis diagnostics, drug resistance, and microbial molecular epidemiology. He currently serves as Coordinator of the National Tuberculosis Reference Laboratory at RIVM, where he oversees TB genotyping and supports global collaborations in TB control. Prior to this, he led the TB research group at KIT Biomedical Research, developing molecular assays and initiating the global rollout of LED microscopy for TB screening. Dr. Anthony's career spans over three decades, including roles as a molecular microbiologist at St. Thomas' Hospital and the Institute of Dermatology in London. His Ph.D. from King's College London focused on molecular typing of Malassezia yeasts. His work has been instrumental in empowering international labs and facilitating skill transfer in regions like Eastern Europe, Central Asia, and South America. He is an editor for the Journal of Antimicrobial Chemotherapy, a WHO expert group member, and has coordinated several international and EU-funded TB projects. He is also proficient in Dutch and skilled in genome analysis tools (RStudio, SAMtools).

Brief biography

Invited speaker



Alexander S. Apt
Central TB Research Institute
Moscow, Russia

Prof. Alexander S. Apt is Head of the Laboratory for Immunogenetics at the Central Tuberculosis Research Institute in Moscow, Russia. With a career spanning over five decades, he is an internationally recognized expert in tuberculosis immunology and host genetics. Prof. Apt holds a Ph.D. in Immunology from the N. Gamaleya Institute, and a D.Sc. in Immunology focusing on the genetic control of intracellular infections using tuberculosis as a model. Prof. Apt has held various positions, including a visiting professorship at McGill University's Centre for the Study of Host Resistance, and has served as Professor at the School of Biology, Moscow State University. His research focuses on genetic susceptibility to tuberculosis, immune responses in murine models, and host-pathogen interactions. He has been a Principal Investigator on multiple international grants from the Wellcome Trust, NIH, and Howard Hughes Medical Institute. His scientific contributions include over 130 peer-reviewed publications and significant advances in understanding immune regulation and the role of B cells and MHC molecules in TB pathogenesis. He has received awards and fellowships from WHO, MRC Canada, and served as an ASM Ambassador for Russia and former Soviet Union states.

Brief biography

Invited speaker

Sayera Banu
International Center for Diarrheal Disease Research
Dhaka, Bangladesh

Dr. Sayera Banu is a Bangladeshi scientist and medical doctor with advanced degrees in Microbiology, specializing in mycobacterial infections. As a Senior Scientist at icddr,b, she leads the Program for Emerging Infections and has dedicated over 25 years to tuberculosis (TB) research and programmatic initiatives. She is also leading a well-equipped Mycobacteriology laboratory. Dr. Banu's work has had a significant national and international impact. She established the cutting-edge icddr,b TB laboratory, conducted Southeast Asia's first multidrug-resistant TB sentinel surveillance, and introduced new tools and technologies to advance TB research. Her studies on TB prevalence and transmission in confined prison settings in Dhaka and the development of an innovative public-private model for TB diagnosis and management have been incorporated into Bangladesh's National Strategic Plan. A fellow of the Bangladesh Academy of Sciences and the World Academy of Sciences, Dr. Banu has received prestigious awards, published extensively, and secured major research funding. She is widely recognized as an expert in tuberculosis globally. She has received several grants from various funding agencies, including USAID, GFATM, and the Stop TB Partnership, etc. She maintains strong collaborations with scientists both nationally and internationally and works closely with the National TB Control Program in Bangladesh.'s National Strategic Plan.

Brief biography

Invited speaker

Virasakdi Chongsuvivatwong
Faculty of Medicine, Prince of Songkla University, Songkla
Songkla, Thailand

Virasakdi Chongsuvivatwong MD, PhD is a Professor in Community Medicine at Prince of Songkla University. He founded Epidemiology Unit in 1986 and started the International Programme for Graduate Study in Epidemiology in 1992. Currently, he is the Curriculum Chairman of the Programme. He has published 245 research articles in PubMed database and has over 3,000 citations (excluded all authors). Over the past 28 years, the Programme has produced over 128 PhD and over 83 MSc graduates who came from 17 countries in Asia and Africa. He has received Senior Research Scholar title from Thailand Research Fund, Outstanding Research in Medical Science Award from the National Research Council of Thailand, NSTDA Research Chair from the National Science and Technology Development Agency and National Outstanding Teacher Award from the National Academic Senate. He is currently serving the National Health Security Office as a consultant on utilization of the national claim data for research purpose. One of the grants that he currently receives is for training of health planners and IT officers in all provinces of Thailand to make use of the existing data routinely collected from the hospitals

Brief biography

Invited speaker

David Couvin
Institut Pasteur de la Guadeloupe
Associate Professor at the Université des Antilles

David Couvin is a bioinformatician and researcher at the Institut Pasteur de la Guadeloupe (as well as Associate Professor at the Université des Antilles), specializing in bioinformatics (particularly in the study of infectious diseases). David contributes to the training and supervision of bioinformatics students. His research focuses on bioinformatics applied to molecular epidemiology, with particular emphasis on genomic sequencing, metagenomics and phylogenetic analysis of pathogens such as *Mycobacterium tuberculosis*. He has developed specific genomic databases and software tools for a better understanding of whole genome sequencing (WGS) data (particularly for bacteria). In addition to his research activities, David Couvin is involved in the structuring of bioinformatics in Guadeloupe. He is also involved in the local organization of bioinformatics theme days and workshops.

Brief biography

Invited speaker

Kiatichai Faksri
Department of Microbiology, Faculty of Medicine, and Dean of Graduate School, Khon Kaen University
Khon Kaen Thailand

Prof. Kiatichai Faksri is a Dean of the Graduate School at Khon Kaen University (KKU), Thailand and also serves as Director of the Research and Diagnostic Center for Emerging Infectious Diseases at KKU. Prof. Faksri earned his B.Sc. in Medical Technology from Naresuan University and a Ph.D. in Medical Microbiology (Royal Golden Jubilee Scholar) from Mahidol University's Faculty of Medicine Siriraj Hospital. He completed postdoctoral training in whole-genome sequencing of mycobacteria at the National University of Singapore in 2015. He has held multiple academic and administrative positions, including Assistant Dean for Research and Planning at the Faculty of Medicine, KKU, and Deputy Head of the Department of Microbiology. Currently, he holds key roles on the boards of graduate and academic service programs both at KKU and nationally. As a respected academic, he serves as Associate Editor for the European Journal of Medical Research and Academic Editor for PLOS Global Public Health. He is also a certified assessor for Thailand's TQA and EdPEx programs. Prof. Faksri has been recognized with numerous awards for his research and leadership, including multiple Outstanding Researcher Awards from KKU, and national fellowships. He has published over 90 research articles indexed in Scopus and leads several international projects, including a major grant from the Open Philanthropy Foundation to develop Raman spectroscopy-based diagnostics for tuberculosis. His academic influence and leadership continue to shape microbiology and infectious disease research in Thailand and the region.

Brief biography

Invited speaker

Amador Goodridge
Instituto de Investigaciones Científicas y Servicios de Alta Tecnología (INDICASAT-AIP)
Panamá Province, Panama

Amador Goodridge; Bachelor's Degree in Medical Technology from the Faculty of Medicine at the University of Panama. He also holds a Master of Science with a specialization in Biotechnology from Universidad Santa María la Antigua, and a Ph.D. in Infectious Diseases and Immunity from the University of California, Berkeley, United States. Recently, he earned a Diploma in Project Management from Florida State University at Ciudad del Saber. Currently he is principal investigator of the Tuberculosis Biomarker Research Unit at INDICASAT-AIP, City of Knowledge, Panamá. He has also collaborated with government and non-government organizations in building scientific capacity for R&D. For more than 20 years he has carried out scientific research on human and animal tuberculosis. Additionally, he collaborates in antimicrobial resistance, nosocomial infections, perinatal infections, nutrition and water quality.

Brief biography

Invited speaker

Tomasz Jagielski
University of Warsaw
Warsaw, Poland

Tomasz Jagielski, PhD, DSc received a PhD in medical sciences from the National Tuberculosis and Lung Diseases Research Institute, which serves as the National Tuberculosis Reference Laboratory for Poland. He currently works as an assistant professor at the University of Warsaw, where he established and now heads the Department of Medical Microbiology. His research interests are interdisciplinary and span a breadth of topics related to infectious diseases, with special emphasis on developing new molecular markers and diagnostic algorithms to be used in everyday clinical practice. The primary areas of his expertise include mycobacteriology, fungal infections, and antimicrobial resistance. He is also actively involved in forging a new realm of microbiology, called medical phycology. The PI of several national and international research projects and (co-)author of more than 100 articles in peer-reviewed journals. He acts as a reviewer for numerous scientific journals and is a member of the editorial boards of Infection, Genetics and Evolution, Microbial Biotechnology, and One Health Mycology. He is affiliated with several international societies and research networks. He also serves as the Country Liaison of the American Society for Microbiology (ASM) and the International Society for Human & Animal Mycology (ISHAM). He is a founder and coordinator of the international research consortium on TB and other mycobacterial diseases – Fight Against TB in Central and Eastern Europe (FATE). Since 2005, he has worked on various aspects of TB and nontuberculous mycobacteria (NTM) infections, including diagnostics, drug resistance, and molecular epidemiology. He was among the first to demonstrate the transmission of multidrug-resistant TB in Poland using genotyping methods. His research have also extensively contributed to the taxonomy and diagnostics of the *Mycobacterium kansasii* complex.

Brief biography

Invited speaker

Surakameth Mahasirimongkol
Assistant Permanent Secretary, Ministry of Public Health
Nonthaburi, Thailand

Dr. Surakameth Mahasirimongkol, MD, MSc, PhD has worked in several institutes in the Ministry of Public Health, Thailand. He specializes in epidemiology, genetic epidemiology, and tuberculosis research, with a focus on integrating human and pathogen genomic data to support TB control programs. He currently leads research projects on pharmacogenomics for precision drug use and develops genome-informed TB diagnostics. With a robust publication record of nearly 200 peer-reviewed articles and over 4,000 citations and h-index of 30, Dr. Surakameth is a respected authority in genomics, bioinformatics, and public health. He is proficient in R, next-generation sequencing, and computational genomics. Based at the Ministry's Department of Medical Sciences, Dr. Surakameth also contributes to regional and international collaborations aimed at improving infectious disease surveillance and personalized medicine in Thailand.

Brief biography

Invited speaker

Mi Kaixia
Institute of Microbiology, Chinese Academy of Sciences
Beijing, China

Dr. Mi earned her PhD in Genetics from the Institute of Microbiology, Chinese Academy of Sciences. She began her research on tuberculosis (TB) during a postdoctoral fellowship at the Albert Einstein College of Medicine in New York in 2003. Dr. Mi's research focuses on key pathogenic microorganisms, especially MTB. Her work spans a broad spectrum of topics including drug resistance mechanisms, novel drug target discovery and host-pathogen interactions. A major focus of her research is on the molecular mechanisms underlying MTB latency and reactivation. She systematically studied the universal stress protein family, notably Rv2623 and Rv2624c, and uncovering how these proteins regulate bacterial metabolism and signaling pathways critical for latent infection. Recently, Dr. Mi's team has uncovered new insights into the multi-functional roles of antibiotic resistance proteins, particularly their involvement in bacterial virulence. Her lab's work on dual-target strategies offers promising avenues to combat resistant TB strains and improve therapeutic outcomes. In the field of drug resistance, Dr. Mi has conducted in-depth studies on fluoroquinolone resistance, notably revealing the structure of the MfpA-DNA gyrase complex and demonstrating MfpA's protective function. By integrating omics technologies, synthetic biology, and structural biology, her group aim to uncover the deeper molecular basis of resistance in mycobacteria and translate these insights into potential therapeutic innovations.

Brief biography

Invited speaker

Taisei Mushiroda
Laboratory for Pharmacogenomics, RIKEN Center for Integrative Medical Sciences
Kobe, Japan

He graduated from the Graduate School of Pharmaceutical Sciences at Kanazawa University in 1988 and subsequently joined Hokuriku Seiyaku Co., Ltd. (now AbbVie), where he spent 15 years conducting preclinical and clinical pharmacokinetic studies for drug discovery and development. In 2000, he earned his Ph.D. from Hokkaido University. He joined RIKEN in 2003 and began research to identify SNPs and genes associated with drug efficacy and adverse drug reactions. His current research focuses on integrating patients' genomic information and drug responses to establish stratified drug therapy based on pharmacogenomics, with the goal of providing the right drug at the appropriate dose for each individual patient.

Brief biography

Invited speaker

Oleg Ogarkov
Scientific Centre for Family Health and Human Reproduction Problems
Irkutsk, Russia

Dr. Oleg B. Ogarkov is Director of the Institute of Epidemiology and Microbiology at the Scientific Centre for Family Health and Human Reproduction Problems (SC FHHRP) in Irkutsk, Russia. With a strong foundation in genetics, epidemiology, and molecular microbiology, he received his Cand. Sci. (PhD) in Genetics from the Institute of Cytology and Genetics, SB RAS, and later earned a Doctor of Science (Dr. Sci.) in Epidemiology in 2014. He also completed training in management at Baikal International Business School. Dr. Ogarkov has extensive experience in infectious disease research, particularly in the molecular and epidemiological aspects of socially significant infections. He held various leadership roles, including Head of Molecular Biology at the Irkutsk Regional Diagnostic Center, and conducted postdoctoral research at Rutgers University in the U.S. His career spans work in public health institutions, academic research centers, and international collaborations. He has authored over 35 publications, with more than 1,700 citations and an h-index of 19 (Google Scholar). His research focuses on microbial communities in tuberculosis, molecular diagnostics, and the epidemiology of infectious diseases. Dr. Ogarkov is recognized for his significant contributions to public health microbiology in Russia and beyond.

Brief biography

Invited speaker

Nawamin Pinpathomrat
Faculty of Medicine, Prince of Songkla University
Songkla, Thailand

Dr. Nawamin Pinpathomrat, MD, DPhil, is an Associate Professor of Immunology and Assistant Dean of International Affairs at the Faculty of Medicine, Prince of Songkla University (PSU), Thailand. He earned his MD with First Class Honors from PSU, followed by an MSc in Immunology from Imperial College London and a DPhil in Clinical Medicine from the University of Oxford's Jenner Institute. His expertise spans immunology, vaccinology, tuberculosis and COVID-19 vaccine development, emerging infectious diseases, and biosafety level 3 research. Dr. Nawamin has led multiple national research projects on TB and COVID-19 vaccines, including those using viral vectors and mRNA platforms. He also serves as Vice Director of the Medical Science Research and Innovation Institute at PSU. With extensive experience in preclinical vaccine development and immunological studies in autoimmune diseases, he has authored over 25 peer-reviewed publications in high-impact journals and continues to contribute significantly to translational research and vaccine innovation in Thailand.

Brief biography

Invited speaker

Marisa Ponpuak
Department of Microbiology, Faculty of Science, Mahidol University
Bangkok, Thailand

Dr. Marisa Ponpuak was awarded a prestigious national scholarship from Thailand's Development and Promotion of Science and Technology Talent Project (DPST) to pursue her studies in the United States. She earned her Bachelor's degree with honours in Molecular Biology from the University of Wisconsin–Madison in 2001. She then completed her Ph.D. in Molecular Microbiology at Washington University School of Medicine under the mentorship of Prof. Daniel E. Goldberg, a Howard Hughes Medical Institute Investigator. Her doctoral research focused on the biology of *Plasmodium falciparum*, the parasite responsible for malaria. Following her Ph.D., Dr. Ponpuak conducted postdoctoral research in the laboratory of Prof. Vojo Deretic at the University of New Mexico, where she gained extensive experience in host immunity against *Mycobacterium tuberculosis*. In 2010, she joined the Department of Microbiology at the Faculty of Science, Mahidol University. Her current research centres on host cellular immunity in the context of globally significant infectious diseases, with a particular emphasis on tuberculosis. Her work includes drug discovery, biomarker identification, and vaccine development to combat *M. tuberculosis* infection

Brief biography

Invited speaker

Egor Shitikov

Lopukhin Federal Research and Clinical Center of Physical-Chemical Medicine of Federal Medical Biological Agency

Moscow, Russia

Dr. Egor Shitikov, D.Sc., is Head of the Laboratory of Molecular Genetics of Microorganisms at the Federal Research and Clinical Center of Physical-Chemical Medicine of the Federal Medical Biological Agency (Russia). His research spans two major areas: multi-omics analysis of *Mycobacterium tuberculosis* and therapeutic applications of bacteriophages. In tuberculosis research, Dr. Shitikov's team has made significant contributions to understanding the genomic diversity of *M. tuberculosis*. His work has introduced advanced genotyping schemes and provided novel insights into regions of difference, establishing their correlation with existing typing systems for the first time. His group has conducted detailed characterization of Lineage 2 strains, developing novel typing schemes and investigating IS6110 evolution within this genotype. The team has described major recombination events in Beijing B0/W148 strains and studied molecular mechanisms of drug resistance and pathogenicity in Russian-endemic strains using multi-omics approaches. In bacteriophage research, Dr. Shitikov focuses on developing phage-based therapies against ESKAPE pathogens and mycobacteria. His studies include optimizing phage-antibiotic combinations and personalized phage cocktails for multidrug-resistant infections. His team has also characterized the first comprehensive collection of Russian mycobacteriophages. Dr. Shitikov is the author of more than 100 publications and has 3 patents. He serves as an active reviewer for Infection, Genetics and Evolution, PLoS One, and Scientific Reports. His contributions to molecular microbiology were recognized with the Moscow Government Award (2019).

Brief biography

Invited speaker

Christophe Sola
INSERM-Université Paris-Cité, Université Paris-Saclay
Paris France

Prof. Christophe Sola, holds a PharmD and a PhD in Life Sciences. He is a former Resident of Lyon's Hospitals, a former research fellow of the Institut Pasteur, Paris, and of the Clinical Research Institute of Montreal (IRCM). He holded various R&D positions in French (Limagrain Seed Group), German (Boehringer-Mannheim) and American (Parexel Corporation) Biotechnology and Pharmaceutical companies between 1989-1994, before moving to Guadeloupe, where he worked as senior scientist within the International Network of Pasteur Institutes. Christophe Sola holds since September 2007 a Full Professorship position at the University of Paris-Saclay (UPSay) ; he created and was the Principal Investigator from 2007 to 2020, of the Infection Genetics Emerging Pathogen Evolution (IGEPE) research team, within the CNRS-UPSay funded Institute for Integrative Cell Biology (I2BC). Since January 1st 2021, He joined the INSERM IAME laboratory Infection Antimicrobials, Modeling Evolution, and the French NRL for tuberculosis as a senior scientist. His main field of interest is Evolutionary Biology of Tuberculosis and Public Health. He is working on the understanding of the consequences of the genetic diversity in relation to anthropology, systems epidemiology, virulence, molecular adaptation and drug resistance mechanisms, and uses machine learning and artificial intelligence. He was very active in CRISPR research using CRISPR diversity for molecular typing of pathogens. He is an associated Editor of PloS ONE, BMC Infectious Diseases, Frontier in Microbiology, the author of >170 international peer-reviewed papers, a member of the steering committee of the European Society for Mycobacteriology since 2023, and a member of the Latin American Society for Mycobacteriology.

Brief biography

Invited speaker

Margarita Shleeva
Federal Research Centre “Fundamentals of Biotechnology” of the Russian Academy of Sciences
Moscow, Russia

Dr. Margarita O. Shleeva, Ph.D., D.Sc., is a leading biochemist and Head of the Laboratory of Biochemistry of Stresses in Microorganisms at the Federal Research Centre “Fundamentals of Biotechnology” of the Russian Academy of Sciences. Her extensive research is dedicated to understanding dormant and “non-culturable” bacterial forms and their biochemistry, with a particular focus on bacterial adaptation to stress, the formation of non-sporulating dormant bacteria, bacterial viability under stress, and mechanisms of cell division. Dr. Shleeva’s significant scientific contributions are centered on the biochemistry of microorganisms, especially mycobacteria, and on devising effective strategies against the dormant forms of tuberculosis and mycobacteriosis pathogens. Her research interests encompass the biochemical processes driving bacterial adaptation to stressful environments, the intricate biochemistry and physiology of mycobacterial dormancy, and the mechanisms governing the formation and reactivation of dormant and “non-culturable” bacterial states. A notable breakthrough from her laboratory is the discovery of porphyrin accumulation in dormant mycobacteria, which has paved the way for developing novel antibacterial photodynamic therapy approaches against these pathogens. Dr. Shleeva’s research has resulted in over 70 co-authored publications, garnering more than 1,400 citations and an h-index of 19. She continues to lead her laboratory, driving advancements in microbial stress responses with broad implications for biotechnology and medicine.

Brief biography

Invited speaker

Violeta Valcheva

Head, Laboratory of molecular biology of mycobacteria, Department of Infectious Microbiology, The Stephan Angeloff Institute of Microbiology, Bulgarian Academy of Sciences

Sofia, Bulgaria

Violeta Valcheva is an Associate Professor in the The Stephan Angeloff Institute of Microbiology (SAIM), Bulgarian Academy of Sciences, Sofia, Bulgaria. In 2009 she received her Ph.D and did the first comprehensive study of molecular characterisation and drug resistance of *Mycobacterium tuberculosis* strains in Bulgaria. The main research topics of her work are the molecular epidemiology, phylogeny and evolution of mycobacteria, bioinformatics, bacterial pathogenesis and virulence; new synthesized compounds with chemical and natural products, drug development, pharmacokinetics, anti-TB chemotherapy. Over the years, she gained experience and high qualifications in the international institutions in various international institutes in the field of molecular epidemiological research, bioinformatics (France, Russia, China, Japan) with visible results (projects, publications, establishing new innovations and collaborations by participating in various COST, ERASMUS+, NATO projects and programs). She was responsible for public relations for the SAIM (2009 - 2020) and responsible for the scientific relation for the SAIM in the International Pasteur Network. She was a secretary of the Microbiology department in the Bulgarian Union of Scientists in the period of 2009-2013.

Brief biography

Invited speaker

Robin Warren
Stellenbosch University
Stellenbosch, South Africa

Professor Robin Warren is a Distinguished Professor at Stellenbosch University (SU) and heads the TB Genomics research group in the Division of Molecular Biology and Human Genetics in the Faculty of Medicine and Health Sciences. In 2015 he was awarded the SAMRC Gold Medal award for scientific excellence and in 2018 the Chancellors award for his contribution to research at SU. Prof Warren has published over 475 papers and 15 book chapters. His research is based on a foundation molecular epidemiology which has led to numerous landmark publications in the field of Tuberculosis (TB). Through his research he has challenged dogmas with respect to recurrent TB, demonstrated mixed infection, identified outbreaks, mapped acquisition of resistance and highlighted programmatic limitations in the standard of care. Critical questions currently under investigation include determining the association between genotype and phenotype for new and repurposed drugs to enable the transition from culture-based methods to molecular methods for drugs susceptibility testing. His research is directly linked whole genome sequencing (WGS) to correlate genome sequence variation to phenotype (virulence and transmission). Prof Warren continues to contribute to global initiatives to improve diagnostics by being a major contributor to WHO technical guides, a global repository of WGS data and the development of a WGS analysis pipeline that is being adopted by the WHO. He continues to play a pivotal role in the archiving of clinical TB isolates in collaboration with the National Health Laboratory Service which houses over 60000 drug-susceptible and drug-resistant isolates and is a national and international resource. Prof Warren collaborates extensively in Africa to ensure skills transfer and postgraduate education.

Brief biography

Invited speaker

Danila Zimenkov
Engelhardt Institute of Molecular Biology, Russian Academy of Sciences
Moscow, Russia

Dr. Danila Zimenkov is a senior scientist in Engelhardt institute of molecular biology, Russian Academy of Sciences. He graduated from Moscow Physics-Engineering Institute in 1999 and got his Ph.D in 2005 at the Institute of Genetics and Selection of Industrial Microorganizms in the field of genetics of the E. coli central metabolism. Dr. Zimenkov has over 25 years research experience in molecular biology of procaryotes. His research is focused on genomics of *M. tuberculosis* and non-tuberculous mycobacteria, molecular mechanisms of drug resistance and tolerance, phylogenetics and genome-wide association studies. The research topics allsio include: development of molecular diagnostics technologies, particularly DNA microarrays, nucleic acids amplification and hybridization techniques, integrated microfluidic device design, engineering of portable systems for clinical diagnostics. Sinnce 2014 he was involved into the study of bedaquilne resistance development upon the start of the drug use for tuberculosis treatment. He described the acquisition and development of the resistance in a small, but noticeable part of cases. Mutations in the atpE gene, encoding the bedaquiline target were decribed for the first time in clinical samples. Many new types of mutations were described, also as novel determinants of high-level resistance to bedaquiline including substitution in MmpL5 and loss-of-function mutations in mmpS4-L4 operon. In 2022-2024 the research group headed by Dr Zimenkov developed the highly specific moolecular test for mycobacterial species identification and tested more than 3000 clinical samples from patients with suspected non-tuberculous infections. More than 70 different species were found, also as species from other genera of Mycobacteriales. Four new mycobacterial species were isolated and described in Moscow, St Petersburg, Novosibirsk (Russia) and Bulgaria sets of samples.

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1. **Taane G. Clark** (London School of Hygiene and Tropical Medicine, UK)

What can 'omics tell us about tuberculosis?

Tuberculosis, caused by bacteria in the *Mycobacterium tuberculosis* complex, remains a major global health challenge, with drug resistance and the absence of an effective vaccine continuing to hinder control efforts. Advances in sequencing technologies and analytical methods - including bioinformatics, data science, and AI - are transforming the generation and interpretation of 'omics data, enabling the design of improved diagnostics, therapies, and vaccines. Many countries now use whole-genome and amplicon-based sequencing to characterise circulating *M. tuberculosis* strains, uncover transmission clusters, and detect genotypic drug-resistance variants, providing actionable intelligence for clinical settings, surveillance and infection-control programmes. Evidence of host-pathogen co-evolution is also driving genome-to-genome studies that seek to pinpoint genetic interactions shaping disease risk, progression, and treatment outcomes. This talk will highlight applications of 'omics - particularly genomics and transcriptomics - across both host and pathogen, and will discuss emerging opportunities, including the use of AI-driven approaches, to accelerate insights and deliver tools that support global tuberculosis control.

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2. **Christophe Sola** (IAME, INSERM-Université Paris-Cité, Sorbonne Paris-Nord, Université Paris-Saclay)

Reconstructing a global evolutionary history of tuberculosis: what are the still unanswered questions?

During this presentation we tackle the issue of the global and local history of tuberculosis through space and time. We try to provide an up-to date synthesis on some evolutionary issues on tuberculosis origin, ecology, and current academic research, focusing on recent results obtained suing comparative genomics of *Mycobacterium tuberculosis* complex (MTBC) infections; How sure are we that MTBC was a human disease at emergence? How old is the most recent common ancestor between animal and human MTBC ecotypes? What is the relative importance of human demography and bacterial transmissibility in epidemic success of tuberculosis? What kind of host-pathogen adaptation are we dealing with: co-divergence or co-evolution? After having reviewed the most important changes of paradigm that appeared with genomic results, we try to tackle the great diversity of the issues remaining to be solved and show how explaining the past of the pandemia may also help us to finally eradicate the disease.

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3. **Kiatichai Faksri** (Director, Research and Diagnostic Center for Emerging Infectious Diseases (RCEID), Department of Microbiology, Faculty of Medicine, Khon Kaen University, Thailand; Dean Graduate School, Khon Kaen University)

Application of Genomics and OMICS Approaches for the Diagnosis and Control of *Mycobacterium* and Related Pathogens

Tuberculosis (TB) control in high-burden settings such as Thailand requires both precise genomic surveillance of drug-resistant strains and innovative approaches for population-level screening. Multidrug-resistant (MDR) and extensively drug-resistant (XDR) TB continue to spread, while latent TB infection (LTBI) remains an underdiagnosed reservoir for future disease. To address these challenges, we combined four complementary approaches. First, whole-genome sequencing (WGS) of MDR/XDR isolates from hospitals and provincial laboratories nationwide revealed multiple interprovincial transmission clusters and silent spread of XDR strains, underscoring the urgent need for cross-province genomic surveillance. Second, we systematically evaluated and updated the drug-resistance (DR) mutation catalog, identifying rare variants in second-line drug targets that were absent from existing references but correlated with phenotypic resistance. This improved the accuracy of mutation-based diagnostics and provided insights into emerging resistance mechanisms. Third, we developed TB-LandScape, a national genomic analysis platform incorporating 3,354 *Mycobacterium tuberculosis* genomes to establish Thailand's first comprehensive TB genomic database. The platform integrates drug-resistance prediction, lineage classification, and phylogenetic analysis through a user-friendly interface equipped with customizable mutation databases, IGV visualization, and geo-temporal analytics (Phylomap). It supports both short- and long-read sequencing data, facilitating applications in clinical, surveillance, and research contexts. Validation using 594 reference samples demonstrated >98% accuracy for lineage and resistance prediction compared with TB-Profiler, confirming its reliability as a national bioinformatics resource. Finally, to address the lack of effective LTBI screening tools, we evaluated a label-free surface-enhanced Raman spectroscopy (SERS) approach using 1,000 plasma samples from Northeast Thailand, equally divided between IGRA-positive and negative individuals. Raman mapping (7 × 7 grid) was completed within 10 minutes per sample. Optimized machine-learning models achieved 81% accuracy in train-test analysis and 75% in leave-one-out cross-validation across all batches, improving to 93% with optimized chip design and preprocessing using logistic regression. Collectively, the integration of genomics, informatics, and AI-enhanced spectroscopy provides a rapid, scalable framework to strengthen TB diagnosis, surveillance, and LTBI screening—accelerating Thailand's progress toward the End TB Goal.

Go to TOCs

4. **Amador Goodridge** (INDICASAT-AIP, City of Knowledge, Panamá, agoodridge@indicasat.org.pa)

Endemic transmission of *Mycobacterium tuberculosis* Sublineage L2.2.M3 within Panama

Mycobacterium tuberculosis lineage 2 (L2) remains a globally significant lineage associated with increased drug resistance and rapid transmission. The L2 lineage exhibits a hotspot for genetic diversity and evolution in Panama, requiring an in-depth analysis. In this talk, we will present the prospective analysis of *Mycobacterium tuberculosis* L2 isolates from Colon City, Panama. Using a ASO-PCR we identified all 31.7 % (86/271) isolates as Modern L2.2. WGS analysis confirmed all isolates belonged to the L2.2.1 sublineage. 96.9 % (62/64) classified as pan-susceptible and 3.1 % (2/64) as rifampicin/pyrazinamide-resistant. The sublineage analysis based on SNPs using the TB-gen tool identified a SNP at position 1219683G > A, which genotyped all strains as L2.2.M3 sublineage. We found a correlation with geographical distribution compared to other Latin American L2 isolates with a relatively low evolutionary rate within Panama. When using TB annotator tool to compare to1,578 L2.2.M3 strains worldwide, our strains form a separate monophyletic cluster within the sublineage, containing all the strains from the province of Colon, Panama, and three additional strains identified in non-Asian countries. The closest relative branches had higher proportions of drug-resistant strains with most strains from, but not limited to, East and Southeast Asian countries. All together these findings suggest endemic transmission of the *Mycobacterium tuberculosis* L2.2.M3 sublineage in Colon, Panama. We recommend combining genomic information with epidemiological data to accurately track and identify the source hotspot for the L2.2.M3 sublineage local and globally.

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5. **Igor Mokrousov** (St. Petersburg Pasteur Institute, St. Petersburg, Russia)

Genomic insight into *Mycobacterium tuberculosis* adaptation to external stress in the in vivo and in vitro models

Full author list: Igor Mokrousov (1), Tatiana Vinogradova (2), Natalia Solovieva (2), Ivaylo Slavchev (3), Marine Dogonadze (2), Dmitry Polev (1), Georgi Dobrikov (3), Violina T. Angelova (4), Violeta Valcheva (5), and Anna Vyazovaya (1)

(1) St. Petersburg Pasteur Institute, St. Petersburg, Russia
(2) St. Petersburg Research Institute of Phthisiopulmonology, St. Petersburg, Russia
(3) Institute of Organic Chemistry with Center of Phytochemistry, Bulgarian Academy of Sciences, Sofia, Bulgaria
(4) Medical University of Sofia, Sofia, Bulgaria
(5) Stephan Angeloff Institute of Microbiology, Bulgarian Academy of Sciences, Sofia, Bulgaria

Different spontaneous mutations emerge in *Mycobacterium tuberculosis* and those beneficial for bacterial survival are selected leading to bacterial drug resistance, tolerance and ultimately - persistence. We studied *M. tuberculosis* genetic variation in response to selective pressure of antibiotics and candidate anti-tuberculosis compounds in vivo and in vitro. C57Bl/6 mice were infected with different MDR clinical strains followed by treatment with moxifloxacin, linezolid, and bedaquiline. Bacterial isolates were recovered from the lungs of euthanized mice after 2 and 5.5 months of treatment. For in vitro study, H37Rv reference strain was cultured under elevated concentrations of new candidate anti-TB compounds (nitrofuranes and aroylhydrazones); resistant clones were subjected to WGS. The treatment course reduced the bacterial burden of the lungs of mice; no resistance mutations to new drugs emerged. However, in few isolates, mutations beyond drug resistance were identified. The in vitro study of spontaneous resistant clones revealed *M. tuberculosis* response to nitrofuranyl amide through multiple pathways, reportedly counteracting oxidative and nitrosative stress. Mutations in several genes were detected in clones resistant to aroylhydrazones including frameshift mutations in glpK and ppgK linked to drug tolerance, and nonsynonymous mutations in possibly efflux genes. To conclude, long-term treatment of mice infected with hypervirulent strain resulted in selection of mycobacteria with a mutation inactivating the tgs3 gene. This gene is associated with lipid metabolism and promotes dormancy, which ensures pathogen persistence. Its inactivation, conversely, leads to increased mycobacterial growth. The in vitro study revealed a complex *M. tuberculosis* response to nitrofuranes and aroylhydrazones. The short-term action of these compounds on slow-growing *M. tuberculosis* primarily lead to the emergence and selection of mutations in various unrelated genes within nonspecific tolerance mechanisms (efflux pumps and slow growth rate), or mechanisms to combat oxidative and nitrosative stress (nitrofuranyl amides).

The study was supported by Russian Science Foundation (grant 24-44-00004).

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6. **Danila Zimenkov** (Engelhardt Institute of Molecular Biology, Russian Academy of Sciences, Russia)

The hidden diversity of *Mycobacterium*

Full author list: Danila Zimenkov[1], Anastasia Ushtanit[1], Marina Filippova[1], Uliana Semenova[1], Vyacheslav Zhuravlev[2], Natalia Solovieva[2], Peter Yablonsky[2], Maria Sviridenko[3], Anastasia Khakhalina[3], Svetlana Safonova[3], Marina Makarova[3], Elizaveta Gordeeva[4], Elena Guselnikova[4], Yakov Schwartz[4], Natalia Stavitskaya[4], Yuliana Atanasova[5], Stanislava Yordanova[5], Ana Baykova[5], Elizabeta Bachiyska[5], Igor Mokrousov[6]

[1]Engelhardt Institute of Molecular Biology, Russian Academy of Sciences, 119991 Moscow, Russia

[2]Saint-Petersburg State Research Institute of Phthisiopulmonology of the Ministry of Healthcare of the Russian Federation, 191036 Saint-Petersburg, Russia

[3]The Moscow Research and Clinical Center for Tuberculosis Control of the Moscow Government Health Department, 107014 Moscow, Russia

[4]Federal State Budgetary Institution "Novosibirsk TB Research Institute" of the Ministry of Health of Russian Federation, 630040 Novosibirsk, Russia

[5]National Reference Laboratory of Tuberculosis, Department of Microbiology, National Center of Infectious and Parasitic Diseases, 44A General Nikolai Stoletov Boulevard, 1233 Sofia, Bulgaria;

[6]St. Petersburg Pasteur Institute, St. Petersburg, Russia

Infections caused by nontuberculous mycobacteria are becoming increasingly significant due to the increasing number of vulnerable individuals worldwide. Understanding the evolutionary relationships within the genus *Mycobacterium* is critical for improving species identification and, consequently, enhancing diagnosis, treatment, and epidemiological tracking.

Pairwise comparisons of average nucleotide identity, genome-genome distance calculations, Mash values, multilocus sequence analyses, and average amino acid identities (AAI) revealed that the AAI metric is the best to distinguish *Mycobacterium* from other genera of Mycobacteriales and the phylogenetic tree inferred displayed the lowest overall topology error calculated from the probabilities of alternative local quadruplex topologies.

Furthermore, separate genes encoding 16S and 23S rRNAs could also be used for the genus delineation: the previously established threshold of 94.5-95.0% of the *rrs* identity measured by Jukes-Cantor was confirmed, and the same/analogous value for the *rrl* gene was estimated at 88.5-89.0%.

The genus delineating thresholds does not confirm the proposed splitting of the Mycobacteria into five genera, and the overall correlation of rare evolutionary events used as the basis of the splitting with particular clades was not satisfactory. On the other hand, the distribution of AAI distances inside the Mycobacteria allows to suppose the existence of separate genus corresponding to *M. chelonae-abscessus* complex, however it is still questionable, and other considerations regarding the clinical importance should be accounted for the decision. We estimated that Mycobacteria contain at least 402 distinct species, 246 of which were identified in clinical human specimens.

Based on the analysis of *gyrB* fragment a hybridization assay 'Myco-biochip' was developed and evaluated in three clinical antituberculosis centres in Moscow, Saint Petersburg, Novosibirsk (Russia) and Sofia (Bulgaria) in 2022-2024. In total, 71 mycobacterial species were identified in 3119 samples from 2221 patients in Russia and 48 samples from 48 patients isolated in Bulgaria. The performance of the assay was also tested using the laboratory collection, allowing to state the reliable identification of more than 80 species.

Four novel mycobacterial species phylogenetically related to *M. duvalii*, *M. lentiflavum*, and *M. talmoniae*, and *M. iranicum* were identified in Novosibirsk, Saint-Petersburg, Moscow and Sofia, respectively. The identification of a close relative of *M. talmoniae* adds to the existence of separate

clade placed between *M. terrae*, *M. triviale* complexes and other slow-growing Mycobacteria, which supports the thesis against the splitting of Mycobacteria into five separate genera.

The diversity of acid-fast bacilli identified in tuberculosis-suspected persons was not limited to the Mycobacteria genus and includes species from genera Nocardia, Gordonia, Corynebacterium, Tsukamurella, and Rhodococcus of the order Mycobacteriales. All the findings underscore the importance of accurate species identification and genotyping for understanding epidemiology, informing public health strategies, and enhancing diagnostic accuracy and treatment protocols.

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7. **Nawamin Pinpathomrat** (Department of Biomedical Sciences and Biomedical Engineering, Faculty of Medicine, Prince of Songkla University, Thailand)

TB vaccine platforms and delivering system

Full author list: Ratchanon Sophonmanee[1], Elena Stylianou[2], Helen McShane[2], Nawamin Pinpathomrat[1*]

[1]Department of Biomedical Sciences and Biomedical Engineering, Faculty of Medicine, Prince of Songkla University, Hat Yai, Songkhla, Thailand

[2]The Jenner Institute, University of Oxford, Old Road Campus Research Building, Roosevelt Drive, Oxford, United Kingdom

Tuberculosis (TB) remains one of the world's leading infectious causes of mortality, underscoring the urgent need for more effective and durable vaccines beyond the century-old Bacille Calmette–Guérin (BCG). Recent advances in immunology, molecular biology, and biomaterials have catalyzed the development of next-generation TB vaccine platforms designed to induce robust, long-lasting, and tissue-specific immunity. This talk provides an overview of emerging TB vaccine platforms, including live-attenuated and recombinant mycobacterial vaccines, viral-vectored vaccines, protein subunit vaccines with novel adjuvants, and nucleic acid-based approaches such as mRNA vaccines.

Equally critical to vaccine efficacy is the delivery system, which governs antigen presentation, immune polarization, dose-sparing potential, and scalability. The presentation will explore innovative delivery strategies, including lipid nanoparticle-based systems, viral and non-viral vectors, and skin-targeted delivery methods such as microneedle arrays, which exploit the high density of antigen-presenting cells in the dermis. Special emphasis will be placed on how delivery platforms can be tailored to enhance cellular immunity, particularly Th1 and $CD8^+$ T-cell responses, which are central to protection against *Mycobacterium tuberculosis*.

By integrating advances in vaccine platform design with optimized delivery technologies, this talk highlights a translational pathway toward more effective TB vaccination strategies. The discussion will also address key challenges in clinical development, manufacturing, and implementation in high-burden settings, outlining future directions for TB vaccine innovation in the era of precision vaccinology.

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8. **Qian Gao** (School of Basic Medical Science, Fudan University, Shanghai, China)

Molecular Epidemiology of Tuberculosis in China

This study aimed to clarify tuberculosis (TB) transmission patterns (recent transmission vs. endogenous reactivation), high-risk groups, and transmission hotspots in urban-rural China using genomic epidemiological methods (whole-genome sequencing combined with epidemiological investigation), providing evidence to optimize control strategies in high-burden areas. Carried out from 2009 to 2023 in Shanghai Songjiang, Shenzhen Longhua (urban sites), and Sichuan Wusheng, Heilongjiang Wuchang, Henan Linzhou (rural sites), it defined recent transmission as ≤12 single nucleotide polymorphisms (SNPs) and analyzed 2,212 urban and 2,418 rural culture-positive pulmonary TB patients.

Key findings revealed significant urban-rural disparities in TB transmission: Urban areas had low recent transmission clustering rates (25.2% in Songjiang, 15.4% in Longhua), with 70–74.7% of patients being migrants. Transmission mainly occurred within migrant (61%) and local (17%) populations, with unmanaged migrants serving as core infection sources; 70% of migrants developed TB within 2 years of arriving in cities, and transmission risk declined sharply with increasing spatial distance. Rural areas had higher clustering rates (26.9–44.7%), with *Mycobacterium tuberculosis* predominantly belonging to lineage L2 (72.8%). Close contacts (42% of cases) and students (3.84–4.82 times higher clustering risk) were high-risk groups, and transmission patterns varied by geography.

The study confirmed TB in high-burden areas is primarily driven by recent transmission, though clustering rates are underestimated due to factors like sequencing technology and population mobility. Developed countries' high-risk group-focused models are inapplicable to China. Active case finding remains the core of TB control, requiring context-specific identification of high-risk groups and hotspots to optimize migrant population management, student protection, and gathering place controls, thereby reducing widespread community transmission.

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9. **Katsushi Tokunaga** (Genome Medical Science Project, National Institute of Global Health, Japan Institute for Health Security, Tokyo, Japan)

Genomic approach to infectious diseases

We have recently been engaged in several human whole-genome sequencing (WGS) projects. We have also investigated human genomic variation relevant to a range of diseases, including multiple infectious diseases. We have conducted genome-wide association studies (GWAS) and high-resolution typing of human leukocyte antigen (HLA) genes to identify human genetic factors that influence disease susceptibility, drug response, and vaccine response.

One of the most interesting results concerns interactions between pathogen genomes and the human genome. We recently reported interactive effects between the hepatitis B virus (HBV) genome and human HLA genes. Patients carrying specific combinations of HBV genome mutations and HLA-DPB1 alleles showed markedly increased risks of progression from chronic hepatitis to hepatocellular carcinoma.

In addition, both high and low responses to HB vaccination showed significant associations with specific HLA-DRB1 alleles. Likewise, we observed associations between adverse effects following COVID-19 vaccination and variation in the human genome, including variants in the IL1RL1/IL18R1/IL18RAP region and in HLA genes.

We also present our findings on the interactions between tuberculosis lineages and human genomic variation. Furthermore, we are contributing to the “Infectious Disease Clinical Research Network with National Repository” by performing WGS of patient samples.

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10. **Surakameth Mahasirimongkol** (Office of Permanent Secretary, Ministry of Public Health, Thailand)

The Dual-Genome Strategy: Operationalizing Host Genetics (NAT2) and Pathogen WGS to Reduce TB Mortality and Transmission

While global TB control strategies have historically focused on the genome of *Mycobacterium tuberculosis*, the genetic architecture of the human host remains the overlooked half of the equation in determining clinical outcomes. As we aim for the End TB targets of <5% mortality, we must confront the biological reality that "standard" treatment is metabolically toxic for a significant proportion of the Thai and Southeast Asian population. This presentation argues for the immediate clinical integration of host genetic profiling alongside pathogen surveillance.

We focus first on the urgent implementation of pharmacogenomics (PGx) to mitigate Drug-induced liver injury (DILI), a primary driver of treatment interruption and mortality. We present data emphasizing the critical role of NAT2 (N-acetyltransferase 2). In Southeast Asia, the prevalence of NAT2 slow acetylator alleles (specifically NAT2*5, NAT2*6, and NAT2*7) creates a high-risk landscape where standard Isoniazid dosing leads to toxic accumulation. We further explore the role of rapid acetylator in increase mortality, especially in HIV infected TB patients.

Beyond toxicity, we address host susceptibility through the lens of pathogen-host co-evolution. We highlight lineage-specific genetic risk, specifically linking HLA-DRB1*09 to susceptibility against Lineage 2 (Beijing family) strains, while identifying CD53 variants as distinct risk factors for Lineage 1 (Indo-Oceanic) infection. This data challenges the model of universal susceptibility, suggesting that host immune failure is often strictly context-dependent on the infecting strain.

Crucially, we pair this host susceptibility data with *Mycobacterium tuberculosis* whole genome sequencing (WGS) to map transmission dynamics with unprecedented precision. WGS enables the detection of cryptic outbreak clusters and distinguishes recent transmission from reactivation. By overlaying host genetic risk onto WGS-defined transmission networks, we can identify "super-spreader" nodes where specific host-pathogen combinations facilitate rapid community spread.

We conclude by proposing a "Dual-Genome Triage" model. By deploying regional level genotyping for NAT2 alongside pathogen WGS, we can stratify patients into "Standard" vs. "Precision" dosing pathways while simultaneously severing transmission chains. This shift from a "one-size-fits-all" regimen to a host-informed, pathogen-aware strategy is the necessary evolution required to eliminate preventable deaths.

Keywords: Host Genetics, NAT2, Pharmacogenomics, HLA-DRB1, CD53, Whole Genome Sequencing (WGS).

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11. **Taisei Mushiroda** (RIKEN Center for Integrative Medical Sciences, Japan)

Toward Patient-Centered, Stratified Tuberculosis Treatment Through Pharmacogenomics

Isoniazid (INH) is primarily metabolized by N-acetyltransferase 2 (NAT2), and the slow acetylators (SA) have been shown to have a higher risk of developing INH-induced liver injury compared to the rapid acetylators (RA). In other words, NAT2 genetic testing enables the prediction of both drug efficacy and the risk of adverse drug reactions even before initiating tuberculosis (TB) treatment. In particular, in the Thai population—where the frequency of the NAT2 SA is higher than that in Japanese individuals—the importance of establishing a TB treatment regimen based on preemptive NAT2 testing is considered greater than in Japan. The Thai National Tuberculosis Control Programme Guideline (2018 edition) states that INH dosage adjustment based on NAT2 test results is possible for patients who develop INH-induced liver injury. This recommendation is based on findings from retrospective studies conducted through a long-term international collaboration between the Department of Medical Sciences, Ministry of Public Health, Thailand, and a Japanese research team. However, the relatively low level of evidence compared with that of prospective studies, as well as the fact that the collaborative research findings were limited to evaluating the risk of liver injury, are thought to be reasons why NAT2 testing has not yet become widespread in Thailand. Recently, our research team reported findings from two cohort studies conducted in Thailand: among 1,065 TB patients treated with INH, RA patients (n = 198) had a 1.7-fold higher all-cause mortality rate within one year compared with intermediate acetylators (IA, n = 490) (95% CI: 1.03–2.80, P = 0.04). These findings suggest that a stratified treatment strategy involving INH dose adjustment based on NAT2 genotype may improve outcomes in TB patients. By evaluating the clinical utility of NAT2 testing through a prospective clinical trial, NAT2 testing is expected to become more widely implemented.

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12. **Margarita Shleeva** (Federal Research Centre 'Fundamentals of Biotechnology' of the Russian Academy of Sciences, Moscow, Russia)

A novel biochemical reaction in mycobacteria: coproporphyrin III tetramethyl ester synthesis and its adaptation significance

Full author list: Margarita Shleeva (1), Daria Bagaeva (1), Galina Demina (1), Maria Khrenova (1,2), Michael Agaphonov (1), Alexander Savitsky (1), Arseny Kaprelyants (1)

(1) A.N. Bach Institute of Biochemistry, Federal Research Centre 'Fundamentals of Biotechnology' of the Russian Academy of Sciences, Moscow, Russia

(2) Chemistry Department, Lomonosov Moscow State University, Moscow, Russia

Mycobacteria like *Mycobacterium smegmatis* (Msm) and *Mycobacterium tuberculosis* exhibit remarkable persistence and survival strategies, particularly during the transition to dormancy. This dormancy is characterized by the accumulation of tetramethyl coproporphyrin III (TMC) within their cellular membranes. Using fluorescence anisotropy of BODIPY FL C16 probes, we observed a significant decrease in membrane fluidity (anisotropy increasing from 0.05 to 0.22) in dormant Msm cells compared to viable ones. This reduced fluidity, mirrored by increased TMC levels induced by 5-aminolevulinic acid in viable Msm, was associated with inhibited respiratory chain activity, evidenced by decreased oxygen consumption and DCPIP redox acceptor reduction. Upon reactivation of dormant Msm, both porphyrin content and membrane fluidity returned to viable levels within 8 hours. We propose that TMC accumulation during dormancy stiffens the membrane, leading to respiratory chain inhibition. We identified and characterized of novel mycobacterial methyltransferases, MSMEG_0614 and Rv0281, which catalyze the S-adenosyl-L-methionine-dependent conversion of coproporphyrin (CP) into TMC through sequential methylation of its carboxyl groups. To confirm the role of MSMEG_0614 in TMC biosynthesis, we generated a deletion mutant (Δ0614) in *M. smegmatis*. This mutant exhibited significantly reduced TMC levels during the late stationary phase and dormancy compared to the wild-type, validating MSMEG_0614's contribution to TMC accumulation. Overexpression of MSMEG_0614 in both species significantly elevated intracellular TMC and reduced respiratory activity, directly linking this enzymatic pathway to dormancy. Furthermore, Msm strains overexpressing MSMEG_0614 demonstrated substantial resistance to heat shock (90-fold) and oxidative stress (7-fold). These findings unveil a new porphyrin modification pathway contributing to mycobacterial stress tolerance and dormancy, offering crucial insights into pathogen survival.

The work was carried out within the Russian Science Foundation grant 24-15-00221.

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13. **Egor Shitikov** (Lopukhin Federal Research and Clinical Center of Physical-Chemical Medicine of Federal Medical Biological Agency Medicine, Russia)

Mycobacteriophages: from laboratory research to practical applications in medicine

Full author list: Egor Shitikov (1), Sofya Kuznetsova (1), Marina Zaychikova (1), Ksenia Klimina (1), Arina German (2), Margarita Shleeva (2) and Maja Malakhova (1)

(1) Lopukhin Federal Research and Clinical Center of Physical-Chemical Medicine of Federal Medical Biological Agency Medicine, Russia

(2) Federal Research Centre 'Fundamentals of Biotechnology' of the Russian Academy of Sciences, Russia

The growing prevalence of multidrug-resistant *Mycobacterium tuberculosis* and nontuberculous mycobacteria (NTM) underscores the urgent need for alternative therapeutic approaches. Mycobacteriophages represent a promising alternative; however, the potential of Russian isolates remains largely unexplored despite extensive global discovery efforts. To address this gap, we established the first Russian collection of mycobacteriophages and identified specific candidates exhibiting strong therapeutic potential. Phages were isolated from environmental samples using *Mycobacterium smegmatis* mc(2)155 as a host. The host range was determined against clinical *M. tuberculosis* isolates as well as various NTM species. Genome sequencing was performed on the Illumina platform. Twenty-one phages were isolated, with electron microscopy revealing a predominance of the siphovirus morphology. The collected phages represented six of the 31 known global mycobacteriophage clusters (A, B, F, K, S, and the rare cluster Y). Notably, we identified phage Arbat as a genomic singleton, sharing less than 5% similarity with any known phage and featuring a large, unique genome (108.9 kb). Phages Nadezda (Y), Yasnaya_Polyana (K), Vic9 (B), Cat (A), and Ksenia (S) have been deposited in NCBI. Lytic activity against *M. tuberculosis* H37Rv was demonstrated for phages Vic9, Yasnaya_Polyana, Nadezda and five cluster A phages. Phage Yasnaya_Polyana had the highest efficacy ($5x10^{-2}$). Against *M. abscessus*, *M. fortuitum*, and *M. avium*, activity was observed in cluster A phages. Cat and KV phages had deletions in the integration module affecting integrase or repressor genes. A lytic derivative (YPΔ47) of temperate phage Yasnaya_Polyana was obtained by deleting the repressor gene via BRED (Bacteriophage Recombineering of Electroporated DNA). In conclusion, the phages from this collection expand the known global diversity of mycobacteriophages. Among them, phages Cat and the engineered lytic derivative YPΔ47 emerge as particularly promising candidates for further development as therapeutic agents.

This study was supported by the Russian Science Foundation (project no. 24-15-00514, https://rscf.ru/en/project/24-15-00514/).

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14. **Marisa Ponpuak** (Department of Microbiology, Faculty of Science, Mahidol University, Thailand)

Monocyte transcriptional responses to *Mycobacterium tuberculosis* associated with natural resistance to tuberculosis infection

Full author list: Fabien Loison1#, Pinidphon Prombutara2,3#, Sureeporn Phlaetita1, Sornram Songpukdee4, Bodin Kummamueng4, Israt Chowdhury1, Tegar Adriansyah Putra Siregar1, Olabisi Flora Davies-Bolorunduro1, Wuthiwat Ruangchai5, Natthakan Tipkrua6, Prapaporn Srilohasin7, Phalin Kamolwat8, Pakorn Aiewsakun1,5, Surakameth Mahasirimongkol9, Prasit Palittapongarnpim1,5 and Marisa Ponpuak1,5*

1 Department of Microbiology, Faculty of Science, Mahidol University, Bangkok, Thailand.
2 Mod Gut Co., Ltd., Bangkok, Thailand.
3 Omics Sciences and Bioinformatics Center, Chulalongkorn University, Bangkok, Thailand.
4 Tuberculosis Clinic, Makarak Hospital, Kanchanaburi, Thailand.
5 Pornchai Matangkasombut Center for Microbial Genomics, Faculty of Science, Mahidol University, Bangkok, Thailand.
6 Office of Prevention and Control Disease region 5, Department of Disease Control, Ministry of Public Health, Ratchaburi, Thailand.
7 Department of Microbiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand.
8 Department of Disease Control, Tuberculosis Division, Ministry of Public Health, Nonthaburi, Thailand.
9 Medical Life Sciences Institute, Department of Medical Sciences, Ministry of Public Health, Nonthaburi, Thailand.

Outcomes following exposure to *Mycobacterium tuberculosis* (Mtb) range from clearance and containment to latent infection and active disease, reflecting substantial interindividual heterogeneity shaped by long-standing host-pathogen coevolution. Notably, a subset of heavily exposed household contacts remains persistently IGRA-negative, suggesting the presence of naturally protective immune mechanisms. We hypothesized that human monocytes exhibit genetically encoded, Mtb-specific transcriptional responses that contribute to resistance to Mtb infection and IGRA conversion. To test this hypothesis, we performed RNA-seq on primary monocytes isolated from tuberculosis household contacts in the Makarak District, Kanchanaburi, Thailand. Monocytes from 51 IGRA-negative “resisters” and 53 IGRA-positive “converters” were profiled at baseline and following ex vivo Mtb infection. Differential gene expression and pathway enrichment analyses were performed to define monocyte-specific, Mtb-dependent transcriptional programs associated with resistance to IGRA conversion. Differentially expressed genes and enriched biological pathways distinguishing resister from converter monocytes in response to Mtb infection will be presented. These transcriptional signatures are expected to provide insight into cellular pathways regulating susceptibility versus resistance to Mtb infection and to identify candidate host-directed targets that enhance intrinsic myeloid restriction of intracellular Mtb.

This study was supported by the Health Systems Research Institute, Thailand.

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15. **Alexander S. Apt** (Laboratory for Immunogenetics, Central TB Research Institute, Moscow, Russia)

MHC-II polymorphism in TB control: new lessons from genetic and immunologic studies in recombinant congenic mice

Full author list: Nadezhda Logunova, Marina Kapina and Alexander Apt
Laboratory for Immunogenetics, Central TB Research Institute, Moscow, Russia

Numerous studies demonstrated that the major histocompatibility complex genes are involved in the control of susceptibility to and severity of TB. Since $CD4^+$ T-cells are critical for effective anti-mycobacterial immune response, it is not surprising that the MHC-II genes have a prominent impact on TB control. Our recent genetic mapping and functional analyses provided new insight in the influence of MHC-II genetic polymorphisms on: (i) expression levels of corresponding molecules, and (ii) TB control by the mouse host. We established a large panel of H2-congenic recombinant strains, one of which differs from its B6 ancestor only by the allele of a single Class II gene encoding the H2-A molecule. Immunologically, this difference was sufficient to decrease the size of CD4 T-cell population and change the Th1: Th17 ratio, which resulted in an increase of neutrophil population, an important factor in TB pathogenesis. These shifts occurred before TB challenge providing mechanistic explanation for true genetic susceptibility to infection. After TB challenge, an increased severity of TB infection was underlined by intrinsically elevated level of CD4 T-cell non-specific activation followed by immune exhaustion and apoptotic death. Genetically, a higher level of TB resistance was associated with the MHC-II dominant allele determining earlier capacity for mycobacteria-specific IFN-γ production followed by its more rapid down-regulation. Genetic analysis of two previously mapped QTLs associated with TB control demonstrated that the control of immune and inflammatory responses involving functionally distant, but interacting, immune cell populations depend upon QTLs which were mapped as two separate loci during the whole genome screen study, but appeared to be the outcome of allelic segregation of a single polymorphic MHC-II gene.

The work was supported by the Russian Science Foundation (grant 23-14-00030).

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16. **Tomasz Jagielski** (University of Warsaw, Poland)

A water tale - new insights into the ecology of nontuberculous-mycobacteria

Abstract

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17. **David Couvin** (Institut Pasteur de la Guadeloupe, France)
SITVIT++: Next-Generation *Mycobacterium tuberculosis* databases and biobanks for genomic surveillance, drug resistance monitoring, and predictive intelligence

David Couvin, Damien Cazenave, Nalin Rastogi
Institut Pasteur de la Guadeloupe, France

The *Mycobacterium tuberculosis* complex (MTBC) comprises closely related bacterial species causing tuberculosis (TB), one of the world's deadliest infectious diseases. Research on MTBC is vital for understanding its evolution, and for advancing diagnostics, treatment, and prevention. Genomic and molecular epidemiology studies have highlighted the diversity of MTBC lineages and their influence on transmission and disease outcomes. A major obstacle to TB control is the rise and spread of drug-resistant strains. The slow development of new antibiotics and limited access to effective therapies further intensify this threat. Strengthening surveillance systems to rapidly detect resistance, monitor spread, and inform treatment decisions is therefore crucial. Integrating molecular, clinical, and epidemiological data can greatly enhance the monitoring and management of antibiotic resistance. This project aims to: (i) elucidate mechanisms underlying antibiotic resistance using endogenous (epidemiological) and exogenous (socioenvironmental) data; (ii) create the next generation of SITVIT databases as well as biobanks incorporating artificial intelligence (AI) and machine learning (ML) for predictive querying; and (iii) make these tools openly accessible to the scientific and public health communities. By leveraging AI and ML to analyze heterogeneous datasets, this initiative seeks to strengthen global TB surveillance, refine MTBC taxonomy, promote collaborative research, and support more precise prevention and treatment strategies.

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18. **Urvashi Singh** (All Indian Institute of Medical Sciences, Delhi and Head of National TB program, India)

Mycobacterium tuberculosis genomics and transmission tracing in India

Abstract

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19. **Virasakdi Chongsuvivatwong** (Prince of Songkla University, Thailand, cvirasak@gmail.com)

Genomic and Epidemiological Interpretation of a Disease Outbreak

Classic epidemiology defines a disease outbreak as abnormal sudden increase of cases. Genomics advancement indicates the necessity to prove the genotype linkage of the cases. Tuberculosis is a chronic infectious disease with long incubation and latent period. Scopes of time and space are ill defined. Modern genomics technology is the nearly the only key to outbreak investigation. However, there are still many potential limitations. Genotypic outbreaks are often reported from analysis of samples stored in the lab without information on social relatedness of the cases. As far as all TB cases are unequally accessible for genomics investigation, the genotypes are over-represented by samples from health facilities acquainted with the lab. Bio-diversity in these lab-based sample is under-estimated and high proportion genotypes could be mis-considered as the cluster outbreak. We propose that epidemiological and community-based microbial evolution theory should be combined in the analysis. All TB patients should have their sputum cultured followed by genomic analysis to enable community-based microbial genetic mapping. A real genotype outbreak calls for further investigation on possible failure of the health systems or changes in host-agent relationship. The abnormally highly infectious strain may require special control measures.

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20. **Richard M. Anthony** (Tuberculosis Reference Laboratory, Centre for Infectious Disease Control, National Institute for Public Health and the Environment (RIVM), the Netherlands)

Micro-evolution in clustered cases of tuberculosis a useful signal or noise?

Whole genome sequencing (WGS) can be used to rule out recent clustering of *Mycobacterium tuberculosis* (MTB) isolates on the basis of pre-defined single nucleotide polymorphism (SNP) thresholds. Limited genetic variability within transmission chains hampers epidemiological investigations. SNP variability between serial isolates from a single individual can be as large as between isolates from multiple individuals within a cluster. Non-the-less as MTB is clonal newly emerging SNPs may be informative if analyzed correctly. In order to do this it is critical to avoid over calling SNPs and ensure only informative SNPs are considered. A strategy to do this was recently validated in isolates from an extended cluster (>150 cases) that has been epidemiologically monitored for more than 30 years in the Netherlands. Genomic positions that varied within the cluster isolates were carefully screened for minority populations in other isolates from the cluster. A transmission scheme was generated on the basis of WGS data alone then compared to the epidemiological information available. Fifty-two informative SNPs were identified, eight of which were also detected as mixed variants. There was high concordance between the transmission chains suggested on basis of the newly emerging SNPs and scenarios identified using classical epidemiological cluster investigations (doi.org/10.1371/journal.pone.0319630). Analysis of filtered SNPs accumulating in the genome of *M. tuberculosis* in large clusters contains information on transmission dynamics and can be used to support epidemiological investigations. The approach developed to analyze this cluster has subsequently been prospectively applied to other recently clustered isolates within the Netherlands to support ongoing epidemiological investigations.

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21. **Sayera Banu** (Infectious Diseases Division, icddr,b, Bangladesh, sbanu@icddrb.org)

Targeted next-generation sequencing for detection of drug-resistant tuberculosis: Challenges and insights from high burden settings in Bangladesh

Full author list: Sayera Banu (1), Mohammad Khaja Mafij Uddin (1), Rumana Nasrin (1), Jannatul Ferdous (1), Afsana Akter Rupa (1), Syed Mohammad Mazidur Rahman (1), Tanjina Rahman (1), Shahriar Ahmed (1), and Aung Kya Jai Maug (1)

(1) Infectious Diseases Division, icddr,b, 68, Shaheed Tajuddin Ahmed Sarani, Dhaka-1212, Bangladesh

Background and rationale: Incomplete drug susceptibility testing (DST) profiles remain a major barrier to effective management of drug resistant (DR) tuberculosis (TB) in resource limited countries like Bangladesh. Existing DST methods are time-consuming and limited to a few drugs. Targeted next-generation sequencing (tNGS) has emerged as a comprehensive alternative. We aimed to investigate the performance and feasibility of tNGS for detecting TB resistance profile directly from clinical samples in Bangladesh, and to explore the challenges of implementation.

Methods: A total of 591 rifampicin-resistant (RR)-TB patients were enrolled between February'22 and December'24. We performed tNGS directly from clinical specimens, while phenotypic DST (pDST) was performed on culture-positive isolates. Resistotypes of tNGS by using the Deeplex Myc-TB kit were compared with pDST results.

Result: Among 591 samples, tNGS identified 362 (61.3%) as multi-drug resistant, 101 (17.1%) as RR, 94(15.9%) as pre-extensively drug-resistant (pre-XDR), and 4 (0.7%) as extensively drug-resistant (XDR). The tNGS showed high concordance with pDST for key drugs, including rifampicin (90.0%), isoniazid (91.2%), fluoroquinolones (96.1%), and aminoglycosides (99.2%). The implementation of tNGS comprised two important phases: a preparatory phase focusing on procurement, laboratory infrastructure, and training, and an implementation phase emphasizing practical workflow with samples. Following successful implementation, tNGS was sustained with services supporting the National TB Control Program (NTP). Key challenges include suitable laboratory infrastructure, lack of a quality assurance program, high reagent cost, limited target genes for newer drugs like pretomanid, delamanid, bedaquiline etc.

Conclusions: The tNGS is a valuable approach to identify comprehensive drug resistance profiles directly from clinical samples with a much faster turnaround time than pDST. With careful planning and mitigation of current challenges, tNGS can be integrated with regular clinical use, e.g. initially at the National TB Reference Laboratory and gradually at the Regional TB Reference Laboratory in the country.

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22. **Pakorn Aiewsakun** (Emeritus Professor Pornchai Matangkasombut Center for Microbial Genomics (CENMIG), Department of Microbiology, Faculty of Science, Mahidol University, Bangkok Thailand)

Whole-genome sequence analysis to detect *Mycobacterium tuberculosis* transmission clusters

Tuberculosis (TB) remains a major public health challenge in Thailand, one of the world's top 30 high-burden countries for TB and TB/HIV. Although national surveillance data indicate that TB incidence has been declining, the rate of reduction has been slow. Substantially more effective control strategies are needed if Thailand is to achieve the World Health Organization's End TB Strategy target of a 90% reduction in TB incidence by 2035 relative to 2015 levels.

Whole-genome sequencing (WGS) analysis has emerged as a promising method for investigating *Mycobacterium tuberculosis* (MTB) transmission clusters. Insights derived from WGS analyses have the potential to inform more targeted and effective interventions for TB control and transmission prevention.

In this talk, I will present progress from an on-going project that applies WGS to detect MTB transmission clusters in Chiang Rai, Thailand. I will focus, in particular, on the limitations of the commonly used SNP-distance-based approach in this high TB burden setting with persistent transmission and incomplete WGS coverage. Potential alternative strategies for identifying transmission clusters will be discussed.

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23. **Robin Warren** (Faculty of Medicine and Health Sciences, Stellenbosch University, South Africa)

The genesis and transmission of drug-resistant tuberculosis

Robin Warren on behalf of the TB Genomics Group
SAMRC Centre for Tuberculosis Research, Division of Molecular Biology and Human Genetics, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa

Drug resistance continues to threaten TB control and has had a devasting impact on mortality and morbidity. The science of molecular epidemiology in combination with whole genome sequencing now allows research to track *Mycobacterium tuberculosis* strains through space and time as well as to map the evolutionary trajectory of their genomes. The emergence of resistance within a patient is driven by drug concentration at the site of disease which is in turn dependent on the types of drugs, their combination and whether they are taken regularly. In South Africa there are estimated 14,000 RR- and MDR-TB cases occur each year. These cases are infected with endemic drug-resistant (DR) strains that form large clusters of both pre-XDR and XDR-TB. Lineage 2 dominates the DR-TB landscape with common progenitor strains evolving additional resistance and subsequent spread. Urbanization has contributed to the influx of highly resistant DR-TB genotypes into the Cape metropole while in rural towns novel clones continue to spread. The longest documented outbreak spans a period of 25 years in a suburb of Cape Town. However, this outbreak probably reflects the complexity of ongoing transmission with associated genomic evolution as well as influx and efflux of closely related strains. We also note that the persistence of certain DR-TB genotypes probably reflecting a combination of inadequate treatment as well as periods of lost to follow-up. To combat the DR-TB epidemic South Africa has rapidly moved to implement novel diagnostics and was instrumental in being one of the first countries to introduce injection free drug regimens for DR-TB. This has brought new challenges with the observed rapid emergence of BDQ resistance. The potential for implementing NGS technologies for patient management is most crucial. These technologies provide important surveillance information but also provide insight into the trajectory of resistance emergence is patients exposed to novel and repurposed drugs.

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24. **Mi Kaixia** (Institute of Microbiology, Chinese Academy of Sciences, China)

Elucidating the Dual Roles of Mycobacterial MfpA in Fluoroquinolone Resistance and Virulence Regulation

Drug-resistant tuberculosis (DR-TB) remains a major challenge to global tuberculosis control efforts. Urgent basic research into the drug resistance mechanisms of *Mycobacterium tuberculosis* (Mtb) is essential to support the discovery of novel anti-tuberculosis therapies. Our research team has long been dedicated to studying drug resistance mechanisms in *M. tuberculosis*, with particular emphasis on fluoroquinolone resistance. We successfully determined the crystal structure of the quinolone resistance protein MfpA in complex with DNA gyrase, revealing how MfpA protects DNA gyrase and elucidating its critical role in mediating resistance. More recently, we have uncovered additional multifunctional roles of MfpA, including its significant contribution to bacterial pathogenesis and virulence. Building on these discoveries, our team proposes a “dual-target intervention strategy” that provides a promising new approach to effectively counter drug-resistant *M. tuberculosis*, overcome resistance barriers, and improve clinical treatment outcomes.

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25. **Violeta Valcheva** (Stephan Angeloff Institute of Microbiology, BAS, Sofia, Bulgaria)

Development and pharmacological evaluation of novel hydrazide - hydrazone derivatives and nitrofuranyl amides as potential antituberculosis drug candidates

Full author list: Violeta Valcheva (1), Simeon Dimitrov (1), Rumyana Simeonova (2), Milka Mileva (1), Ivaylo Slavchev (3), Violina Angelova (2) and Georgi Dobrikov (3)

(1) Stephan Angeloff Institute of Microbiology, BAS, Sofia, Bulgaria
(2) Medical University of Sofia, Pharmacy Faculty, Sofia, Bulgaria
(3) Institute of Organic Chemistry with Center of Phytochemistry, BAS, Sofia, Bulgaria

Background: The global escalation of multidrug-resistant tuberculosis (MDR-TB) necessitates the development of novel therapeutic agents with unique mechanisms of action. Hydrazide - hydrazone derivatives and nitrofuranyl amides represent promising chemical classes due to their structural adaptability and potential biological efficacy.

Aim: The aim of this study was to evaluate the antimycobacterial activity, toxicity profile, and pharmacokinetic properties of two novel aroylhydrazone derivatives (3a and 3b) and two nitrofuranyl amides (DO 209 and DO 190) as potential drug candidates.

Methodology: In vitro antimycobacterial potency was determined using REMA assays against reference *Mycobacterium tuberculosis* H37Rv. Safety profiles was assessed through acute and sub-acute toxicity studies in murine models, including histopathological analysis of the liver, kidneys, and intestines. Pharmacokinetic evaluation focused on redox-modulating capacity via oxidative stress biomarkers and gastrointestinal permeability across various pH gradients. Molecular docking simulations were utilized to characterize protein-ligand interactions with essential bacterial targets.

Main findings: All four compounds demonstrated significant antimycobacterial activity and a favorable safety profile, with no observed histological or behavioral toxicity. All derivatives exhibited robust antioxidant properties and high gastrointestinal permeability. Molecular docking confirmed high binding affinities for key mycobacterial proteins, with compound 3a and DO 190 showing superior interaction stability.

Conclusion: These findings suggest that the novel aroylhydrazone derivatives and nitrofuranyl amides are viable leads for further antituberculosis drug development, offering a dual-action approach through direct bacterial inhibition and host-protective antioxidant effects.

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26. **Oleg Ogarkov** (Institute of Epidemiology and Microbiology, Scientific Centre for Family Health and Human Reproduction Problems, Irkutsk, Russia)

Formation of a polybacterial community in caseous necrosis: a common and adverse consequence of tuberculosis

Full author list: Oleg Ogarkov (1), Elizaveta Orlova (1), Alexey Suzdalnitsky (2,3), and Igor Mokrousov (4)

(1) Institute of Epidemiology and Microbiology, Scientific Centre for Family Health and Human Reproduction Problems, Irkutsk, Russia
(2) Irkutsk Regional Clinical Tuberculosis Hospital, Irkutsk, Russia
(3) Irkutsk State Medical University, Irkutsk, Russia
(4) St. Petersburg Pasteur Institute, St. Petersburg, Russia

Caseum, the central necrotic material found in tuberculosis lesions, serves as a reservoir for drug-resistant *Mycobacterium tuberculosis*. However, it is not the only type of bacteria residing within these lesions. We obtained data through metagenomic and 16S rRNA amplicon sequencing of caseous necrosis derived from surgically excised tuberculosis foci. This approach enabled us to characterize the biological diversity and potential biochemical pathways of these bacterial communities. In addition to *M. tuberculosis*, we identified anaerobic, lipophilic satellite bacteria within the caseum. This finding is significant because the caseum can exist in two distinct states: "true" tuberculosis necrosis, which comprises 99.9% *M. tuberculosis*, and a polymicrobial community where anaerobic bacteria predominate. Furthermore, the isolation and genomic characterization of Corynebacterium and Staphylococcus species corroborate this observation. Co-cultivation of *Corynebacterium kefirresidentii* with *Mycobacterium bovis* BCG enhanced robust biofilm formation, as a distinct surface pellicle with cord-like structures of acid-fast bacilli (BCG). Staining revealed a polysaccharide-rich matrix surrounding these two bacterial consortia. These findings suggest that satellite bacteria can stimulate or/and enhance production of biofilm in necrotic sites of TB focuses. Immunological profiling of tuberculosis patients revealed that Corynebacterium and Staphylococcus strains isolated from caseum triggered a heightened immune response compared to healthy controls. IGRA and ELISA assays showed these bacteria differentially stimulated IFN-γ, IL-4, and IL-10 release in patients, suggesting their potential role in modulating Th1/Th2 responses during infection. We believe that this immunogenicity may influence granuloma development and TB progression.

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27. **Prasit Palittapongarnpim**, M.D. (Emeritus Professor Pornchai Matangkasombut Center for Microbial Genomics (CENMIG), Department of Microbiology, Faculty of Science, Mahidol University, Bangkok Thailand)

Structural Variants in *Mycobacterium tuberculosis* Genomes

The genomes of *Mycobacterium tuberculosis* are relatively homogeneous compared to most pathogenic bacteria. However, the variations have been correlated with various important phenotypes. Apart from single nucleotide polymorphism, *M. tuberculosis* genomes also contain various structural variants, which have been targets of classical genotyping methods: IS6110-RFLP, MURU-VNTR, CRISPR region-for spoligotyping and RDs for LSP. Another highly polymorphism element is the pe/ppe gene family, which in total contributes to about 7% of the *M. tuberculosis* genome. The available complete genomes of different genotypes revealed considerable structural variations in addition to the single nucleotide variants. Indeed, some of the perceived SNVs are results from erroneous read mapping due to the structural variants. We investigated the highly polymorphic pe_pgrs3-pe_pgrs4 among clinical isolates and revealed that there actually are 4 highly similar genes, pe_pgrs3, pe_pgrs4, pe_pgrs3*, pe_pgrs4*, two or three of which are present in each genotype. The structural variants of some pe/ppe, such as ppe38, have significant physiological and pathogenic consequences. The others remain to be studied. The information may be useful for vaccine development as many pe/ppe proteins are surfacely exposed, interact with host surface proteins, such as TLR2 or TLR4 and highly immunogenic.

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28. O-01: Oren Tzfadia (Institute for Tropical Medicine, Antwerp, Belgium)
A next-generation Mycobacterial knowledge base

Full author list: Klaas Dewaele (1), Oren Tzfadia (1)
(1) Institute for Tropical Medicine, Antwerp, Belgium

Leading computer scientists predict smarter-than-human AI in 2027. Already today, Large Language Models (LLMs) can process book-volumes of information, can be chained in autonomous, agentic workflows, and perform reasoning tasks – properties expected to enable a revolution in biological hypothesis generation and testing. To leverage these capabilities for mycobacterial research, access to domain-specific knowledge is key. However, existing mycobacterial databases, such as TBDB and Mycobrowser are defunct. We present a suite of tools to build and dynamically extend a next-generation, LLM-interrogable, mycobacterial knowledge base (KB). This KB is gene-centric, enabling the formulation and testing of hypotheses related to gene function and biological networks. It is constructed as a knowledge graph, enabling plug-and-play extension with novel data types. This suite includes scripts to interrogate functional protein association databases (comprising co-expression, gene neighborhood and co-occurrence data). The network is augmented with regulatory information, including transcriptional control and protein-level modulation, based on curated experimental literature sets. Labeling of genes and their interactions is done using our automated literature querying tool – retrieving, storing, and interpreting abstracts and open access papers. Gene functional markers, including conservation, evolutionary patterns (dN/dS, regions-of-difference) and immune-pressure signatures (epitope quantity and conservation) are supplied by our public domain strain variant calling pipeline. Ultimately, we aim to enable autonomous hypothesis testing using LLM agents and software for protein interface prediction (Boltz-1) and coevolution studies (EVcouplings, Pyseer). In summary, we present a methodological framework and several tools for compiling a next-generation LLM-enhanced mycobacterial knowledge base, preparing for mycobacterial research in the AI era.

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29. **O-02: Mohammad Khaja Mafij Uddin** (Infectious Diseases Division, icddr,b, Bangladesh, kmuddin@icddrb.org)

Genomic Insights into Drug Resistance and Transmission Dynamics of Multidrug-Resistant Tuberculosis Strains in Bangladesh

Full author list: Mohammad Khaja Mafij Uddin[a], Rumana Nasrin[a], Jannatul Ferdous[a], Afsana Akter Rupa[a], Omar Faruk Bhuiyan[a], S. M. Mazidur Rahman[a], Shahriar Ahmed, Aung Kya Jai Maug[a], and Sayera Banu[a]

[a]Infectious Diseases Division, icddr,b, 68, Shaheed Tajuddin Ahmed Sarani, Dhaka-1212, Bangladesh

Background: Understanding the epidemic determinants of multidrug-resistant tuberculosis (MDR-TB) is essential to control transmission. However, a major gap exists in understanding the genetic determinants underlying drug resistance and the transmission dynamics of the MDR-TB strains circulating in Bangladesh. The study aimed to characterize the population structure, drug resistance profiles, and transmission dynamics of MDR-TB strains in Bangladesh.

Methods: A total of 429 rifampicin-resistant (RR)-TB patients were enrolled from Programmatic Management of Drug Resistant-TB sites across the country between February 2022 and December 2024. Targeted next-generation sequencing (tNGS) was utilized to determine drug resistance profiles and lineage distribution. Additionally, Mycobacterial Interspersed Repetitive Unit-Variable Number of Tandem Repeat (MIRU-VNTR) was performed to investigate transmission of MDR-TB.

Results: Out of 429 isolates, tNGS identified 264 (61.5%) as MDR, 74 (17.2%) as RR, 67 (15.6%) as pre-extensively drug-resistant (pre-XDR), and 4 (0.9%) as extensively drug-resistant (XDR). Four major lineages based on single-nucleotide polymorphism (SNP) were found: L1 (137; 31.9%), L2 (108; 25.2%), L3 (56;13.1%), and L4 (128; 29.8%). MDR-TB was mainly linked to L4 (128; 29.8%), while L2 was strongly associated with pre-XDR-TB (25.9%). MIRU-VNTR revealed 336 distinct patterns with 37 clusters comprising 130 isolates. The clustering rate was 30.3%. A combination of MIRU-VNTR and spoligotyping, and the phylogenetic relationship demonstrated that the majority of the clustered isolates belonged to L2 and L4. The estimated recent transmission rate was 14.0%.

Conclusion: MDR-TB exhibited high genetic diversity along with lineage-specific resistance patterns. The recent transmission rate suggests that the majority of the TB cases in Bangladesh result from reactivation of prior infections. These findings underscore the urgent need to strengthen active case finding, screening for latent infection, and lineage-specific surveillance to control MDR-TB transmission.

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30. O-03: Dyshelly Nurkartika Pascapurnama (Universitas Padjadjaran, Indonesia)

Proportion of pathogenic non-tuberculous mycobacteria identified by partial-gene sequencing among presumptive tuberculosis patients in Indonesia

Full author list: Dyshelly Nurkartika Pascapurnama (1,2), Yoopie Setiawan (1,3) and Lidya Chaidir (2,4)

(1) Doctoral Program in Medical Sciences, Faculty of Medicine, Universitas Padjadjaran, Bandung, West Java, Indonesia
(2) Center for Translational Biomarker Research, Universitas Padjadjaran, Bandung, West Java, Indonesia
(3) Department of Biomedical Sciences, Faculty of Medicine, Universitas Katolik Parahyangan, Bandung, West Java, Indonesia
(4) Department of Biomedical Sciences, Faculty of Medicine, Universitas Padjadjaran, Sumedang, West Java, Indonesia

The burden of Non-Tuberculous Mycobacteria (NTM) cases in Indonesia remains unknown. Early detection is challenging, leading to under- and misdiagnosis. The paucity of data concerning this disease contributes to the neglect of NTM in the country. This study aimed to identify NTM by utilizing a partial gene sequencing of superoxide dismutase A (sodA) in presumptive tuberculosis (TB) patients from an Indonesian setting. Retrospective samples from two cohorts were included: the first cohort mostly enrolled patients from community clinics, and the second was a hospital-based cohort. The stored isolates from individuals suspected of having pulmonary NTM infection were re-cultured. Extracted genomic DNA was subjected to polymerase chain reaction (PCR) and was subsequently sequenced. The sequences were analyzed using the DNA Baser software. Consensus sequences were compared with reference sequences from the NCBI GenBank database to determine NTM species. A total of 3,426 patients presenting for pulmonary TB were enrolled. Half of the patients (n=1,713) were positive on either solid or liquid culture for TB. NTM was detected in 54 (3.2%) culture-positive cases. The proportion of NTM among culture-positive cases was higher in the hospital-based cohort (7.6%) versus 2.2% in the other cohort. Sequencing of sodA in 43 samples showed that *M. fortuitum* complex was predominant (39.5%), followed by *M. abscessus* group (13.9%), *M. chelonae* (11.6%), and several other slow-growing NTM. No species identification was possible for 11 samples due to failure in re-culture or during sequencing. The proportion of predominant species was not different in both settings. Current screening for NTM among presumptive TB cases remains challenging in Indonesia. These findings highlight the need to refine NTM case-finding strategies and identify patient groups at higher risk of NTM infection. The incorporation of molecular identification methods offers a promising direction for future NTM research and surveillance in Indonesia.

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31. O-04: John Carlo Malabad (Department of Science and Technology, Philippines)

A molecular epidemiologic analysis of drug-resistant *Mycobacterium tuberculosis* isolates derived from the Third Philippines TB Drug Resistance Survey 2018 and community-based study

Full author list: John Carlo Malabad (1), Concepcion Ang (2), Sam Lopez (3), Alma Palparan (4), Michellin Roxanne Baje (4), Dodge Lim (4), Chona Daga (4), Kuang-Hung Liu (5), Ruwen Jou (5), Charles Yu (2), and Jaime Montoya (1, 3)

(1) Department of Science and Technology – Philippine Council for Health Research and Development, Philippines
(2) De La Salle Medical and Health Sciences Institute, Philippines
(3) College of Medicine, University of the Philippines Manila, Philippines
(4) National Tuberculosis Reference Laboratory, Research Institute for Tropical Medicine, Department of Health, Philippines
(5) Tuberculosis Research Center, Centers for Disease Control, Taiwan, R.O.C.

The Philippines remains a high burden country for tuberculosis (TB), multidrug-resistant TB (MDR-TB) and TB/HIV co-infection. The World Health Organization Global TB Report 2024 ranks the country as fourth in having the highest number of incident TB cases in the world. Previous molecular epidemiologic analyses of *Mycobacterium tuberculosis* isolated from Filipino TB patients revealed that the dominant genotype is EAI2-Manila (Lineage 1.2.1). The aim of this study is to determine the genomic profiles of drug-resistant isolates and characteristics of TB patients. We analyzed 66 *M. tuberculosis* isolates, including 37 and 29 collected from TB patients enrolled in the Third National TB Drug Resistance Survey 2018 (DRS) and a community-based study (COACH-DRTB) in Cavite, Philippines, respectively. Drug-resistant isolates were revived, subcultured and whole genome sequenced using the Illumina NovaSeq 6000 SP and analyzed using the TB-Profiler. The majority of the studied TB patients were male (49, 74.2%), re-treatment/previously treated cases (34, 51.5%), with chest x-ray findings suggestive of TB (41, 62.1%) and acid-fast bacilli smear-positive (44, 66.7%). Of the 66 isolates, 1, 57, 2 and 6 were rifampicin-resistant, MDR, pre-XDR and others, respectively. Consistent with previous studies, EAI2-Manila (Lineage 1.2.1) (53, 80.3%) is the most prevalent genotype, followed by LAM (Lineage 4.3) (12, 18.2%), and Beijing (Lineage 2.2) (1, 1.5%). Based on the 2021 WHO Catalogue of mutations in *M. tuberculosis* complex, 59 variants in 12 drug resistance-associated genes, including 32 and 27 high confidence and uncharacterized variants, respectively. Findings from this study contribute to the enrichment of the genomic and molecular characteristics data of isolates in the Philippines and improvement of existing TB prevention and control programs in the country to prevent further disease transmission.

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32. **O-05: Pundharika Piboonsiri** (Medical Life Sciences Institute, Department of Medical Sciences, Ministry of Public Health, Thailand)

Whole Genome Sequencing of *Mycobacterium tuberculosis* Reveals Emerging Bedaquiline Resistance Variants in Thailand

Full author list: Pundharika Piboonsiri[1], Charintip Yenyuvadee[1], Naparat Naowanat[1], Woraporn Thuansuwan[2], Natthakan Thipkrua[3], Boonchai Chaiyasirinroj[4], Jaluporn Chumpol[5],Sukanya Wattanapokayakit[1], Waritta Sawaengdee[1]

[1] Medical Life Sciences Institute, Department of Medical Sciences, Ministry of Public Health
[2] Central Chest Institute of Thailand, Department of Medical Services, Ministry of Public Health
[3] Office of Disease Prevention and Control 5, Ratchaburi Province, Department of Disease Control
[4] TB/HIV Research Foundation, Chiang Rai Province
[5] Office of Disease Prevention and Control 7, Khon Kaen Province, Department of Disease Control

Background: The BPaLM/BPaL regimen is essential for treating multidrug-resistant tuberculosis (MDR-TB). In Thailand, phenotypic drug-susceptibility testing (DST) for Bedaquiline (BDQ) is restricted to central laboratories. To enhance surveillance, the Medical Life Sciences Institute (DMSc) conducted a pilot study using WGS to investigate the genetic landscape of BDQ resistance.

Methods: From 2022 to the present, 2,782 *Mycobacterium tuberculosis* isolates were collected from the Central Chest Institute (n=184), Chiang Rai province (n=670), Health Region 5 (n=754), and Health Region 7 (n=1,174). WGS was performed via the Illumina platform (30X average coverage), and resistance mutations were analyzed using TB-profiler version 6.6.5.

Results: Thirteen isolates (0.48%) possessed mutations associated with BDQ resistance. These cases were sporadic, with no evidence of clonal outbreaks. The majority were MDR-TB strains belonging to Lineage 1 (66.67%). Resistance was first detected in 2022 in HR7, followed by occurrences in all other pilot sites. The most frequent mutations occurred in the mmpR5 gene, including missense variant p.Leu117Arg (n=3), and frameshift mutations c.144dupC (n=2) and c.198delG (n=2). Most mutations were heterozygous, indicating bacterial heteroresistance. Notably, six patients with these mutations had no prior BDQ treatment history, suggesting pre-existing resistance. To date, none of these isolates have undergone phenotypic DST for BDQ.

Conclusion: The detection of BDQ-resistance mutations in Thailand is a significant public health concern, particularly as the country scales up BPaLM/BPaL regimens. These findings underscore the urgent need for a robust national genomic surveillance system integrated with phenotypic DST to monitor MDR-TB clinical outcomes. This study demonstrates that WGS provides the comprehensive detection, high sensitivity, and rapid turnaround time essential for guiding national TB treatment guidelines and preserving the efficacy of new drug regimens.

Keywords: Bedaquiline, Drug Resistance, Whole Genome Sequencing, *Mycobacterium tuberculosis*, mmpR5 gene

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33. **O-06: Motunrayo Badejo** (Faculty of Medicine and Health Sciences, Stellenbosch University, South Africa)

Superparamagnetic iron oxide nanoparticles perturb mycobacterial homeostasis and unveil gene expression signatures of antimicrobial action

Full author list: Motunrayo Badejo (1), Kudakwashe Nyambo (1), Hleziphi Mpundu (1), Lucinda Baatjies (1), Kudzanai Tapfuma (1), and Vuyo Mavumengwana (1)

(1) South African Medical Research Council Centre for Tuberculosis Research; Division of Molecular Biology and Human Genetics, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town 7505, South Africa.

Transition metals such as iron, copper, and nickel are indispensable for the metabolic functions and survival of *Mycobacterium tuberculosis* (Mtb). However, their dysregulation can exert toxic effects, making metal homeostasis a critical aspect of Mtb physiology. In this study, we examined the antimicrobial activity and transcriptional responses of *Mycobacterium smegmatis* mc²155 to iron-based nanoparticles. Superparamagnetic iron oxide nanoparticles (SPIONs) were synthesized via chemical co-precipitation and functionalized with either monometals (Ag, Cu, Ni), yielding Ag@SPIONs, Cu@SPIONs, and Ni@SPIONs, or bimetals (Ag-Cu, Ag-Ni), yielding Ag-Cu@SPIONs and Ag-Ni@SPIONs. Antimicrobial efficacy was assessed using time-kill kinetics, while transcriptomic profiling was performed through RNA sequencing. The average particle size of the functionalized SPIONs was ~10 nm. Time-kill assays demonstrated that bimetallic SPIONs exhibited superior antimicrobial activity compared with their monometallic counterparts, with minimum inhibitory concentrations (MICs) of 1.95 µg/mL (Ag-Cu@SPIONs) and 3.9 µg/mL (Ag-Ni@SPIONs), versus 3.9 µg/mL, 62.5 µg/mL, and >62.5 µg/mL for Ag@SPIONs, Cu@SPIONs, and Ni@SPIONs, respectively. Transcriptomic analysis of *M. smegmatis* exposed to Ag@SPIONs, Cu@SPIONs, and Ag-Cu@SPIONs revealed significant upregulation of genes involved in sulfur metabolism, ATP-binding cassette (ABC) transporters, redox homeostasis, and cell envelope remodeling, including regulators such as GntR and MraZ. In contrast, genes encoding the DnaK operon and PASTA domain-containing proteins, associated with protein folding and cell wall integrity, were downregulated. These transcriptional changes were accompanied by phenotypic alterations as observed via electron microscopy. Collectively, these findings highlight the enhanced antimicrobial potential of surface-functionalized SPIONs and provide novel insights into the molecular stress responses of mycobacteria to metal-based treatments.

Keywords: metals, *Mycobacterium*, SPIONs, transcriptomics

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34. **O-07: Noppadon Nuntawong** (National Electronics and Computer Technology (NECTEC), National Science and Technology Development Agency, Thailand)

Engineering a robust SERS-based POC system for tuberculosis screening

Full author list: Saksorn Limwichean (1), Ratthasart Amarit (1), Tawee Pogfay (1), Pitak Eiamchai (1), Pacharamon Somboonsaksri (1), Uraiwan Waiwijit (1), Benjawan Kaewseekhao (2), Mati Horprathum (1), Kiatichai Faksri (2) and Noppadon Nuntawong (1)

(1) National Electronics and Computer Technology (NECTEC), National Science and Technology Development Agency (NSTDA), Pathum Thani, Thailand

(2) Research and Diagnostic Center for Emerging Infectious Diseases (RCEID), Khon Kaen University, Khon Kaen, Thailand

Surface-Enhanced Raman Spectroscopy (SERS) has revolutionized molecular diagnostics by amplifying weak Raman signals through plasmonic nanostructures, enabling detection of trace-level biomarkers with exceptional sensitivity and molecular specificity. Unlike conventional diagnostic methods, SERS provides label-free, multiplex analysis of complex biological samples, making it particularly attractive for medical applications. Recent advances in SERS-based biosensors have demonstrated successful detection of various pathogens, cancer biomarkers, and disease-specific molecular signatures. However, translating SERS technology from research laboratories to clinical point-of-care (POC) settings remains a formidable engineering challenge, particularly for tuberculosis diagnosis in resource-limited environments. This presentation examines the engineering perspective on developing robust SERS-based POC systems for latent tuberculosis infection (LTBI) screening, addressing three critical pillars: SERS substrate quality control, portable instrumentation design, and intelligent system integration. First, we tackle batch-to-batch reproducibility in SERS substrates, the primary obstacle to clinical translation. Through systematic optimization of nanofabrication processes and establishment of rigorous quality control metrics, we achieved relatively consistent substrate performance across multiple production batches, ensuring reliable diagnostic outcomes independent of manufacturing variations. Second, we present our custom-designed portable Raman mapping system that overcomes fundamental limitations of commercial single-point spectrometers. Our engineering approach balances optical sensitivity, spectral resolution, laser stability, and portability while incorporating spatial mapping capabilities essential for heterogeneous sample analysis. Comprehensive performance validation against benchtop systems demonstrates that optimized portable instrumentation, when synergistically coupled with SERS enhancement, achieves clinically relevant diagnostic accuracy. Finally, we discuss system-level integration strategies combining hardware optimization with advanced machine learning algorithms to compensate for inherent constraints of portable systems. Our preliminary engineered POC platform demonstrates high diagnostic accuracy for LTBI screening, proving that carefully designed portable SERS systems can deliver performance comparable to laboratory-grade instruments while meeting stringent requirements for deployment in resource-limited, high-TB-burden settings.

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35. **O-08: Saradee Warit** (National Center for Genetic Engineering and Biotechnology (BIOTEC), National Science and Technology Development Agency, Thailand)

Advancing Tuberculosis Diagnosis in Macaques: A One Health Approach

Full author list: Saradee Warit (1), Sarinya Jaitrong (1), Suthirote Meesawat (2), Taratorn Kemthong (3), Mutchamon Kaewparuehaschai (4), Kirana Noradechanon (4), Therdsak Prammananan (1), Reka Kanitpun (5), Prapaporn Srilohasin (6), Tanapat Palaga (7), Angkana Chaiprasert (8), and Suchinda Malaivijitnond (2, 9)

(1) Industrial Tuberculosis Team, Industrial Medical Molecular Biotechnology Research Group, National Center for Genetic Engineering and Biotechnology, National Science and Technology Development Agency, Thailand
(2) Department of Biology, Faculty of Science, Chulalongkorn University, Thailand
(3) Biological Sciences Program, Faculty of Science, Chulalongkorn University, Bangkok,
(4) Thailand Wildlife Conservation Office, Department of National Parks Wildlife and Plant Conservation, Thailand
(5) National Institute of Animal Health (NIAH), Kaset Klang, Thailand
(6) Department of Microbiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand
(7) Department of Microbiology, Faculty of Science, Chulalongkorn University, Thailand
(8) Office for Research, Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand
(9) National Primate Research Center of Thailand, Chulalongkorn University, Thailand

Background: Tuberculosis (TB), primarily caused by *Mycobacterium tuberculosis* (Mtb), is a chronic airborne disease that affects humans and non-human primates. Recent interactions between humans and long-tailed macaques (*Macaca fascicularis*) in Southeast Asia, including Thailand, raise concerns about zoonotic and reverse zoonotic transmission of mycobacterial agents between these two species. The challenges of diagnosing Mtb infection and determining the stages of TB disease in macaques stem from the lack of specific methods developed for this species. This study explored the pathogenesis and infection dynamics of TB in a cohort of naturally Mtb-infected long-tailed macaques in Chachoengsao Province, central Thailand. Various methods for cell-mediated immunity and humoral immunity responses, as well as methods for detecting Mtb antigens, were also developed concurrently.

Results: Over a six-year longitudinal study, we developed and validated several diagnostic tools for TB in macaques, integrating traditional gold-standard methods such as culture and tuberculin skin test with advanced molecular and immunological techniques. These included the monkey interferon-gamma releasing assay (mIGRA) (Warit et al., 2020; 2024), GeneXpert-ultra (Srilohasin et al., 2024), IS6110-nested PCR (Meesawat et al., 2023a, 2023b), enzyme-linked immunosorbent assay (ELISA), multiple antigens printed immunoassay (MAPIA), and chest radiography (Kemthong et al., 2025). Our study confirmed that a single diagnostic tool cannot determine whether the animal is Mtb-infected or the stage of infection, and an algorithm is necessary for interpreting TB in long-tailed macaques. The spectrum of TB disease spanned from non-TB, incipient, latent, subclinical, to active TB infection.

Conclusion: Effective identification of TB infection in long-tailed macaques necessitates the application of multiple diagnostic tools, as no single method is sufficient due to the complexity of pathogen-host interactions. This multifaceted approach enhances our understanding of TB dynamics in both human and non-human primate contexts, underscoring the importance of integrated diagnostic strategies in managing zoonotic diseases within One Health programs.

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36. **O-09: Narisa Mohthong** (Department of Biomedical Sciences and Biomedical Engineering, Faculty of Medicine, Prince of Songkla University, Thailand)

Investigating immune profiles in healthy and latent tuberculosis-infected participants

Full author list: Narisa Mohthong (1), Ratchanon Sophonmanee (1), Jomkwan Ongarj (1), Yasumin Kerdsri (5,6,7,8), Sarintip Nguantad (5,6,7,8), Damita Jevapatarakul (3), Narita Thungsatianpun (3), Sahasawat Suksan (1), Pyae Sone Oo (1), Natapohn Saowaphong (1), Supattra Uppanisakorn (2), Ponpan Matangkasombut (3,4), Varodom Charoensawan (5,6,7,8,9,10) and Nawamin Pinpathomrat (1)

(1) Department of Biomedical Sciences and Biomedical Engineering, Faculty of Medicine, Prince of Songkla University, Songkhla, 90110, Thailand,
(2) Clinical Research Center, Faculty of Medicine, Prince of Songkla University, Songkhla, 90110, Thailand
(3) Department of Microbiology, Faculty of Science, Mahidol University, Bangkok, 10400, Thailand
(4) Single-cell Omics and Systems Biology of Diseases Research Unit, Faculty of Science, Mahidol University, Bangkok, 10400, Thailand
(5) Division of Medical Bioinformatics, Research Department, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, 10700, Thailand
(6) Department of Biochemistry, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, 10700, Thailand
(7) Siriraj Genomics, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, 10700, Thailand
(8) Integrative Computational BioScience (ICBS) Center, Mahidol University, Nakhon Pathom, 73170, Thailand
(9) Department of Biochemistry, Faculty of Science, Mahidol University, Bangkok 10400, Thailand.
(10) School of Chemistry, Institute of Science, Suranaree University of Technology, Nakhon, Ratchasima 30000, Thailand.

Introduction: Latent tuberculosis infection (LTBI) is associated with a persistent immune response to stimulation by *Mycobacterium tuberculosis* antigen without signs of active TB. This condition can develop into active TB (in approximately 5–10% of LTBI cases) depending on the host-bacterial interactions. Challenges remain in disease control due to the unclear immune correlate of protection in LTBI, the difficulty of detecting LTBI status or TB progression in LTBI patients, and the inefficiency of vaccination in providing long-term protection.

Method: The participants had blood collected before the isolation of peripheral blood mononuclear cells (PBMCs). We used flow cytometry to analyze cellular immune responses by staining surface markers and measuring cytokine production after PPD stimulation (11 healthy and 11 LTBI subjects). Single-cell RNA sequencing (scRNA-seq) was then introduced to evaluate gene expression at the cellular level between two conditions (a total of 6 healthy and 6 LTBI individuals).

Result: The flow cytometry analysis observed differences in antigen-specific cytokine production from CD4+ T cells such as IFN-g, IL-2 and IL-17. There was a trend toward an increase in LTBI compared to healthy subjects. For scRNA-seq analysis, we identified subpopulations within PBMCs and observed the differences in overall expression profiles between conditions.

Conclusion: The findings from this study demonstrated that healthy and LTBI subjects have differences in their immune profiles in both stimulated and unstimulated PBMCs. Furthermore, scRNA-seq highlights its impact on tuberculosis research, as it reveals cellular heterogeneity and distinct gene expression patterns between the conditions. Using scRNA-seq to investigate the immune response in LTBI subjects may reveal their immune correlates of protection and serve as a potential target for future vaccine development.

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37. **O-10: Yoopie Setiawan** (Department of Biomedical Sciences, Faculty of Medicine, Universitas Katolik Parahyangan, Indonesia)

The interferon-gamma response to Latin American Mediterranean and Modern Beijing sub-lineages of *Mycobacterium tuberculosis* in drug-sensitive and resistant tuberculosis

Full author list: Yoopie Setiawan (1,2), Agnes Rengga Indrati (3), Ramdan Panigoro (4) and Lidya Chaidir (4,5)

(1) Department of Biomedical Sciences, Faculty of Medicine, Universitas Katolik Parahyangan, Bandung, West Java, Indonesia
(2) Doctoral Program in Medical Sciences, Faculty of Medicine, Universitas Padjadjaran, Bandung, West Java, Indonesia
(3) Department of Clinical Pathology, Faculty of Medicine, Universitas Padjadjaran, Bandung, West Java, Indonesia
(4) Department of Biomedical Sciences, Faculty of Medicine, Universitas Padjadjaran, Sumedang, West Java, Indonesia
(5) Center for Translational Biomarker Research, Universitas Padjadjaran, Bandung, West Java, Indonesia

Tuberculosis (TB) remains a major global health challenge caused by *Mycobacterium tuberculosis* (Mtb), a pathogen exhibiting diverse clinical manifestations and variable outcomes influenced by complex host–pathogen interactions. Among these, differences in Mtb lineages have been shown to affect immune responses. Certain lineages may have evolved specific adaptations to host immune profiles within particular geographic regions. In Indonesia, the two predominant Mtb lineages are Lineage 4 (Euro-American, L4) and Lineage 2 (East-Asian, L2). This study aimed to evaluate differences in interferon-gamma (IFN-γ) responses produced by peripheral blood mononuclear cells (PBMCs) from healthy individuals following stimulation with lysates of Mtb L4 sub-lineage Latin American-Mediterranean (LAM) and L2 sub-lineage Modern Beijing, each in drug-sensitive (DS) and isoniazid-monoresistant (Hr-TB DR) phenotypes. PBMCs were stimulated for 48 hours, and IFN-γ levels were quantified using an enzyme-linked immunosorbent assay (ELISA). Stimulation with the Modern Beijing sub-lineage elicited significantly lower IFN-γ levels (mean 15.30 pg/mL) compared with the LAM sub-lineage (mean 19.16 pg/mL). Stratified analysis by drug-susceptibility status showed that both DS and Hr-TB DR Modern Beijing isolates consistently induced lower IFN-γ responses than their LAM counterparts. Within LAM, the Hr-TB DR group (mean 17.74 pg/mL) elicited lower IFN-γ responses than the DS group (mean 20.59 pg/mL), though this difference was not statistically significant. In contrast, within Modern Beijing, IFN-γ levels induced by the Hr-TB DR group (mean 13.14 pg/mL) were significantly lower than those caused by the DS group (mean 17.45 pg/mL). These findings indicate that both Mtb lineage and drug-resistance status influence host immune responses, underscoring the importance of considering lineage-specific immune interactions in the development of vaccines and host-directed therapies.

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38. **O-11: Pyae Sone Oo** (Department of biomedical sciences and biomedical engineering, Faculty of medicine, Prince of Songkla university Thailand)

Differential immune responses to novel and established *Mycobacterium tuberculosis* antigens among tuberculosis patients in Southern Thailand

Full author list: Pyae Sone Oo (1), Ratchanon Sophonmanee (1), Narisa Mohthong (1), Sahasawat Suksan (1), Natapohn Saowaphong (1), and Nawamin Pinpathomrat (1)

(1) Department of biomedical sciences and biomedical engineering, Faculty of medicine, Prince of Songkla university Thailand

Background and rationale: Tuberculosis (TB) is a disease which is inflexible to eradicate. The current vaccine Bacillus Calmette-Guérin (BCG) offers limited protection, particularly against pulmonary TB in adults, necessitating a deeper understanding of immune responses to improve diagnostic and therapeutic strategies.

Aim: To assess antigen-specific T-cell responses to PPD, IrtA, PE9, and PPE68 across BCG-vaccinated, LTBI, and ATB groups using ELISpot and flow cytometry.

Method: Peripheral blood mononuclear cells (PBMCs) were collected from HC (n=20), LTBI (n=20), and ATB (n=20) groups and analyzed using flow cytometry and ELISpot assays after stimulation with PPD, IrtA, PPE-68 and PE-9. Cytokine productions were quantified, compared and correlated.

Results: In the ELISpot assay, PPD elicited the highest IFN-γ responses across all groups, compared to IrtA, PE9, and PPE68 ($p < 0.0001$) followed by PPE68.The frequencies of CD4+ and CD8+ T cells cytokine responses, memory subsets' cytokines responses, were heterogeneous among the groups in the flow cytometry assay. A strong positive correlation was observed between ELISpot and flow cytometry PPD-stimulated IFN-γ+ CD4+ T cells and CD4+ TCM in both HC and LTBI groups.

Conclusion: The strong correlation between PPD-stimulated IFN-γ responses measured by ELISpot and flow cytometry, especially in $CD4^+$ T cells and central memory subsets, supports using these assays together for immunodiagnostic evaluation.

Implication: The strong correlation between PPD-stimulated IFN-γ responses measured by ELISpot and flow cytometry, particularly within $CD4^+$ T cells and central memory subsets, supports the complementary use of these assays for immunodiagnostic evaluation.

Keywords: immune responses, *Myobacterium tuberculosis*, cytokines, flow cytometry, ELISpot

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39. O-12: Tania Jim (Department of Chemistry, National University of Singapore, Singapore)
The use of a novel conjugated oligoelectrolyte molecule to potentiate antibiotic efficacy against Non-Tuberculous Mycobacteria

Full author list: Tania Jim (1,2), Aniket Kulkarni (3), Jakkarin Limwongyut (4), Alex Moreland (5), Kaixi Zhang (6)*, Kevin Pethe (2,7)* and Guillermo Bazan (1,2,5,8)*

(1) Department of Chemistry, National University of Singapore, Singapore
(2) Singapore Centre for Environmental Life Sciences Engineering, Singapore
(3) Department of Chemistry, National University of Singapore, Singapore
(4) Suranaree University of Technology, Nakhon Ratchasima, Thailand
(5) Xiretsa Incorporated, California, United States of America
(6) Antimicrobial Resistance Interdisciplinary Research Group, Singapore-MIT Alliance for Research and Technology Center, Singapore
(7) Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore
(8) Institute for Digital Molecular Analytics and Science, Nanyang Technological University, Singapore

Antimicrobial resistance (AMR) is a critical global threat that undermines the foundation of modern medicine. As conventional antibiotics lose efficacy, infections become harder to manage, leading to procedural complications and the rise of multi-drug resistant pathogens. The development of novel antimicrobial agents is paramount. *Mycobacterium abscessus* (MAB) is amongst one of the most drug-resistant non-tuberculous mycobacteria. Its multifaceted intrinsic resistance mechanisms to many antibiotics and the need for prolonged drug regimens complicate treatment, underscoring the need for more effective therapeutic strategies.

Conjugated oligoelectrolytes (COEs) are a promising class of antimicrobial candidates, featuring a rigid conjugated backbone with cationic pendant groups. They are hypothesised to disrupt membrane integrity by intercalating into the lipid bilayer. Given that combination therapy is a treatment option to enhance efficacy, limit resistance development, and broaden antimicrobial coverage, this study examines the potential of COEs as an adjuvant with commercial antibiotics. Understanding the interactions of COES can also shed light on individual and complementary mechanisms.

Using MAB ATCC 19977 as a reference strain, synergy screening was performed with the checkerboard assay and kill kinetics studies were conducted with selected drug combinations. Minimal inhibitory concentration (MIC) assay was performed using the broth dilution method.

The results demonstrate that COEs display strong synergy with commercial antibiotics against MAB. Kill kinetics studies revealed that combining COE-1b with a macrolide gives rise to strong synergistic and bactericidal effects, which is of relevance given the inducible macrolide resistance in MAB as well as the bacteriostatic nature of macrolides.

COEs can be strategically combined with an antibiotic in-vitro to optimise antibacterial activities against MAB. The implications of this research are far-reaching. Further work in this project will entail the use of a molecular approach to elucidate the mechanism(s) of synergy.

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40. **O-13: Kishan Kumar Parida** (National Institute of Pharmaceutical Education and Research (NIPER), India)

Structure Based Identification and Validation of Benzothiazole Derivatives as Potent Dpre1 Inhibitors Against *Mycobacterium tuberculosis*

Full author list: Kishan Kumar Parida (1), Rabiya Samoon (2), Syed Shafi (2) and Nitin Pal Kalia (1)
(1) Department of Biological Sciences (Pharmacology and Toxicology), National Institute of Pharmaceutical Education and Research (NIPER), Hyderabad, Telangana 500037, India
(2) Department of Chemistry, School of Chemical and Life Science, Jamia Hamdard, New Delhi 110062, India

Decaprenylphosphorl-β-D-ribose 2'-epimerase (DprE1) has emerged as a compelling target for anti-tuberculosis drug development due to its essential role in the biosynthesis of the *Mycobacterium tuberculosis* (Mtb) cell wall. In this study structure based virtual screening was performed using the crystal structure of DprE1 (PDB ID: 4KW5) to identify novel inhibitors through rational drug design benzothiazole based derivatives were sourced from ZINC 15 and ChemSpider databases and evaluated using molecular modelling techniques including docking score binding energy fitness score and ADME profiling. Two benzothiazole analogues demonstrated strong non covalent interaction at DPR 1 active sites, with talking score of -7.164 and -6.168 respectively. These compounds exhibited potent in vitro activity against Mtb with minimum inhibitory concentrations (MIC) of 1µg/ml and 45 µg/ml. Further derivatization of a bis- benzothiazole scaffold yielded analogue with enhanced efficacy against drug resistant Mtb strains improved safety profiles and time and dose dependent bactericidal activity. Target validation of the optimized lead compound was achieved through the generation of one-step resistant mutants, revealing cross-resistance with TCA-1 and a single nucleotide polymorphism (SNP) resulting in a tyr314His substitution in DprE1. Mechanistic insights were supported by molecular docking, GFP-release fluorescence assay, and luminescence-based pini-luc assays. These findings underscore the therapeutic potential of benzothiazole-based DprE1 inhibitors and provide a robust framework for the development of next-generation anti-TB agents targeting cell wall biosynthesis.

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41. O-14: **Hleziphi Violah Mpundu** (Division of Molecular Biology and Human Genetics, Faculty of Medicine and Health Sciences, Stellenbosch University)

Targeting Drug-Tolerant Tuberculosis Through Repurposing of Approved Drugs

Full author list: Mpundu HV, Julius L, Nyambo K, Tapfuma K, Badejo MV, Kinnear C, Mavumengwana V, and Baatjies L.

DSI-NRF Centre of Excellence for Biomedical Tuberculosis Research; South African Medical Research Council Centre for Tuberculosis Research; Division of Molecular Biology and Human Genetics, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town. Correspondence should be addressed to H.V. Mpundu (hlezipihm@sun.ac.za).

Introduction: *Mycobacterium tuberculosis* (Mtb) causes over 10.6 million cases and 1.6 million deaths annually. Its persistence through immune evasion and drug tolerance complicates treatment, which is lengthy, toxic, and increasingly compromised by resistance. Repurposing FDA-approved drugs with antimycobacterial and host-directed immunomodulatory properties offers a promising, cost-effective strategy to improve TB therapy and antimicrobial stewardship.

Objectives: To evaluate the antimycobacterial activity, synergy, and host-directed effects of selected repurposed drugs against Mtb to support novel combination therapies.

Methods: MICs of 29 repurposed drugs were determined against Mtb H37Rv via broth microdilution in a BSL-3 lab. Synergy was assessed by checkerboard assays, with bactericidal effects evaluated by time-kill kinetics. Transcriptomic profiling of treatments was performed using RNA sequencing and bioinformatic analysis (STAR, DESeq2), with RT-qPCR validation.

Results: Eighteen compounds showed activity, including miconazole (MIC 0.98 µg/mL), sulfameter, and 4-(Trifluoromethyl)phenylboronic acid. Synergistic drug pairs maintained bacteriostatic effects for up to 18 days at reduced doses, demonstrating potential for enhanced TB treatment.

Conclusion: Repurposed drug combinations offer a promising, accelerated route to effective TB therapies, aligning with global infection control goals and addressing resistance in high-burden, resource-limited settings.

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42. **O-15: Arnab Roy** (National Institute of Pharmaceutical Education and Research (NIPER), India)

Overcoming metabolic redundancy in *Mycobacterium tuberculosis* via dual inhibition of terminal oxidases

Full author list: Arnab Roy (1) and Nitin Pal Kalia (2)

(1) Department of Biological Sciences (Pharmacology and Toxicology), National Institute of Pharmaceutical Education and Research (NIPER), Hyderabad. Telangana.500037. India.
(2) Department of Biological Sciences (Pharmacology and Toxicology), National Institute of Pharmaceutical Education and Research (NIPER), Hyderabad. Telangana.500037. India.

The functional redundancy between the cytochrome bc_1:aa_3 and cytochrome bd oxidase (Cyt-bd) allows *Mycobacterium tuberculosis* (Mtb) to evade killing by the cytochrome bc_1:aa_3 inhibitor, Telacebec (Q203), a promising clinical candidate. This highlights the critical need for inhibitors targeting the Cyt-bd to disrupt this protective mechanism and achieve potent bactericidal activity. To address this, a whole-cell phenotypic screen was employed, leading to the identification of BD-2, a small-molecule inhibitor targeting the Cyt-bd. When assessed individually, BD-2 exhibited limited bactericidal activity; however, its combination with Q203 yielded a profoundly synergistic effect. This dual inhibition strategy potently suppressed cellular respiration and catastrophically depleted intracellular ATP levels, effectively dismantling the bacterium's core bioenergetic pathways. The resulting metabolic disruption translated into potent, synergistic bactericidal activity that was effective against both replicating and non-replicating Mtb populations, which are often associated with chronic infection and antibiotic tolerance. Furthermore, this combination therapy demonstrated significantly enhanced efficacy in a THP-1 macrophage infection model, showing improved clearance of intracellular Mtb compared to Q203 monotherapy. In conclusion, the simultaneous pharmacological targeting of both terminal oxidases with BD-2 and Q203 successfully overcomes inherent metabolic flexibility and redundancy of Mtb. By completely blocking oxidative phosphorylation, this dual-targeting strategy induces a bactericidal state that is effective against heterogeneous populations of mycobacteria, thereby presenting a highly promising and robust therapeutic approach for tuberculosis that could potentially shorten treatment duration and combat persistent infections.

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43. **P-01: Xiaoming Liu** (Beijing Chest Hospital, Capital Medical University; Beijing Tuberculosis and Thoracic Tumor Research Institute, China)

Global burden of childhood tuberculosis (1990–2021): a systematic analysis from the Global Burden of Disease Study 2021

Full author list: Xiaoming Liu1,2, Hui Jiang1,2*, Weimin Li1,2†

1. Beijing Chest Hospital, Capital Medical University, Beijing, 101149, China.
2. Beijing Tuberculosis and Thoracic Tumor Research Institute, Beijing, 101149, China.

* Contributed equally to this work.

†Corresponding authors on this study.Weimin Li: 1711362459@qq.com

Childhood tuberculosis (TB) remains a substantial global health challenge. However, comprehensive studies examining childhood TB burden, trends, and risk factors across three distinct age groups at global, regional, and national levels remain scarce.

Methods: Data on childhood TB incidence and mortality from 1990 to 2021 were extracted from the Global Burden of Disease (GBD) 2021 database. This study analysed three age groups (<5 years, 5–9 years, and 10–14 years), with regions categorised using the Socio-demographic Index (SDI). Multiple statistical approaches were employed, including estimated annual percentage change (EAPC), Joinpoint regression, age-period-cohort (APC) models, and Bayesian APC (BAPC) models, to analyse trends and project future burden. Health inequality and decomposition analyses were conducted to explore the contributions of socioeconomic factors and demographic changes to the TB burden.

Findings: In 2021, an estimated 759,300 incident cases and 70,659 deaths from childhood TB occurred globally. The global age-standardised incidence rate (ASIR) was 38·1 per 100,000 population, and the age-standardised mortality rate (ASMR) was 3·7 per 100,000 population. Since 1990, childhood TB incidence and mortality rates have declined annually by 2·61% and 4·48%, respectively. The SDI showed a negative correlation with childhood TB incidence and mortality. Sub-Saharan Africa accounted for more than 80% of global childhood TB deaths. In 2021, children aged 0–5 years represented 78·01% of TB mortality. Projections to 2045 indicate continued declines in both incidence and mortality; however, achieving the goal of eliminating childhood TB by 2035 remains challenging.

Conclusion: Improvements in diagnostic and treatment technologies have driven global reductions in childhood TB incidence and mortality, yet substantial disparities persist across regions. Global investment in low-income countries is essential to reduce TB mortality among children aged 0–5 years. Active case-finding and preventive treatment strategies should be implemented to interrupt transmission and reduce incidence.

Keywords: Childhood tuberculosis, incidence, mortality, Socio-demographic Index, disease burden

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44. **P-02: Zaidah Abdul Rahman** (School of Medical Sciences, Universiti Sains Malaysia, Malaysia)

Latent tuberculosis infections (LTBI) among healthcare workers & laboratory staff: is screening mandatory?

Full author list: Zaidah Abdul Rahman[1], Mohd Jazman Che Rahim[1], Mohamad Zikir Ismail[1], Nik Zuraina Nik Mohd Noor[1], Nurul Husna Hashim[1], Nor Suhana Mohd Satar[2], Mohd Zuhaili Norhashim[2], Ayub Mohamad[2] and Zulhurairah Fikriah Abu Bakar[2]

[1]School of Medical Sciences, Universiti Sains Malaysia, Health Campus, 16150, Kubang Kerian, Kelantan, MALAYSIA.

[2]Medical Microbiology & Parasitology Department, School of Medical Sciences, Universiti Sains Malaysia, Health Campus, 16150, Kubang Kerian, Kelantan, MALAYSIA.

Background: Healthcare workers (HCWs) and microbiology laboratory personnel (MLP) are at increased risk of latent tuberculosis infection (LTBI) due to occupational exposure. Timely identification and management of LTBI are crucial components of tuberculosis (TB) control in healthcare settings. This study aimed to determine the prevalence of LTBI among HCWs and MLPs using the Interferon-Gamma Release Assay (IGRA).

Methods: A cross-sectional screening was conducted among HCWs and MLPs at a hospital on the East Coast of Malaysia using the QuantiFERON-TB Gold IGRA test. HCWs were selected based on a history of contact with patients diagnosed with active TB. Demographic data were collected, and individuals with positive IGRA results were further evaluated for symptoms of active TB and history of TB exposure.

Results: Of the 198 individuals screened, 80 were HCWs and 18 were MLPs. LTBI was detected in 12 participants (6.1%), including 10 HCWs and 2 MLPs. No cases of active TB were identified among those with positive results. The majority of LTBI-positive individuals were female (n=10). Of those diagnosed, 9 received treatment, and none developed active TB during the follow-up period.

Conclusion: The 6.1% prevalence of LTBI among HCWs and MLP highlights the possibility of ongoing occupational risk of TB infection in healthcare settings. Routine IGRA-based screening can support early detection and preventive treatment, contributing to TB control efforts among HCWs. Continued surveillance and targeted interventions are recommended to minimize occupational TB transmission.

Keywords: Latent tuberculosis infection, healthcare workers, IGRA, TB screening, occupational health

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45. **P-03: Lapasrada Pattarapreeyakul** (Medical Life Sciences Institute, Department of Medical Sciences, MOPH, Thailand)

Geographical Distribution and Characteristics of Cutaneous Non-tuberculous Mycobacterial Infections in Thailand from 2015 to 2024

Full author list: Lapasrada Pattarapreeyakul (1), Sunisa Kanchanasutthiyakorn (1), Pichanee Watthanasiri (1), Kan Khemnak (2), Sarrote Boonkerd (2), Panadda Dhepakson (1) and Surakameth Mahasirimongkol (3)

(1) Medical Life Sciences Institute, Department of Medical Sciences, Ministry of Public Health, Thailand

(2) Information and Communication Technology Center, Office of the permanent secretary, Ministry of Public Health, Thailand

(3) Technical and Planning Division, Department of Thai Traditional and Alternative Medicine, Ministry of Public Health, Thailand

Non-tuberculous mycobacteria (NTM) are an increasingly recognised global public health concern with prevalence associated with environmental exposure. Extrapulmonary manifestations, notably cutaneous NTM infections, remain an area that requires further investigation. This retrospective study aimed to determine the geographical distribution and characteristics of confirmed cutaneous NTM infections in Thailand over a ten-year period (January 2015– December 2024). Data were retrieved from the national health database using ICD-10 diagnostic codes for outpatient visits, identifying 1,137 cases of cutaneous NTM infection (A31.1) from 297 hospitals. The mean patient age was 46.3 years, with a slight female predominance (54.44%). Eighteen percent of cases were reported among individuals in occupations involving environmental exposure, particularly agriculture and livestock. Geographically, the Central and Northeastern regions accounted for the largest proportions of patients (31.75% and 27.97%, respectively). Clinical information indicated highly variable incubation periods, ranging from a few days to several years. Among patients with available comorbidity records, the most frequent conditions were tuberculosis, hypertension, and diabetes. Overall, this study highlights that cutaneous NTM infections in Thailand indicate distinct geographical clustering, associations with environmental occupations, and variable incubation periods. These findings underscore the importance of strengthening clinical and public health awareness, enhancing the completeness of health record systems, and supporting future policy planning and targeted prevention strategies.

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46. **P-04: Mahfuza Talukder Flowra** (Oslo Metropolitan University, Oslo, Norway)

Barriers of multi-drug-resistant Tuberculosis (MDR- TB) detection from the community perspective in Bangladesh: A mixed method Study

Full author list: Mahfuza Talukder Flowra (1,2), Muhammad Asaduzzaman (3)
(1) Oslo Metropolitan University, Oslo, Norway
(2) Gadjah Mada University, Yogyakarta, Indonesia
(3) University of Oslo, Oslo, Norway

Multi-drug-resistant Tuberculosis (MDR-TB) is becoming a significant global health issue, particularly for developing countries due to delays in diagnosis and reporting of cases. We, therefore, aimed to understand community perceptions about the challenges and obstacles that hinder the timely detection of MDR-TB under the National Tuberculosis Control Program (NTP) of Bangladesh. We conducted a mixed-method study in both urban and rural areas of the Mymensingh division. For the quantitative component, we distributed semi-structured questionnaires to total 61 MDR-TB patients, 23 from households and 38 from two hospitals. For qualitative insights, we conducted focus group discussion (n=1), in-depth interviews (n=12) and key informant interviews (n=3), including community members, caregivers, and service providers. This helped us to explore the community perceptions of the barriers as well as the knowledge, attitudes, practices, and healthcare-seeking behaviors of patients. Our findings indicated a significant lack of awareness about MDR-TB among community members. Many patients reported inadequate knowledge of the disease until they were diagnosed. Majority of patients both in hospitals (73.9%) and community (85.7%) documented lack of information about the services of NTP before their disease detection which indicates a gap in public awareness strategies. The major barriers to timely MDR-TB detection in NTP included insufficient information about the program among the community, poor publicity of this specific issue, lack of essential diagnostic tools like the Gene Xpert machine at sub-district levels, and insufficient personnel and funding, and lack of motivation for the community level health care service providers without risk incentives. However, social stigma and job insecurity seem to be major restricting factors to seek timely healthcare service. To ensure community perception and optimum functioning, our study emphasizes the need for a comprehensive approach to improve MDR-TB detection in Bangladesh, advocating for community engagement, addressing stigma, providing economic support, and incentivizing healthcare workers.

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47. **P-05: Ayush Bhutada** (Indira Gandhi Government Medical College Nagpur, India)

Open Negative Syndrome in Tuberculosis: A Rare Diagnostic Dilemma Post-Treatment

Full author list: Ayush Bhutada, Gyanshankar Mishra and Radha Munje
Indira Gandhi Government Medical College Nagpur, India

Background and Rationale: Open Negative Syndrome (ONS) in tuberculosis refers to the persistence of a lung cavity on radiological imaging despite successful microbiological clearance of *Mycobacterium tuberculosis* (MTB). Although the patient is non-infectious, the retained cavity mimics active disease, creating diagnostic confusion, especially in high TB-burden regions. Due to its rarity and resemblance to relapse or secondary infections, ONS remains an under-recognized clinical entity.

Aim: To describe a case of Open Negative Syndrome following completion of anti-tubercular therapy and highlight the diagnostic complexity associated with this condition.

Brief Methodology: A detailed clinical evaluation, serial sputum analyses, gene-based testing, and radiological imaging were reviewed for a 23-year-old female diagnosed with pulmonary TB. Baseline and follow-up clinical, microbiological, and imaging findings were compared over a one-year treatment period and subsequent follow-up.

Main Findings: The patient initially presented with fever, cough, weight loss, and an X-ray showing a cavitary lesion with an air-fluid level. Sputum smear and CBNAAT confirmed MTB positivity. Following one year of anti-tubercular therapy, the patient demonstrated complete clinical recovery, including weight gain and symptom resolution. Repeat sputum smear and CBNAAT were negative, confirming microbiological cure. However, follow-up imaging continued to show a persistent cavity without air-fluid level or any radiological signs of active infection. These findings fulfilled diagnostic criteria for ONS- initial cavitary TB, sustained sputum negativity for at least six months, and persistent cavity one year post-treatment.

Conclusion: Open Negative Syndrome represents a rare but significant post-treatment radiological paradox in TB. Despite microbiological cure, the persistent cavity may falsely suggest ongoing disease.

Implication: Recognizing ONS is crucial to prevent misdiagnosis, unnecessary re-treatment, and patient anxiety. Greater clinician awareness can improve decision-making and avoid overtreatment in high TB-burden settings.

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48. **P-06: Ayush Bhutada** (Indira Gandhi Government Medical College Nagpur, India)

Unveiling Gender and BMI influences on outcome of hospitalization in TB cases: Insights from a Central India hospital study

Full author list: Ayush Bhutada, Radha Munje and Gyanshankar Mishra
Indira Gandhi Government Medical College Nagpur, India

Background and Rationale: Gender differences and nutritional status profoundly influence tuberculosis (TB) outcomes, yet their combined effect in hospitalized patients remains inadequately understood. Undernutrition is a well-recognized risk factor for poor TB prognosis, but evidence on how varying BMI categories and gender modify hospitalization outcomes is scarce in high-burden regions such as Central India. Understanding these interactions is essential for risk stratification and optimizing inpatient management.

Aim: To assess gender-wise hospitalization outcomes among TB patients and evaluate the impact of BMI and CBNAAT semi-quantitative bacterial load on clinical outcomes in a tertiary care hospital in Central India.

Brief Methodology: A retrospective analysis was conducted on TB patients admitted to the Department of Respiratory Medicine at Indira Gandhi Government Medical College (IGGMC), Nagpur. Outcomes were classified as: Discharged after improvement / cure
Discharge Against Medical Advice (DAMA) Death Patients were stratified by gender and categorized BMI (BMI <15, 15–20, 20–25, >25). CBNAAT semi-quantitative categories (Very Low, Low, Medium, High) were documented. Associations between gender, BMI, bacterial load, and outcomes were assessed using the chi-square test.

Main Findings: A total of 210 patients (142 males, 68 females) with complete BMI data were analyzed. Severe undernutrition (BMI <15) showed a strong association with adverse outcomes. Mortality reached 38.3% in undernourished males and 26.1% in females, while DAMA occurred in 29.8% and 43.5%, respectively. Compared with normal BMI (20–25), undernourished females exhibited nearly 2.5-fold higher odds of DAMA and 2-fold increased mortality. Outcomes improved progressively with increasing BMI, indicating a dose–response relationship. BMI was significantly associated with outcomes in females ($\chi^2 = 18.90$, $p = 0.004$), with borderline significance in males ($\chi^2 = 11.73$, $p = 0.068$). CBNAAT bacterial load showed no significant association with outcomes ($\chi^2 = 6.72$, $p = 0.347$).

Conclusion: Gender and nutritional status significantly influence hospitalization outcomes in TB patients. Severe undernutrition, especially in females, markedly increased mortality and DAMA rates, whereas higher BMI correlated with improved outcomes.

Implication: Routine nutritional assessment and gender-sensitive risk stratification should be prioritized in TB inpatient care. CBNAAT bacterial load offers limited prognostic utility, underscoring the need to integrate nutritional metrics into clinical decision-making.

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49. **P-07: Rashmi Ratnam** (Microbiology, King George's Medical University, Lucknow, India)

Influence of Diabetes and Socioeconomic Variables on Treatment Response in Pulmonary Tuberculosis Patients

Full author list: Rashmi Ratnam[1], Parul Jain[1], Mehul Saxena[1], Amita Jain[1], R A S Kushwaha[2], Varun Pratap Singh[2]

[1]Microbiology, King George's Medical University, Lucknow, India

[2]Respiratory Medicine, King George's Medical University, Lucknow, India

Background: India faces a dual burden of tuberculosis (TB) and diabetes mellitus (DM), both compromising immune function and complicating TB treatment. Delayed sputum culture conversion prolongs infectiousness and increases the risk of poor outcomes. This study assessed the impact of diabetes and socioeconomic factors on sputum culture conversion among pulmonary TB patients in North India.

Methods: We conducted a retrospective cohort study including 100 bacteriologically confirmed pulmonary TB patients treated at a tertiary center. Fifty patients had diabetes, and 50 did not. Demographic, clinical, and behavioral data were collected from laboratory records, the Ni-kshay portal, and telephonic interviews. Kaplan-Meier survival analysis and Cox regression were performed to identify factors influencing sputum culture conversion time.

Results: Diabetic TB patients were significantly older and more likely to have drug-sensitive TB than non-diabetics. Mean culture conversion time was longer in diabetics (27.1 weeks) versus non-diabetics (23.7 weeks). In drug-sensitive TB, diabetes was significantly associated with delayed conversion (HR=0.325, p=0.03), while no significant effect was observed in drug-resistant TB (HR=1.46, p=0.68). Multivariable analysis identified diabetes (HR=0.66, p=0.001), older age, low socioeconomic status, smoking, and alcohol use as significant predictors of delayed conversion, while urban residence favored faster conversion.

Conclusion: Diabetes significantly delays sputum culture conversion in drug-sensitive TB, underscoring the need for integrated TB-diabetes care. Socioeconomic disadvantages and behavioral risk factors further prolong infectiousness. Strategies addressing these determinants are essential for optimizing TB control efforts in India.

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50. **P-08: Rashmi Ratnam** (Microbiology, King George's Medical University, Lucknow, India)

Emerging Phenotypic Resistance to Delamanid and Pretomanid in MDR-TB: Co-resistance Patterns from a North Indian Reference Laboratory

Full author list: Rashmi Ratnam[2] , Parul Jain[1] , R A S Kushwaha[2] , Varun Pratap Singh[2] , Amita Jain[1] , Urmila Singh[1]

[1]Microbiology, King George's Medical University, Lucknow, India

[2]Respiratory Medicine, King George's Medical University, Lucknow, India

Introduction: The increasing use of delamanid (DLM) and pretomanid (Pa) in multidrug-resistant tuberculosis (MDR-TB) regimens necessitates early detection of baseline resistance. However, phenotypic resistance to these nitroimidazoles remains under-characterized in India.

Methods: 70 MDR-TB isolates (55 treatment-naïve; 15 follow-up, culture-positive ≥4 months after treatment initiation) were tested at the Intermediate Reference Laboratory for TB testing, King George's Medical University, Lucknow, India. Drug susceptibility testing (DST) was conducted on the BACTEC MGIT 960 system using WHO-recommended critical concentrations: DLM 0.06 µg/mL; Pa 0.5 µg/mL (low-level) and 2 µg/mL (high-level). Resistance proportions were calculated with 95% Wilson confidence intervals (CI). Group comparisons were performed using Fisher's exact test; odds ratios (OR) were calculated for co-resistance patterns.

Results: No DLM resistance was detected in treatment-naïve isolates (0/55), while DLM resistance occurred in 2/15 (13.3%, 95% CI: 3.7–37.9%) follow-up isolates (p=0.03). Both resistant isolates also showed high-level Pa resistance, BDQ–CFZ co-resistance, and resistance to rifampicin, isoniazid, fluoroquinolones, second-line injectables, and linezolid. One of these patients, a 15-year-old female, died. Low-level Pa resistance was observed in 5/55 (9.1%) treatment-naïve isolates and 1/15 (6.7%) follow-up isolate (p=1.00). Odds of Pa resistance were significantly higher among BDQ–CFZ co-resistant isolates (OR 6.7, 95% CI: 1.1–39.1, p=0.03).

Conclusion: Phenotypic DLM resistance was absent in treatment-naïve MDR-TB but emerged in follow-up isolates, all of which demonstrated extensive co-resistance. Pretomanid resistance, although low, clustered with BDQ–CFZ co-resistance, suggesting possible cross-resistance or selection pressure. These findings support the urgent need for routine phenotypic DST for new drugs and early identification of highly resistant TB strains to guide individualized therapy and improve outcomes.

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51. **P-09: Nenekazi Masikantsi** (to be checked)

CRISPR interference-mediated discovery of antitubercular compounds from South African medicinal plants

Full author list: Nenekazi Masikantsi (1), Rendani Mbau (1), Lubabalo Macingwana (4), Peter Masoko (3), and Gabriel Mashabela (1,2).

Division of Molecular Biology and Human Genetics, Department of Biomedical Sciences, Faculty of Medicine and Health Sciences, Centre for Tuberculosis Research. Stellenbosch University, Cape Town

South African Medical Research Council, Parow, Cape Town.

Department of Biochemistry, Microbiology and Biotechnology, Faculty of Science and Agriculture, University of Limpopo, Polokwane.

Department of Human Biology, Faculty of Health Sciences, Walter Sisulu University, Mthatha.

Tuberculosis remains a global health burden despite the impetus in drug discovery and development, mainly due to increasing *Mycobacterium tuberculosis* (Mtb) resistance against the available treatment regimens. This has led to an urgent need to discover and develop new antibiotics with distinct mechanisms of action. In this study, essential gene products and mediating reactions in different Mtb essential metabolic pathways were identified as potential drug targets for the development of antitubercular drugs. CRISPR interference (CRISPRi) was utilized to deplete intracellular levels of the target gene products, generating knockdown strains of *Mycobacterium smegmatis* (Msmeg) as a surrogate for *M. tuberculosis* (Mtb). These CRISPRi strains were utilized as screening models in innovative screening assays to identify compounds from medicinal plants that disrupt mycobacterial essential metabolic pathways. Here, medicinal plants were acetone-extracted and screened against a panel of CRISPRi strains to identify those whose antimicrobial activities are potentiated more than fourfold in the CRISPRi strains than in the wild-type strains. Thereafter, activity-guided fractionation, comprising a series of chromatographic techniques, was carried out to isolate and purify the bioactive compound(s) responsible for the extract's selective activities in the CRISPRi knockdown strains. Finally, high-resolution mass spectrometry was utilised for structural elucidation of the bioactive compounds. To this end, this study identifies molecules as potential antitubercular compounds.

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52. **P-10: Nuhu Ibrahim Tukur** (Department of Biomedical Sciences, Faculty of Medicine and Health Sciences, Stellenbosch University, South Africa)

Discovery of potent DnaK-targeting Cyclomarin-A derived BacPROTACs as a potential anti-tuberculosis therapeutic modality

Full author list: [1]Tukur N.I, [1]Mbau R.D, [2]Kigondu E, Mashabela [1]G.T.M*

[1]DSI-NRF Centre of Excellence for Biomedical Tuberculosis Research, SAMRC Centre for Tuberculosis Research, Division of Molecular Biology and Human Genetics, Department of Biomedical Sciences, Faculty of Medicine and Health Sciences, Stellenbosch University, Cape Town, South Africa.

[2]Center For Traditional Medicine and Drug Research (CTMDR), Kenya Medical Research Institute, Nairobi, Kenya

Tuberculosis (TB) remains a major global health threat, with escalating drug resistance in *Mycobacterium tuberculosis* (Mtb) eroding the efficacy of current therapies and underscoring the urgent need for novel treatment strategies. Traditional drug discovery has largely focused on inhibiting essential bacterial proteins; however, resistance frequently arises. An emerging paradigm "targeted protein degradation" offers a powerful alternative, leveraging the endogenous ClpC1P1P2 protease complex to irreversibly eliminate proteins of interest (POIs) rather than merely suppressing their activity.

Here, we explored the feasibility of targeted degradation as an anti-mycobacterial strategy by developing cyclomarin-based BacPROTACs designed to recruit the ClpC1 unfoldase to the essential chaperone DnaK. Using our established CRISPR interference (CRISPRi) knockdown platform, we demonstrated that depletion of DnaK potentiates the activity of DnaK-targeting BacPROTACs, inferring target engagement and on-mechanism action. Lead BacPROTAC anti-TB candidates showed potent anti-mycobacterial activity with minimum inhibitory concentrations (MICs) in the sub-micromolar ranges and corresponding bactericidal activity (MBCs), while exhibiting low cytotoxicity in mammalian cells and favourable selectivity indices. Collectively, these findings identify a promising early anti-TB lead molecule.

This study provides the first evidence that ClpC1-mediated degradation of DnaK can be exploited to kill Mtb and demonstrates the utility of CRISPRi knockdown strains as a powerful tool to functionally validate and potentiate degrader activity. Our findings establish targeted protein degradation as a viable strategy for anti-TB drug discovery and lay the foundation for developing next-generation therapies to combat drug-resistant TB.

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53. **P-11: Onpreeya Kritwatcharas** (Department of Medical Technology, Faculty of Associated Medical Sciences, Chiang Mai University, Thailand)

Investigation of propolis-loaded niosomes for tuberculosis: anti-mycobacterial activity and three-dimensional granuloma model

Full author list: Onpreeya Kritwatcharas (1), Sirikwan Sangboonruang (1,2), Natthawat Semakul (3) and Khajornsak Tragoolpua (1)

(1) Division of Clinical Microbiology, Department of Medical Technology, Faculty of Associated Medical Sciences, Chiang Mai University, Thailand
(2) Office of Research Administration, Office of the University, Chiang Mai University, Thailand
(3) Department of Chemistry, Faculty of Sciences, Chiang Mai University, Thailand

Tuberculosis (TB) remains a major global health concern, with approximately 95% of the world's population possessing latent TB infection. Most cases are caused by *Mycobacterium tuberculosis* (Mtb), which promotes granuloma formation within host cells. When granuloma breaks down, Mtb is released, leading to active disease. Limited drug penetration into TB granulomas contributes to emergence of drug-resistant TB. Therefore, nanocarrier-based drug delivery systems offer a promising strategy to improve therapeutic efficacy. In this study, ethanolic extract of propolis-loaded niosomes coated with trimethyl chitosan (TMC/EEP-Nio) were fabricated and evaluated for the anti-mycobacterial activity and penetration into three-dimensional (3D) granuloma. EEP-Nio were prepared using a microfluidic technique, followed by dropwise assay to obtain TMC/EEP-Nio. TMC/EEP-Nio were characterized for particle size, zeta potential (ZP), poly dispersity index (PDI). The optimized TMC/EEP-Nio based on central composite design (CCD) exhibited a particle size (188.37±9.41 nm), ZP (-49.41±2.47 mV), and PDI (0.17±0.01). Fourier transform infrared spectrometry (FTIR) was used to confirm the chemical structure of TMC/EEP-Nio. Anti-TB activity was examined against Mtb H37Rv using resazurin microtiter assay (REMA) for 7 days. TMC/EEP-Nio demonstrated effectively inhibit Mtb activity. Cell cytotoxicity was assessed in monocyte-derived macrophages (MDMs), human alveolar epithelial cells (A549), and human fibroblast cells (MRC-5) using REMA. TMC/EEP-Nio exhibit low cytotoxicity in a cell type-dependent manner. A 3D granuloma model comprising *M. smegmatis*-infected MDMs, A549, and MRC-5 was constructed for 3 days to evaluate the penetration of TMC/EEP-Nio. TMC/EEP-Nio demonstrated deeper granuloma penetration compared to EEP-Nio. This approach may overcome current limitations of TB drug delivery by improving granuloma penetration and contributing to an alternative effective TB treatment regimen.

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54. P-12: Sujata Sharma (Department of Biophysics, All India Institute of Medical Sciences, India)
Lactoferrin as a Multifunctional Modulator of Oxidative Stress and Antimycobacterial Immunity in Tuberculosis

Full author list: Sujata Sharma, Surabhi Pandit, Anamika Singh, Mansi Tanwar, Pradeep Sharma and Tej P Singh

Department of Biophysics, All India Institute of Medical Sciences, New Delhi-110029, India

Tuberculosis (TB) remains a global health challenge marked by persistent infection, chronic inflammation, and oxidative tissue injury. Excess reactive oxygen species (ROS) generated during *Mycobacterium tuberculosis* (Mtb) infection cause extensive oxidation of lipids, proteins, and nucleic acids, leading to cellular damage and contributing to bacterial persistence and host pathology. Lactoferrin (LF), an iron-binding glycoprotein of the innate immune system, is known for its antimicrobial, antioxidant, and immunomodulatory properties. This study aimed to elucidate the molecular mechanisms by which LF counteracts oxidative stress and exerts antimycobacterial effects. Using molecular dynamics simulations, fluorescence quenching, and surface plasmon resonance (SPR) assays, we examined LF interactions with two key oxidative-stress biomarkers, 4-hydroxynonenal (4-HNE) and 8-hydroxy-2'-deoxyguanosine (8-OHdG). LF displayed micromolar binding affinities toward both molecules, and structural analyses revealed that its flexible interdomain interface accommodates 4-hydroxynonenal (4-HNE), while the C-lobe binds 8-hydroxy-2'-deoxyguanosine (8-OHdG). Beyond this antioxidant activity, LF exhibited direct bactericidal actions against Mtb through iron sequestration, membrane destabilization mediated by cationic peptides such as lactoferricin, inhibition of biofilm formation, interference with mycolic-acid synthesis, and synergism with standard antitubercular drugs. Collectively, these findings demonstrate that LF acts through dual mechanisms: directly inhibiting Mtb growth and indirectly mitigating oxidative and inflammatory damage within infected tissues.
In conclusion, LF emerges as a multifunctional modulator of host–pathogen interactions in TB, simultaneously targeting bacterial survival and redox imbalance. Its combined antimicrobial and cytoprotective properties highlight lactoferrin as a promising host-directed therapeutic candidate for tuberculosis and other oxidative-stress-driven infections.

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55. **P-13: Nikhat Khan** (Symbiosis International University, India; Regional Medical Research Centre, India)

Population Genetic Analysis of NAT2 Gene in Saharia Tribe: A Particularly Vulnerable Tribal Group of Central India

Full author list: Nikhat Khan (1), (2), Manjari Jonnalagadda (1) and Aparup Das (2)
(1) Symbiosis International University, Pune, India
(2) ICMR- Regional Medical Research Centre, Sri Vijaya Puram, India

The N-acetyltransferase 2 (NAT2) gene plays a pivotal role in metabolization of several exogenous compounds including isoniazid (INH), a first-line drug used extensively to treat tuberculosis (TB). This gene has been found to be variable in populations; different alleles can be phenotypically translated as different types of metabolizers, viz., each allele of the NAT2 gene can be assigned as fast/slow acetylator type. Since TB is endemic to India and the Saharia Particularly Vulnerable Tribal Group is one of the highest contributors of TB (with the incidence goes up to 2-3 times higher than the national average) we wish to conduct a thorough population genetic analyses of the NAT2 gene in this PVTG inhabiting in Madhya Pradesh. For this, we sequenced its exon-2 region (~1.3 kb) in 163 Saharia individuals from three subpopulations. A total of 12 single nucleotide polymorphisms including six globally common and six novel nonsynonymous ones unique to Saharia were identified. Genetic analysis revealed high haplotype diversity (Hd ≈ 0.9) along with low nucleotide diversity ($\pi \approx 0.002$) indicating heterogeneous but evolutionarily constrained gene pool. Furthermore, neutrality tests showed no deviation from the neutral model, whereas McDonald–Kreitman and Ka/Ks analyses revealed signatures of strong purifying selection in Saharia populations. Shared genetic ancestry and gene flow with minimal genetic differentiation (Fst ≈ 0) were some of the features of the Saharia PVTG populations. Overall, the present study indicates NAT2 genetic diversity that appears to be shaped by demographic forces under long-term purifying selection. Our study provides the first evolutionary insights of the NAT2 gene in a PVTG. Furthermore, genetic variations at the NAT2 gene provide the foundation for developing genotype-guided, personalized medicine framework for TB therapy in marginalized tribal populations.

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56. **P-14: Pathida Prakongsup** (Department of Biochemistry, Faculty of Pharmacy, Mahidol University, Thailand)

The association study between DNA methylation on CYP2D6 and CYP2E1 gene promoter and anti-tuberculosis drug-induced liver injury in tuberculosis patients in Thailand

Full author list: Pathida Prakongsup (1), Wanvisa Udomsinprasert (2), Jiraphun Jittikoon (2) and Nuanjun Wichukchinda (3)

(1) Master of Science Program in Biopharmaceutical Sciences, Department of Biochemistry, Faculty of Pharmacy, Mahidol University, Thailand
(2) Department of Biochemistry, Faculty of Pharmacy, Mahidol University, Thailand
(3) Department of Medical Sciences, Ministry of Public Health, Thailand

Anti-tuberculosis drug-induced liver injury (ATDILI) is one of the most frequently reported adverse drug reactions among patients receiving first-line anti-tuberculosis (TB) therapy. This condition eventually contributes to treatment interruption and prolongation, presumably leading to treatment failure and liver failure, especially in highly predisposed patients. Importantly, the incidence of ATDILI is expected to increase continuously due to the widespread implementation of comprehensive TB treatment strategies across all affected populations. In addition, the underlying mechanism of ATDILI is still elusive since several factors including the dysfunction of drug-metabolizing enzymes, were proposed. Given these concerns, this study aimed to investigate the association between DNA methylation (DNAm), a key epigenetic modification, at the promoter regions of drug-metabolizing enzyme genes, including CYP2D6 and CYP2E1, and the occurrence of ATDILI in Thai TB patients. A total of 60 TB patients, divided into ATBILI cases (n=30) and non-ATDILI cases (n=30), and 30 age-matched heathy controls were enrolled. DNAm levels were quantified using pyrosequencing. Although there is no significant difference, results demonstrated higher DNAm levels at the CYP2D6 promoter in patients with ATDILI compared with those without ATDILI. Likewise, no significant differences were also observed for CYP2E1 promoter methylation. Moreover, no significant association was found between DNA hypermethylation of CYP2D6 or CYP2E1 and the risk of ATDILI. Furthermore, DNAm level on CYP2D6 promoter demonstrated significant relation to DNAm level on CYP2E1 prompter, age and liver function-related parameters. Collectively, CYP2D6 and CYP2E1 promoter hypermethylation might represent a potential epigenetic predisposition to ATDILI and could support clinical management of ATDILI, ultimately improving therapeutic outcomes and patient well-being. Nevertheless, considering the dynamic nature of epigenetic regulation, these findings warrant validation in independent cohorts with larger sample sizes before clinical application.

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57. P-15: Taratorn Kemthong (Faculty of Science, Chulalongkorn University, Thailand)
Evaluating the Tuberculin Skin Test as a Practical Tool for Staging *Mycobacterium tuberculosis* Infection in Cynomolgus Macaques

Full author list: Taratorn Kemthong (1)(7) Saradee Warit (2), Sarinya Jaitrong (2), Suthirote Meesawat (1), Mutchamon Kaewparuehaschai (3), Kirana Noradechanon (3), Therdsak Prammananan (2), Prapaporn Srilohasin (4), Tanapat Palaga (5), Angkana Chaiprasert (6), and Suchinda Malaivijitnond (1)(7)

(1) Department of Biology, Faculty of Science, Chulalongkorn University, Thailand
(2) Industrial Tuberculosis Team, Industrial Medical Molecular Biotechnology Research Group, National Center for Genetic Engineering and Biotechnology, National Science and Technology Development Agency, Thailand
(3) Thailand Wildlife Conservation Office, Department of National Parks Wildlife and Plant Conservation, Thailand
(4) Department of Microbiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand
(5) Department of Microbiology, Faculty of Science, Chulalongkorn University, Thailand
(6) Office for Research, Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand
(7) National Primate Research Center of Thailand, Chulalongkorn University, Thailand

Background: Reliable diagnostic and staging tools for *Mycobacterium tuberculosis* (Mtb) infection in non-human primates remain limited. This study aimed to determine whether the Tuberculin Skin Test (TST) can serve as a practical assay for identifying the stage of Mtb infection in cynomolgus macaques (*Macaca fascicularis*).

Methods: TST readings at 24, 48, and 72 hours were assessed in specific pathogen-free (SPF) cynomolgus macaques and compared with those from naturally Mtb-infected animals confirmed by Xpert MTB/RIF Ultra and/or culture. A cohort of 34 naturally infected macaques was subsequently examined both cross-sectionally and longitudinally using multiple diagnostic approaches, including the monkey interferon-gamma release assay (mIGRA), ELISA, Xpert, IS6110-nested PCR, and culture, to classify infection into four distinct stages: incipient–innate, incipient–adaptive, latent, and active tuberculosis (TB). The TST results were then analyzed to evaluate their diagnostic performance and correlation with each infection stage.

Results: Among the three points, the 72-hour TST measurement demonstrated the highest sensitivity, specificity, and accuracy in distinguishing Mtb-infected macaques from SPF controls. When integrated with immunological and molecular assay data, TST responses showed clear differences across infection stages, corresponding to disease progression from incipient to active tuberculosis (TB).

Conclusion: The findings indicate that the TST provides not only reliable diagnostic accuracy but also reflects the immunopathological stage of Mtb infection in cynomolgus macaques. These results support the use of TST as a simple, cost-effective, and stage-informative tool for both detection and staging of Mtb infection in non-human primate models.

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58. **P-16: Prapaporn Srilohasin** (Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand)

Mycobacterium tuberculosis Beijing Lineage from Cynomolgus Macaques Compared with Human Isolates in Thailand

Full author list: Prapaporn Srilohasin (1, 2), Nattakan Thakaew (2), Worawich Phornsiricharoenphant (3), Saradee Warit (4), Suchinda Malaivijitnond (5,6), Sissades Tongsima (3), Mutchamon Kaewparuehaschai (7), Kirana Noradechanon (7), Therdsak Prammananan (4), Reka Kanitpun8, Suthirote Meesawat (5), Taratorn Kemthong (6), Tanapat Palaga (9), Angkana Chaiprasert (2, 10)

(1) Department of Microbiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand
(2) Drug Resistant Tuberculosis Research Fund, Siriraj Foundation, Bangkok, Thailand
(3) National Center for Genetic Engineering and Biotechnology, National Science and Technology Development Agency, Thailand
(4) Industrial Tuberculosis Team, Industrial Medical Molecular Biotechnology Research Group, National Center for Genetic Engineering and Biotechnology, National Science and Technology Development Agency, Thailand
(5) Department of Biology, Faculty of Science, Chulalongkorn University, Thailand
(6) National Primate Research Center of Thailand, Chulalongkorn University, Thailand
(7) Thailand Wildlife Conservation Office, Department of National Parks, Wildlife and Plant Conservation, Thailand
(8) National Institute of Animal Health, Thailand
(9) Department of Microbiology, Faculty of Science, Chulalongkorn University, Thailand
(10) Office for Research, Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand

Background: *Mycobacterium tuberculosis* (M.tb) remains a leading cause of human tuberculosis worldwide. Non-human primates, being the closest living relatives to humans, can be infected with M.tb and play a crucial role in One Health frameworks. The genomic relationship between macaque- and human-derived isolates in endemic regions has not been thoroughly investigated. Understanding these host-pathogen dynamics may provide insights into transmission and host-specific adaptation.

Methods: Twelve M.tb isolates from cynomolgus macaques collected in Thailand (2018–2025) were analyzed and compared with 1,454 human isolates. Pairwise single-nucleotide polymorphism (SNP) distances and clustering thresholds (≤5 and ≤12 SNPs) were applied to infer genetic relatedness and possible transmission events. Phylogenetic analyses were used to determine lineage classification and assess relationships to circulating human strains.

Results: Phylogenetic analysis placed all macaque isolates within lineage 2.2 (Beijing family), forming a monophyletic clade in sublineage L2.2.M1.1. Macaque isolates showed close relatedness, differing by 4–30 SNPs. A tight cluster (≤5 SNPs) was identified among three isolates (MKBK006, MKBK014 and MKBK027), including two obtained from macaques housed within the same gang cage zone. Eleven of the twelve isolates differed from each other by at most 12 SNPs, whereas one isolate was an outlier (MKBK010). Notably, that outlier was from the same gang cage zone as one of the isolates in the tight cluster. Unfortunately, the original capture locations of these macaques and the period when they were housed together are unknown. The most closely related human isolate identified was from Buri Ram province, Thailand, showing a difference of 20 SNPs. The predominant sublineage found in the macaques was different from that observed in humans, suggesting a possible host-specific lineage distribution.

Conclusion/Implication: Macaques in Thailand harbor a distinct Beijing sublineage compared to the major lineage circulating in humans. These findings highlight possible host adaptation and raise important questions about cross-species transmission and the role of wildlife as potential reservoirs.

Integrating genomic surveillance across human and animal hosts will be essential for advancing One Health strategies in TB control.

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59. **P-17: Zhenli Liang** (Guangxi Center for Disease Control and Prevention, China)

The impact of Influenza on TB treatment outcomes: a retrospective matched cohort study in Guangxi, China, 2012-2024

Full author list: Zhenli Liang (1) (2), Xiaoyan Liang (1), Zhezhe Cui (1), Nyi Nyi Zayar (2), Mei Lin (1), Guanghua Lan, Jun Zeng (1), Prasit Palittapongarnpim (3) and Virasakdi Chongsuvivatwong (2).

(1) Guangxi Center for Disease Control and Prevention, China.
(2) Department of Epidemiology, Faculty of Medicine, Prince of Sonkla University, Thailand.
(3) Center for Microbial Genomics, Faculty of Science, Mahidol University, Thailand.

Background: Previous studies have suggested that co-existing influenza may worsen tuberculosis (TB) clinical outcomes, but most evidence has focused on short-term effects or immunological mechanisms, with limited attention to TB treatment outcomes. Existing research mainly originated from western countries, South Africa, or South Korea, with findings that have been inconsistent across settings.

Objective: To assess TB treatment outcomes in patients with influenza according to different inter-disease interval, compared with those without influenza.

Method: We conducted a retrospective matched cohort study using population-based data from the National TB Information System (NTBIS) and the National Notifiable Disease Reporting System (NNDRS) in Guangxi, China. Identify pulmonary TB patients aged ≥15 years diagnosed between January 2012 and October 2024. Combined cases were defined as patients with both TB and laboratory-confirmed influenza occurring concurrently or within 24 months. Combined cases were matched with TB-only patients by age, sex, diagnosis date, and bacteriological results. Each combined case was classified as concurrent (TBcoFlu: influenza ≤90 days after TB diagnosed, or FlucoTB: TB ≤30 days after influenza) or subsequent (Flu_TB: TB >30 days after influenza). Multinomial logistic regression was used to examine associations between disease status and TB treatment outcomes, adjusting for sociodemographic and clinical covariates.

Results: Among 509,882 TB patients, 1,299 (0.25%) had combined influenza - TB disease. Nonfatal-unfavorable treatment outcomes (loss to follow-up and treatment failure) for combined cases were not statistically differed from those for TB-only patients. Notably, the mortality risk was lower in combined disease groups, with relative risk ratios ranging from 0.31 to 0.52 compared to the TB-only group.

Discussion and conclusion: These findings contrast with previous reports and may reflect differences in study design or underreporting due to limited influenza testing, which could bias estimates toward the null hypothesis. Further prospective studies with influenza subtype testing are needed to clarify the impact of influenza on TB treatment outcomes.

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60. **P-18: Natapohn Saowaphong** (Faculty of Medicine, Prince of Songkla University, Thailand)

Evaluation of stability and viability of BCG microneedle vaccine derived from three different conditions

Full author list: Natapohn Saowaphong (1), Julinthip Puttawong (1), Ratchanon Sophonmanee (1), Narisa Mohthong (1), Jomkwan Ongarj (1), Sahasawat Suksan (1), Pyae Sone Oo (1) and Nawamin Pinpathomrat (1)

(1) Department of Biomedical Sciences and Biomedical Engineering, Faculty of Medicine, Prince of Songkla University, Songkhla, 90110, Thailand

Introduction: Tuberculosis (TB) is a public health challenge, particularly in developing countries, despite advancements in treatment and control measures. Currently, the only licensed vaccine against tuberculosis is Bacillus Calmette-Guérin (BCG). However, there are safety and logistical issues with the conventional intradermal BCG immunization, which uses a hypodermic needle. To overcome these limitations, microneedling (MN) patches have become a popular alternative to BCG injections.

Method: The microneedle BCG vaccine patch was created and constructed to provide effective intradermal vaccine administration. The microneedle patch was made using a micro-molding technology. BCG vaccine solution from stock was mixed with biocompatible at a 1:1 ratio and BCG vaccine powder, pellet and was mixed with biocompatible 100 ul per powder-pellet unit, loaded into dissolvable microneedle molds, followed by a 4-h incubation, top-up with Hya/CMC, and further 18-h drying to obtain the final BCG-MNA. We compared Bacille Calmette-Guérin (BCG) microneedle cultures, constructed using BCG vaccine pellets, powder, and BCG Form Stock stored at room temperature and refrigerated (4°C), for stability and viability (%CFU viability) measured by spread plate.

Result: Findings showed that live BCG remained viable within the microneedle matrix for more than seven days, While the standard reconstituted BCG vaccine must be used within 24 hours of opening. The powder form had the best stability at 4°C, Further tuning is required to keep the powder form at high stability in the final microneedle product.

Conclusion: This finding suggests that the microneedle formulation can efficiently sustain BCG viability and may be more stable in storage and easier to handle than traditional vaccination formulations. Further research will examine the immunogenicity and efficacy of the microneedle BCG patch to confirm it as a safer, more accessible, and effective tuberculosis prevention. This technology has the potential to increase vaccine coverage, particularly in resource-limited settings.

Keywords: Microneedle, BCG Vaccine, Tuberculosis, Medical technology

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61. **P-19: Trinh Minh Phuong** (College of Medicine, Gyeongsang National University, Republic of Korea)

Disentangling Relapse and Reinfection in *Mycobacterium intracellulare* Using MIRU-VNTR Genotyping

Full author list: Trinh Minh Phuong[1], Kyu-Min Kim[1], Jung-Wan Yoo[2], and Min-Kyoung Shin[1*]

[1] Department of Microbiology and Convergence of Medical Science, College of Medicine, Gyeongsang National University, Jinju, Republic of Korea

[2] Department of Internal Medicine, Gyeongsang National University Hospital, Jinju, Republic of Korea.

Mycobacterium avium complex (MAC) is one of the most common pathogens responsible for pulmonary diseases caused by non-tuberculous mycobacteria (NTM). The global incidence of MAC pulmonary disease (MAC-PD) has steadily increased over the past decades, particularly in aging populations and in patients with pre-existing lung disorders such as chronic obstructive pulmonary disease, bronchiectasis, or idiopathic pulmonary fibrosis. Once a person is infected with MAC-PD, it is difficult to eradicate the bacilli, as it requires prolonged therapy. Even after prolonged treatment, many patients continue to suffer from microbiological recurrence, which can occur either due to relapse (persistence of the original strain) or reinfection (introduction of a new strain from the environment). Distinguishing between these two scenarios is of high clinical importance, since relapse often indicates treatment failure or antimicrobial resistance, whereas reinfection reflects continuous exposure to environmental reservoirs of MAC. A practical and reliable genotyping approach is needed to evaluate clinical outcome of MAC-PD, which has frequent relapse/reinfection.

We investigated *M. intracellulare*, the most frequently isolated MAC species, from 30 patients with pulmonary disease treated at Gyeongsang National University Hospital, Gyeongsangnam-do, Korea. Antimicrobial susceptibility testing and MIRU-VNTR genotyping were performed to assess strain diversity and to distinguish relapse from reinfection. Selected isolates from antibiotic-treated patients were further subjected to whole-genome sequencing.

A total of 119 strains were examined by MIRU-VNTR. Among the 30 patients, 18 (60%) showed recurrence with the same strain, whereas 12 (40%) experienced reinfection with genetically distinct strains. Six loci including VNTR3, VNTR4, VNTR9, VNTR11, VNTR13, and MIN33, showed genetic changes in relapsed patients, confirming that there are specific sites where genetic mutations are induced as infection persists.

This study provides genotypic criteria for distinguishing relapse from reinfection in MAC-PD using the MIRU-VNTR 23-loci profile and identifies mutation-prone loci potentially linked to bacterial persistence and virulence. These findings may contribute to improved monitoring of treatment outcomes in MAC-PD patients and offer valuable molecular markers for clinical and epidemiological applications.

Keywords: Nontuberculous mycobacteria; *Mycobacterium intracellulare*; *Mycobacterium avium* complex pulmonary disease; multilocus variable-number of tandem-repeat; whole genome sequencing; antibiotic susceptibility

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62. **P-20: Minh Phuong Trinh** (College of Medicine, Gyeongsang National University, Republic of Korea)

Gram-Negative–Driven TLR4 Activation Reshapes Cytokine Dynamics and Host Response during *Mycobacterium avium* Infection

Full author list: Minh Phuong Trinh[1,2], Jeong-Ih Shin[1,2,3], Kyu-Min Kim[1,2], Jung-Wan Yoo[4], and Min-Kyoung Shin[1,2*]

[1] Department of Microbiology, College of Medicine, Gyeongsang National University, Jinju, Republic of Korea

[2] Department of Convergence of Medical Science, Graduate School, Gyeongsang National University, Jinju, Republic of Korea

[3] Department of Biomedicine & Health Sciences and Integrated Research Center for Genomic Polymorphism, Precision Medicine Research Center, College of Medicine, The Catholic University of Korea, Seoul, Republic of Korea

[4] Department of Internal Medicine, Gyeongsang National University Hospital, Jinju, Republic of Korea

Background: *Mycobacterium avium* complex lung disease (MAC-PD) is divided into fibro cavitary and nodular bronchiectasis types, the latter occurring without underlying disease and highly associated with chronic Pseudomonas aeruginosa (PA) infection. While MAC is introduced into macrophages by phagocytosis and retained in the cells, co-infected PAs can impact MAC-infected host cells.

Methods: We evaluated the impact of co-infection with gram-negative bacteria, including PA, in a MAC infection model. To establish a MAC infection model that mimics gram-negative bacterial co-infection, C3H/HeN and C3H/HeJ (TLR4-deficient) mice were used. Bone marrow-derived macrophages (BMDMs) from these mice were colonized and measured for cytokine concentration 24 hours after treatment with MAC and LPS (TLR4 agonist).

Results: There was no difference in the expression of IL-10 and TNF-α between the LPS+MAC and only MAC-treated groups in C3H/HeJ BMDM, whereas in C3H/HeN BMDM, IL-10 expression increased synergistically in the LPS+MAC group. Additionally, the LPS+MAC and only MAC groups in C3H/HeJ BMDM showed the same colonization results, and the intracellular bacterial CFU was decreased in the LPS+MAC group of C3H/HeN BMDM.

Conclusion: The results of this study suggest that co-infection with gram-negative bacteria in MAC infection exhibits a synergistic response to IL-10 secretion by macrophages and may affect the clinical features of MAC-PD.

Keywords: *Mycobacterium avium* complex, *Pseudomonas aeruginosa*, Pulmonary disease, TLR 4, IL-10

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63. **P-21: Sahasawat Suksan** (Department of Biomedical Science and Biomedical Engineering, Prince of Songkhla University, Thailand)

Modeling human tonsil organoids to study adaptive immune responses against BCG

Full author list: Sahasawat suksan(1), Nattarin Nilrat(2), Chayut Kimsri(3), Krongthong Tawaranurak(3), and Nawamin Pinpathomrat(1)a

(1) Department of Biomedical Science and Biomedical Engineering, Prince of Songkhla University, Thailand.
(2) Department of Otolaryngology, Faculty of Medicine, Prince of Songkla University, Songkhla, Thailand.
(3) Department of Pathology, Faculty of Medicine, Prince of Songkla University Hat Yai, Songkhla, Thailand.

Vaccine testing is a crucial part of development. However, preclinical studies using animal models often fail to accurately predict human responses. The responses in animals, such as mice frequently differ from humans due to genetic and environmental variances. This study proposes an in vitro model based on tonsil organoids cultured from human tonsil tissue. Tonsil tissue contains various types of immune cells involved in adaptive immunity, making it an ideal tissue for studying responses to vaccination. This study aimed to optimize a culture protocol for tonsil organoids to model the human adaptive immune response against Bacillus Calmette-Guérin (BCG). Including to develop a model with structures and functions similar to human tonsil tissue. Tonsil tissue from consented pediatric patients was processed and cultured to generate organoids. The optimization process evaluated factors such as growth, antibiotic formulas, timing of antigen stimulation and organoid formation characteristics. Our results showed that a once stimulation with the BCG antigen before culture was sufficient to activate T and B-cell responses. Penicillin/streptomycin in the culture medium yielded the best results in maintaining T-cell and B-cell proportions. The organoids developed into three-dimensional structures that aggregated into distinct clusters under a bright microscope. Functionally, the group that successfully forming organoids had higher CD4+ and CD8+ T-cell responses and significantly higher secretion of key cytokines than the non organoids forming group. This study successfully developed a tonsil organoid culture system that can reliably mimic the immune responses observed in human lymph nodes. This provides a useful approach for the future development and efficacy testing of TB vaccines.

Keyword: Tonsil, Organoid, Adaptive immune, BCG, in vitro

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64. **P-22: Suthirote Meesawat** (Department of Biology, Faculty of Science, Chulalongkorn University, Thailand)

Rapid detection of antibody against *Mycobacterium tuberculosis* complex in synanthropic rhesus (*Macaca mulatta*) and long-tailed (*M. fascicularis*) macaques across Thailand

Full author list: Suthirote Meesawat (1),(2), Saradee Warit (3), Sarinya Jaitrong (3), Taratorn Kemthong (2),(4), Angkana Chaiprasertc (5), and Suchinda Malaivijitnond (1),(2),(4)

(1) Department of Biology, Faculty of Science, Chulalongkorn University, Bangkok, Thailand
(2) Biological Sciences Program, Faculty of Science, Chulalongkorn University, Bangkok, Thailand
(3) Industrial Tuberculosis Team (ITBT), IMBG, BIOTEC, NSTDA, Pathumthani, Thailand
(4) National Primate Research Center of Thailand - Chulalongkorn University, Saraburi, Thailand
(5) Office of Research, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Wild macaques (rhesus, *Macaca mulatta*, and cynomolgus, *M. fascicularis*) in Thailand were reported to have a high prevalence of *Mycobacterium tuberculosis* complex (Mtbc) infection detected using the IS6110 nested-PCR technique, indicating an active tuberculosis stage. This study developed a multi-antigen print immunoassay (MAPIA) for serological screening of latent tuberculosis infection (LTBI) by measuring IgG levels against rESAT-6, rCFP-10, and bovine and avian purified protein derivative (bPPD and aPPD) antigens. Twenty-six populations (1,075 individuals) of wild macaques across Thailand were captured, and serum was collected. The antibody responses were interpreted as infections with Mtbc (for either rESAT-6, rCFP-10, or bPPD) and/or *M. avium* (for aPPD). Of the 1,075 animals tested, antibody responses to mycobacterial antigens were detected in 646 (60.1%) macaques, and only 158 of those 646 (24.4%) had previously tested positive for Mtbc IS6110 nested-PCR. The serological test revealed 4.3 times more infected animals than the antigen test, and this difference was associated with the species and age of animals. A higher antibody response to Mtbc antigens at the individual level was observed in cynomolgus than in rhesus macaques, and in adults than in juveniles that were tuberculosis (TB)-positive. Due to the COVID-19 pandemic, there was a high demand for macaques as experimental animals for vaccine testing; however, the supply of monkeys was limited. Consequently, there was extensive capture of wild macaques in the habitat range countries, including Thailand. Apart from active tuberculosis detection, this study corroborates that the LTBI detection in free-ranging monkeys should be performed. The MAPIA has several advantages for early detection of TB, i.e., no need for specialized equipment, quick turnaround time, and visually readable results. This suggests that MAPIA should serve as an additional tool for TB diagnosis to prevent Mtbc spillover from synanthropic macaques to humans.

Keywords: tuberculosis, MAPIA, *Mycobacterium bovis*, *M. avium*, serological test

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65. **P-23: Anna Vyazovaya** (St. Petersburg Pasteur Institute, Russia)

Overwhelming dominance of the Beijing genotype among pre-extensively drug-resistant *Mycobacterium tuberculosis* strains in western Siberia, Russia

Full author list: Anna Vyazovaya (1), Grigory Sergeev (1), Irina Kostyukova (2), Alena Gerasimova (1), Mikhail Bezruchko (1), Dmitry Polev (1), Oksana Pasechnik (3) and Igor Mokrousov (1)

(1) St. Petersburg Pasteur Institute, Russia
(2) Clinical Anti-Tuberculosis Dispensary, Russia
(3) Omsk State Medical University, Russia

An increasing spread of drug resistant *Mycobacterium tuberculosis* strains, including those with pre-extensive and extensive drug resistance (pre-XDR and XDR)) is a global concern. Here, we performed genomic and phylogenetic analysis of pre-XDR/XDR *M. tuberculosis* strains in the Omsk region in western Siberia, Russia, a region with high rate of multi-drug resistant (MDR) tuberculosis. A total of 720 *M. tuberculosis* strains from newly diagnosed tuberculosis patients in 2019-2023 were studied. Genotyping scheme included spoligotyping and detection of lineage and subtype markers. Whole-genome sequencing was performed on the DNBSEQ-G50 platform (MGI, China), and the obtained data (fastq files) were subjected to bioinformatics analysis. The study was supported by Russian Science Foundation (grant 24-44-00004). Of the 720 *M. tuberculosis* strains, 313 (43.5%) were MDR, including 102 (14.2%) pre-XDR strains. The overall population structure of *M. tuberculosis* comprised strains from diverse genotypes: Lineage 2 (Beijing genotype, 69.6%) and Lineage 4 (30.4%). The major Beijing subtypes were Central Asian/Russian (L2.2.M4.9; 38.6%), B0/W148 (L2.2.M4.5; 19.4%), Central Asia Outbreak cluster (L2.2.M4.9.1; 5.4%), ancient/ancestral sublineage (L2.2; 4.9%). Further analysis of WGS data of 89 pre-XDR strains revealed the predominance of Beijing genotype (92.9%). Among pre-XDR strains, Beijing genotype included: B0/W148 cluster (56%), Central Asian/Russian clade (20%); Central Asia Outbreak cluster (7.9%), ancient sublineage of the Beijing genotype (9.0%). Genotypic resistance to first-line antibiotics was mainly due to mutations in *rpoB*531, katG315, and embB306. The most frequent fluoroquinolone resistance mutations were gyrA Asp94Gly and Ala90Val. In addition, three B0/W148 strains had bedaquiline resistance mutations in mmpR5, i.e. they were XDR. Putative compensatory mutations in rpoC were identified in 39.3% pre-XDR strains. The Beijing genotype dominates among pre-XDR/XDR *M. tuberculosis* strains in western Siberia, Russia. Strains of the Russian epidemic variant Beijing B0/W148 and ancient sublineage of the Beijing genotype endemic for the region require special attention.

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66. **P-24: Nik Mohd Noor Nik Zuraina** (Department of Medical Microbiology & Parasitology, School of Medical Sciences, Universiti Sains Malaysia, Malaysia)

Rapid Detection of *Mycobacterium tuberculosis* SIT745/EAI1-MYS Using a Five-Spacer Multiplex PCR

Full author list: Nik Mohd Noor Nik Zuraina (1), Noreafifah Semail (1), Mohammed Abdullah (1), Zaidah Abdul Rahman (1) and Siti Suraiya (1,2)

(1) Department of Medical Microbiology & Parasitology, School of Medical Sciences, Universiti Sains Malaysia, Kelantan, Malaysia

(2) Hospital Infections Control and Epidemiology Unit, Hospital Pakar Universiti Sains Malaysia, Universiti Sains Malaysia, Kelantan, Malaysia

Background and rationale: The *Mycobacterium tuberculosis* strain SIT745/EAI1-MYS is a unique lineage that has been reported mainly among the Malaysian population. It belongs to the East-African Indian (EAI) family and is characterized by the absence of spacers 37, 38, and 40 in the standard spoligotyping pattern. However, the conventional spoligotyping method is expensive and time-consuming, limiting its use for routine strain identification.

Aims: This study aimed to develop a simple, rapid, and cost-effective multiplex PCR (mPCR) method for detecting SIT745/EAI1-MYS and to evaluate the distribution of this lineage among *M. tuberculosis* clinical isolates.

Methods: A total of 104 *M. tuberculosis* clinical isolates collected between 2017 and 2020 were included. DNA templates were prepared using the boiling method, and primers targeting spacers 37-41 were designed using NCBI Primer-BLAST.

Results: Initial monoplex PCR confirmed that all five spacers were present in the reference strain H37Rv but absent for spacers 37, 38, and 40 in SIT745/EAI1-MYS. The optimized mPCR successfully amplified all five spacers from H37Rv and only two (spacers 39 and 41) from SIT745/EAI1-MYS at an annealing temperature of 58°C. Validation using 16 previously confirmed SIT745/EAI1-MYS isolates showed identical duplex amplicon patterns, consistent with their spoligotyping profiles. Screening of 104 clinical isolates revealed that 16 isolates (11%) shared the same duplex pattern, confirming the presence of SIT745/EAI1-MYS in local TB cases.

Conclusion: The developed five-spacer mPCR assay offers a rapid, reliable, and affordable alternative to conventional spoligotyping. It allows clear differentiation of SIT745/EAI1-MYS from other *M. tuberculosis* lineages and can be applied for routine molecular surveillance. This assay may enhance epidemiological tracking, improve understanding of strain diversity, and support more targeted tuberculosis control strategies in Malaysia.

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67. **P-25: Manu Singh** (Department of Respiratory Medicine, King George's Medical University, India)

Discrepancies in molecular and culture-based detection of central nervous system tuberculosis and its drug resistance profile

Full author list: Manu Singh (1), Parul Jain (2), Rajiv Garg (1), Sushma Yadav (1) Rashmi Ratnam (1) and Urmila Singh (2)

(1) Department of Respiratory Medicine, King George's Medical University, India
(2) Department of Microbiology, King George's Medical University, India

Central Nervous System Tuberculosis (CNS-TB), due to its paucibacillary nature, poses significant diagnostic and therapeutic challenges. This study, conducted jointly by the Departments of Respiratory Medicine and Microbiology at KGMU, aimed to assess the diagnostic yield and resistance patterns in cerebrospinal fluid (CSF) samples using molecular and culture-based methods. In this retrospective analysis, 2,898 CSF samples received between January and December 2024 were tested using CBNAAT (GeneXpert MTB/RIF). A subset of 199 samples underwent liquid culture (MGIT 960, BD) and Line Probe Assay (LPA; MTBDRplus and MTBDRsl v2.0, Hain Lifescience). Of 2,898 samples, 887 (30.6%) were pediatric and 2,011 (69.4%) were adult. CBNAAT detected *Mycobacterium tuberculosis* in 211 samples (7.3%), with rifampicin resistance (RIF-R) in 43 cases (20.4%; 11 pediatric, 32 adult). Culture yielded growth in only 4/199 (2.0%) samples—three drug-sensitive and one identified as pre-XDR-TB. Among the 43 RIF-R cases detected by CBNAAT, only one was confirmed resistant on LPA or phenotypic DST, indicating significant discordance between molecular and conventional methods. The low culture positivity from CSF (2%) restricts comprehensive resistance profiling in CNS-TB. The observed 20% RIF-R rate by CBNAAT reflects a considerable burden of drug-resistant CNS-TB, yet the discrepancies with culture and LPA highlight diagnostic uncertainty. These findings underscore the urgent need for advanced, CSF-compatible molecular diagnostics to support timely and accurate treatment decisions in high-burden settings.

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68. **P-26: Waritta Sawaengdee** (Department of Medical Sciences, MOPH, Thailand)

Whole-genome sequencing reveals the co-dominance of *Mycobacterium tuberculosis* lineages 1 and 2 in Thailand

Full author list: Waritta Sawaengdee (1), Pundharika Piboonsiri (1), Charintip Yenyuvadee (1), Naparat Naowanat (1), Woraporn Thuansuwan (1), Jaluporn Chumpol (1), Sukanya Wattanapokayakit (1), Boonchai Chaiyasirinroj (2), Natthakan Thipkrua (3), Wuthiwat Ruangchai (4), Nurin Dureh (5), Arinda Ma-a-lee (5), Prasit Palittapongarnpim (4), Bharkbhoom Jaemsai (4)

(1) Department of Medical Sciences, Ministry of Public Health, Nonthaburi, Thailand
(2) TB/HIV Research Foundation (THRF), Chiang Rai, Thailand
(3) Office of Prevention and Control Disease region 5, Ratchaburi, Department of Disease Control, Ministry of Public Health, Bangkok, Thailand
(4) Pornchai Matangkasombut Center for Microbial Genomics (CENMIG), Department of Microbiology, Faculty of Science, Mahidol University, Bangkok, Thailand
(5) Department of Mathematics and Computer Science, Faculty of Science and Technology, Prince of Songkla University, Patani, Thailand

Whole-genome sequencing (WGS) provides high-resolution insights into the genetic diversity and antibiotic resistance of *Mycobacterium tuberculosis* (MTB). In this study, we analysed whole-genome sequence data of 2,887 MTB isolates collected between 2022 and 2025, the majority of which (72.98%) were from two health regions (HR) of Thailand: HR 7 (n = 1,204) and HR 5 (n = 903). Phylogenetic and genomic analyses were performed to genotype lineages, determine drug resistance profiles, and reconstruct the phylogenetic tree. The most common lineages were L1 (n = 1,426; 49.4%) and L2 (n = 1,214; 42.0%), followed by L4 (n = 237; 8.21%) and L3 (n = 10; 0.35%). Phylogenetic reconstruction grouped these lineages into four major clades, all supported by high ultrafast bootstrap scores (UFboot = 100). Overall, 1,943 (67.30%) isolates were drug-sensitive, while 944 (32.70%) were drug-resistant (DR). Among these DR isolates, 392 (41.5%) were classified as isoniazid-resistant, 53 (5.61%) were rifampicin-resistant, 220 (23.3%) were multi-drug resistant, 25 (2.65%) were pre-extensively drug-resistant, and 1 (0.11%) was extensively drug-resistant. The remaining 253 (26.8%) samples exhibited resistance patterns that could not be classified into the previous categories and were designated as 'other'. This dataset offers potential benefits for personalised medicine and provides better insight into overall transmission dynamics at the national level when integrated with other sets of WGS data from Thailand.

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69. **P-27: Pornpen Tantivitayakul** (Department of Oral Microbiology, Faculty of Dentistry, Mahidol University, Thailand)

Interactions of human genomes and mycobacterial genomes contribute to severity and transmissibility of pulmonary tuberculosis

Full author list: Pornpen Tantivitayakul (1, 4), Punna Kunhapan (2), Manon Boonbangyang (4), Kridsadakorn Chaichoompu (3), Alisa Wilantho (3), Waritta Sawaengdee (2), Wuthiwat Ruangchai (4), Yuttapong Thawornwattana (4), Hideki Yanai (5), Sukanya Wattanapokayakit (2), Areeya Disratthakit (2), Reiko Miyahara (6), Supalert Nedsuwan (7), Worarat Imasanguan (7), Pacharee Kantipong (7), Boonchai Chaiyasirinroje (8), Jody Phelan (9), Taane G. Clark (9), Martin L. Hibberd (9), Katsushi Tokunaga (6), Surakameth Mahasirimongkol (2), Prasit Palittapongarnpim (4)*

(1) Department of Oral Microbiology, Faculty of Dentistry, Mahidol University, Bangkok, 10400, Thailand.
(2) Department of Medical Sciences, Ministry of Public Health, Tiwanon Road, Nonthaburi, Thailand.
(3) National Biobank of Thailand, 111 Thailand Science Park, Phahonyothin Road, Klong Neung, Khlong Luang, Pathum Thani, 12120, Thailand
(4) Emeritus Professor Pornchai Matangkasombut Center for Microbial Genomics, Department of Microbiology, Faculty of Science, Mahidol University, Bangkok, Thailand.
(5) Fukujuji Hospital and Research Institute of Tuberculosis (RIT), Japan Anti-Tuberculosis Association (JATA), Kiyose, Japan
(6) Genome Medical Science Project, National Center for Global Health and Medicine, Tokyo, Japan.
(7) Chiang Rai Prachanukroh Hospital, Ministry of Public Health, Chiang Rai, Thailand
(8) TB-HIV Research Foundation, Chiang Rai, Thailand
(9) London School of Hygiene and Tropical Medicine, London, UK

Tuberculosis (TB) are influenced by a complex interplay of bacterial (diversity of *Mycobacterium tuberculosis*), the host (host genetics and immune condition), and the environmental factors. These factors could affect disease susceptibility and progression. This study aimed to simultaneously analyze demographic and genomic data from both patients and bacteria in determining epidemiological clustering, treatment outcomes, and pulmonary cavitation of TB. A cohort study of pulmonary TB in Thailand was conducted during 2003-2020. Whole genome analysis of MTB and genome wide SNP genotyping for TB patients were performed. The TB patients were classified into main (n = 899) and minor groups (n = 394) based on difference of population ancestry. Logistic regression analysis was performed to identify factors related to clinical TB phenotypes. Genome-wide association study (GWAS) was conducted in TB patients from main group to identify host genetic variations associated with an increased risk of developing lung cavitation, adverse treatment outcome, and epidemiological TB clustering. This GWAS was stratified by infecting MTB lineage L1 and L2. Regression analysis revealed the unfavorable treatment outcomes and pulmonary cavitation associated with human genetic factors. Bacterial genetic clustering was correlated with bacterial lineages. GWAS conducted on main patient group revealed rs1485302 in COLEC10 (p = 1.91E-8) were significantly associated with TB clustering cases. Furthermore, the study found 15 suggestive significant SNPs in IL-16 (p = 2.20E-7) associated with adverse outcome and 2 suggestive SNPs in OXSR1 gene (p = 8.28E-7) related to develop lung cavity in TB patient infected with MTB L1. These findings highlight the importance of investigating both bacterial and human genomic data to better understand the outcomes of host-pathogen interactions.

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70. **P-28: Manita Yimcharoen** (Department of Medical Technology, Faculty of Associated Medical Sciences, Chiang Mai University, Thailand)

Adaptive genome remodeling and conserved virulence shape interactions between host and pathogen in drug-resistant *Mycobacterium tuberculosis*

Full author list: Manita Yimcharoen (1), Zayar Phyo (1), Pitiporn Noisagul (2), and Bordin Butr-Indr (1)
(1) Division of Clinical Microbiology, Department of Medical Technology, Faculty of Associated Medical Sciences, Chiang Mai University, Thailand
(2) Center of Multidisciplinary Technology for Advanced Medicine (CMUTEAM) Faculty of medicine, Thailand

Mycobacterium tuberculosis (Mtb), the causative agent of tuberculosis (TB), remains a leading cause of infectious disease mortality worldwide, with drug-resistant strains posing significant challenges to global TB control. Understanding how genomic diversity influences virulence, immune evasion, and drug susceptibility is crucial for combating this pathogen. We employed whole-genome sequencing (WGS) with hybrid assembly, phylogenetic analysis, and comprehensive genomic profiling to investigate the relationship between genomic variation and drug resistance phenotypes in clinical Mtb isolates. Our analysis revealed that antimicrobial resistance has emerged independently across multiple evolutionary lineages of Mtb, indicating convergent evolution under selection pressure. Despite phenotypic differences, core pathogenic capabilities were maintained across all strains, suggesting that essential virulence functions are preserved during resistance evolution. However, antimicrobial selection pressure drove substantial genomic reorganization, with variants and structural variations increasing systematically from susceptible strains to extensively drug-resistant isolates. The analysis identified gene sets specific to drug-resistant strains, with virulence and immune evasion factors comprising the largest functional category. Notably, the PE/PPE virulence gene families and ESX secretion systems showed the greatest degree of variation and structural impact, highlighting their critical roles in host–pathogen interactions during resistance development. These findings demonstrate that while Mtb maintains core pathogenic functions across diverse genetic backgrounds, drug selection pressure promotes extensive genomic reorganization and structural variation that may enhance adaptive potential. This comprehensive genomic framework elucidates the molecular mechanisms underlying virulence maintenance and adaptive evolution in drug-resistant Mtb, providing insights essential for the development of targeted therapeutic strategies against resistant tuberculosis strains.

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71. **P-29: Zayar Phyo** (Department of Medical Technology, Faculty of Associated Medical Sciences, Chiang Mai University, Thailand)

Comparative Transcriptional Signatures Reveal Strain-Specific Isoniazid Responses in *Mycobacterium tuberculosis* Under Host-Mimicked Stress Conditions

Full author list: Zayar Phyo, Manita Yimcharoen, Sukanya Saikaew and Bordin Butr-Indr
Division of Clinical Microbiology, Department of Medical Technology, Faculty of Associated Medical Sciences, Chiang Mai University, Thailand

Isoniazid (INH) is a frontline drug of tuberculosis (TB) treatment, primarily targeting mycolic acid synthesis and influencing cell envelope components such as lipoarabinomannan (LAM) in *Mycobacterium tuberculosis* (Mtb). Despite its efficacy, Mtb frequently develops phenotypic drug tolerance by adapting to the hostile host environment, including hypoxia, acidic pH, nitric oxide, and nutrient scarcity within granulomas. To investigate this adaptive mechanism, we cultivated drug-susceptible (H37Rv) and mono-isoniazid-resistant (INH-R) clinical strains in a host-mimicked multi-stress (MS) system and exposed them to INH at its peak plasma concentration (6 µg/ml). Relative gene expression was quantified using real-time PCR targeting stress-response genes (virS, icl1, whiB3, tgs1) and LAM biosynthesis/transport genes (lprG, p55, lmeA, mptA, embC). Upon INH exposure in MS conditions, the INH-R strain displayed significant upregulation of the lipid-storage regulator tgs1 and LAM-related transport and precursor genes (lprG, p55, lmeA), suggesting an adaptive strategy centered on cell-wall remodeling and lipid mobilization. Conversely, the H37Rv strain exhibited increased expression of lipid-utilization genes (icl1, whiB3) but showed general downregulation of LAM-related genes and tgs1. These findings reveal distinct, strain-dependent transcriptional strategies employed by Mtb to achieve drug adaptation under environmental stress, highlighting divergent metabolic shifts (cell wall modification versus lipid utilization). This study underscores that the pre-existing resistance profile dictates the immediate adaptive response to INH. Furthermore, this work provides a critical foundation for future research that will integrate whole-genome sequencing (WGS) and RNA sequencing (RNA-seq) to fully elucidate the complex coding and non-coding regulatory networks underlying drug tolerance across different resistant strains.

Keywords: *Mycobacterium tuberculosis*; isoniazid; stress response; drug tolerance

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72. P-30: Grigorii Sergeev (St. Petersburg Pasteur Institute, St. Petersburg, Russia)

Development of bedaquiline resistance in *Mycobacterium tuberculosis* serial isolates recovered during treatment of MDR/pre-XDR tuberculosis patients

Full author list: Grigorii Sergeev (1), Anna Vyazovaya (1), Gulnora Ahmedova (2), Dmitrii Polev (1), Dmitrii Leontev (2), Natalia Maslennikova (2), Dmitrii Korneev (2), Evgenii Turkin (2) and Igor Mokrousov (1)

(1) St. Petersburg Pasteur Institute, St. Petersburg, Russia

(2) Kaliningrad Regional Anti-Tuberculosis Dispensary, Kaliningrad, Russia

Spread of multi- and extensively drug-resistant (MDR/XDR) strains of *Mycobacterium tuberculosis* is a global public health concern. Northwestern Russia, including Kaliningrad, is one of the first regions where tuberculosis patients receive bedaquiline. We aimed to study development of bedaquiline resistance in *M. tuberculosis* isolates recovered from patients during treatment. The study included 15 MDR/pre-XDR patients and 48 isolates (2-7 from each patient). *M. tuberculosis* isolates were submitted to whole-genome sequencing on the DNBSEQ-G50. The fastq files were subjected to bioinformatics analysis using TB-profiler and TbLG tools to identify drug resistance mutations and assign barcodes. In particular, we searched for mutations associated with resistance to bedaquiline in mmpR5 (Rv0678), atpE (Rv1305), pepQ (Rv2535c), and Rv1979c. The study was supported by Russian Science Foundation (grant 24-44-00004). Most of the enrolled patients were infected with Beijing genotype (L2.2.1, 13 patients) and its B0/W148 subtype (L2.2.M4.5, 10 patients). Other subtypes were Beijing Central Asian Russian (L2.2.M4.9, 13.3%, 2 patients), Beijing Central Asia Outbreak (L2.2.M4.9.1, 1 patients) and Ural (L4.2.1, 2 patients) genotypes. Further analysis demonstrated that isolates from 6 patients have BDQ resistance mutations: 4 infected with B0/W148 subtype, and 2 infected with Ural (L4.2.1). Nine different mutations were detected altogether, 1-3 per isolate, mostly in mmpR5 and once in atpE. In most cases, heteroresistance was observed. Mutations emerged during treatment in 2 patients. Five of 6 patients with genotypic bedaquiline resistance were characterized by ineffective treatment outcome. To conclude, serial *M. tuberculosis* isolates from MDR/pre-XDR patients primarily belonged to the Beijing genotype (86.7%), particularly to the B0/W148 subtype (66.7%). Mutations associated with bedaquiline resistance were found mostly in different regions of the mmpR5 gene, half of them were at codon 198. Early genotypic detection of bedaquiline resistance is critical for informed choice or eventual correction of treatment regimen of MDR/pre-XDR TB patients.

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73. **P-31: SM Rezvi** (Microbiology Department, Faculty of Medicine, Universitas Andalas, Indonesia)

Development and Validation of an RT-PCR Kit for Rapid Detection of *Mycobacterium tuberculosis* in Clinical Samples

Full author list: SM Rezvi (1,2), Andani Eka Putra (1,2), Ayu Novita Trisnawati (2), Puji Oktavia (2), Afrilia Susanti (2), Gusmelly (2) and Yank Olivia Diana (2)

(1) Microbiology Department, Faculty of Medicine, Universitas Andalas, Indonesia

(2) Center of Diagnostic and Research on Infectious Diseases Faculty of Medicine, Universitas Andalas, Indonesia

Tuberculosis (TB) remains a significant public health challenge in Indonesia. According to the Global TB Report 2023, Indonesia ranks second globally in TB burden, with an estimated 1,060,000 cases and approximately 134,000 TB-related deaths in 2022. Early and accurate diagnosis is essential for effective disease control. Conventional diagnostic methods such as smear microscopy and culture have limitations in terms of sensitivity and turnaround time. Therefore, molecular diagnostic methods, particularly RT-PCR, offer promising alternatives. This study aimed to develop and validate an RT-PCR-based diagnostic kit for the detection of *Mycobacterium tuberculosis* in clinical samples. The development process included six optimization models: reaction temperature, reagent composition, detector type, detector volume, and implementation in both conventional PCR and quantitative real-time PCR platforms. Validation was conducted across four parameters: diagnostic accuracy (sensitivity and specificity), cross-reactivity, amplification efficiency, and coefficient of variation (CV). Culture was used as the reference standard for comparison. The developed RT-PCR kit demonstrated a sensitivity of 96.7% and a specificity of 100% when compared to culture. Amplification efficiency reached 99.82%, and the CV was 1.6%, indicating strong reproducibility and stability. Cross-reactivity tests confirmed the specificity of the assay for *M. tuberculosis*, with no amplification observed from non-target bacterial species. The in-house RT-PCR kit provides a rapid, sensitive, and specific method for detecting *Mycobacterium tuberculosis*, offering several advantages over conventional diagnostic methods. Its high accuracy, efficiency, and potential scalability make it a valuable tool to support TB diagnosis and control efforts, particularly in high-burden countries like Indonesia.

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74. **P-32: Sushma Yadav** (King George's Medical University, India)

Identification of Drug-resistant profile of multidrug-resistant patients receiving bedaquiline and delamanid based regimen

Full author list: Sushma Yadav*, Parul Jain*, Surya Kant*, Jyoti Bajpai*
*King George's Medical University, Lucknow, U.P.

Background: Tuberculosis (TB) remains a major global health challenge, with India contributing significantly to the global burden. The rise of multidrug-resistant tuberculosis (MDR-TB), resistant to isoniazid and rifampicin, complicates treatment due to limited options and adverse effects. Newer drugs like Bedaquiline and Delamanid have improved outcomes in drug-resistant TB (DR-TB). However, resistance patterns and adverse reactions often necessitate regimen modification. Evaluating patients transitioned to Delamanid-based therapy provides crucial insights into emerging resistance trends, therapeutic responses, and the importance of drug susceptibility testing (DST) to optimize individualized treatment and prevent further resistance development.

Objectives: To determine the drug-resistance patterns and identify the number of multidrug-resistant tuberculosis (MDR-TB) patients who were transitioned to a Delamanid-based regimen.

Methods: This observational study was conducted in the Department of Respiratory Medicine, King George's Medical University (KGMU), Lucknow. Patients with sputum culture positive for *Mycobacterium tuberculosis* and confirmed multidrug resistance from the Microbiology Laboratory, who initiated treatment between January and December 2022, were included.

Results: Out of 1021 patients with MDR-TB, all were initially started on a Bedaquiline-based regimen. Of these, 177 (17.33%) were shifted to a Bedaquiline–Delamanid-based regimen due to adverse drug reactions or specific drug-resistance profiles. Among these patients, 94 (53.10%) were female and 83 (46.89%) were male. The age distribution was 8–17 years (29 patients) and 18–65 years (148 patients). The observed resistance patterns were: rifampicin, both inhA and katG, and fluoroquinolone (FQ) – 10 (5.6%); rifampicin, katG, and FQ – 33 (18.63%); rifampicin, inhA, and FQ – 1 (0.56%); rifampicin and FQ – 40 (22.59%); and FQ-resistant alone – 93 (52.54%).

Conclusion: Drug-resistant tuberculosis (DR-TB) remains a major public health challenge requiring prolonged, complex therapy. Bedaquiline and Delamanid have shown promising outcomes in DR-TB management. Routine molecular testing for MDR, pre-XDR, and XDR-TB prior to treatment initiation, along with drug susceptibility testing (DST) for Bedaquiline and Delamanid, is essential to ensure effective, individualized therapy and to prevent further resistance.

Keywords: MDR-TB, Bedaquiline, Delamanid, drug resistance, molecular testing, DST

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75. **P-33: Charintip Yenyuvadee** (Medical Life Sciences Institute, Department of Medical Science, MOPH, Thailand)

Comparative Analysis of Phenotypic and Whole Genome Sequencing for Drug Susceptibility Testing in *Mycobacterium tuberculosis* Isolates.

Full author list: Charintip Yenyuvadee (1), Waraporn Thuansuwan (2), Thanyanuch Sanchat (2), Pundharika Piboonsiri (1) and Waritta Sawaengdee (1)

(1) Medical Life Sciences Institute, Department of Medical Science, Ministry of Public Health, Nonthaburi, Thailand

(2) Central Chest Institute of Thailand, Nonthaburi, Thailand

Accurate and rapid detection of drug-resistant tuberculosis is essential for guiding effective treatment and controlling transmission. Whole Genome Sequencing (WGS) offers a genotypic approach to predict drug susceptibility, complementing phenotypic testing. This study quantified and characterized the concordance between WGS and phenotypic solid drug susceptibility testing (pDST) for six key anti-tuberculosis drugs in 233 *Mycobacterium tuberculosis* isolates from the Central Chest Institute of Thailand. Resistance profiles obtained by pDST and WGS were directly compared. For first-line drugs, WGS demonstrated high sensitivity and specificity for isoniazid (97.2% and 98.1%, respectively) and rifampicin (95.0% and 95.6%), while ethambutol showed very high sensitivity (98.2%) but lower specificity (90.4%). Among second-line drugs, WGS achieved moderate sensitivity for moxifloxacin and levofloxacin (86.4% each) with excellent specificity (99.5% for both), and for streptomycin, sensitivity and specificity were 90.8% and 89.6%, respectively. Compared with pooled WHO data from 52,567 isolates, local WGS sensitivity was higher for isoniazid, ethambutol, and streptomycin, while performance for fluoroquinolones was comparable; specificity estimates were generally similar, although slightly lower for some drugs, reflecting regional variation in resistance-associated mutations. Overall, WGS demonstrated reliable performance for detecting resistance to both first- and second-line anti-tuberculosis drugs, supporting its integration into routine diagnostics to enable rapid resistance profiling, inform individualized treatment, and strengthen surveillance of drug-resistant TB.

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76. **P-34: Ye Win Aung** (Department of Microbiology, Faculty of Medicine, Khon Kaen University, Thailand)

Heteroresistance of *Mycobacterium tuberculosis* in the sputum detected by Droplet Digital PCR

Full author list: Ye Win Aung[1], Arunne Sangka[2], Kanchana Tomanakan[3], Kiatichai Faksri[1] and Wises Namwat[1],*

1Department of Microbiology, Faculty of Medicine, Khon Kaen University, Khon Kaen 40002, Thailand

2Faculty of Associated Medical Science, Khon Kaen University, Khon Kaen 40002, Thailand

3Department of Medical laboratory, Khon Kaen Hospital, Khon Kaen 40002, Thailand

*Corresponding author: wisnam@kku.ac.th

Heteroresistance of *Mycobacterium tuberculosis* (MTB) is considered a preliminary stage to full resistance. The prevalence of multidrug- and rifampicin-resistant tuberculosis was 3.5% of new TB cases and 18% of previously treated TB cases shown in Global TB report in 2018. Here, we determined the heteroresistance of MTB in the sputum of new TB cases by using droplet digital PCR. The most common point mutations of *rpoB* and *katG* genes, which associated to rifampicin (RIF) and isoniazid (INH), respectively, were also investigated. Nine (11.4%) of 79 samples of new TB patients were found those mutations. INH mono-resistant TB, RIF mono-resistant TB and MDR-TB were 1.3%, 6.3% and 3.8% of new TB cases, respectively. Among 9 DR-TB cases, 1, 5 and 3 were INH mono-resistant TB, RIF mono-resistant TB and MDR-TB, respectively. Four of 9 DR-TB cases were found as heteroresistance of MTB and only one case was fully resistance of MDR-TB. The percentage of the mutant clone in DR-TB cases varied from 5 to 95% of MTB population. We concluded that these heteroresistance detected in MTB might be naturally occurred in the body because the patients were not given anti-TB drugs yet at the time of sample collection.

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77. **P-35: Arkan Hidayat** (Stem Cell and Cancer Institute, Indonesia)

Performance of Wide-Coverage Open-System RT-PCR to Detect *Mycobacterium tuberculosis*, Rifampicin, and Isoniazid Resistance in Sputum Samples from Presumed Pulmonary Tuberculosis Patients in Indonesia

Full author list: Arkan Hidayat (1), Dilafitria Fauza (1), Bella Valeria (1), Muhammad Yunus (1), Dini Budhiarko (1), Franny Budiono (2), Ida Parwati (3), Lidya Chaidir (4), and Akterono Budiyati (1)

Stem Cell and Cancer Institute, Indonesia
Balai Besar Kesehatan Paru Masyarakat (BBKPM) Bandung, Indonesia
Department of Clinical Pathology, Faculty of Medicine, Universitas Padjadjaran/Dr. Hasan Sadikin General Hospital, Bandung, Indonesia
Department of Biomedical Sciences, Faculty of Medicine, Universitas Padjadjaran, Bandung, Indonesia

Tuberculosis in Indonesia remains a health burden due to its mortality rate. Rapid and reliable diagnostic testing is important and could determine the treatment outcome. The current WHO recommended detection system contributes significantly to rapidly detecting TB infection, particularly in MDR/RR TB cases. However, the recent US funding cut also impacted Indonesia to obtain the cartridge required for sample testing. Despite the urgent need, a low-cost alternative with similar target coverage and performance is currently absent. In this study, we aim to establish an open-system Real-Time PCR (RT-PCR) assay that not only covers IS*6110* and all 81-bp of rifampicin resistance-determining regions but also capable to detect mutations in katG (S315L, S315N, S315T, S315T2) and inhA (T-8A, T-8C, C-15T) genes associated with isoniazid resistance. To assess the performance of the designed assay, sputum specimens were collected from 73 subject with presumed TB who visited BBKPM Bandung and RC3ID Padjajaran University, Indonesia. The specimens were examined using our open-system RT-PCR, acid fast bacillus (AFB) smear microscopy, MTB culture, drug susceptibility testing (DST), and GeneXpert assay. Statistical analysis was done using Fisher's exact test. The results showed that the assay could detect MTB with 100% sensitivity (95%CI [94.22, 100.00]) and specificity (95%CI [71.51, 100.00]) compared to bacterial culture with Kappa value of 1. Compared to DST, sensitivity and specificity of developed assay to detect INH-resistance were 78.57% (95%CI [63.19, 89.70]) and 100% (95%CI [76.84, 100.00]) and RIF-resistance were 94.12% (95%CI [80.32, 99.28%]) and 100% (95%CI [86.77, 100.00]), respectively. This study concludes that the assay demonstrates comparable performance and could serve as a reliable assay to detect MTB along with MDR/RR TB in routine testing.

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78. **P-36: Muhammad Mu'iz Ehsannudin bin Abu Bakar** (National Mycobacteria Reference Laboratory, Department of Laboratory Services, Ministry of Health, Brunei Darussalam)

High prevalence of inducible macrolide resistance in *Mycobacterium abscessus* Complex revealed by nationwide implementation of the GenoType NTM-DR Assay in Brunei Darussalam.

Muhammad Mu'iz Ehsannudin bin Abu Bakar

National Mycobacteria Reference Laboratory, Department of Laboratory Services, Ministry of Health, Brunei Darussalam

Background: Non-tuberculous mycobacteria (NTM), particularly the *Mycobacterium abscessus* complex, pose a significant therapeutic challenge due to their intrinsic and acquired resistance to antibiotics, especially macrolides. The GenoType NTM-DR line probe assay enables rapid detection of subspecies and resistance-determining mutations, guiding critical early treatment decisions. This study presents the first nationwide data from Brunei Darussalam on the molecular epidemiology and resistance markers of NTM using this advanced assay.

Methodology: A laboratory-based analysis was conducted on all clinical NTM isolates subjected to the GenoType NTM-DR assay (Hain Lifesciences, Germany) at the National Mycobacteria Reference Laboratory. Results were compiled from the national NTM registry, encompassing data from the assay's implementation through September 2025.

Results: As of September 2025, a total of 127 NTM isolates were characterized using the NTM-DR assay. The *Mycobacterium abscessus* complex was the most prevalent group, accounting for 71 isolates (55.9%). Within this complex, *M. abscessus* subsp. *massiliense* was the dominant subspecies (n=44, 62.0% of complex), followed by *M. abscessus* subsp. *abscessus* (n=27, 38.0%). Critically, analysis of the erm(41) gene revealed that 13 of the 27 *M. abscessus* subsp. *abscessus* isolates (48.1%) harbored the T28 sequevar, conferring inducible resistance to macrolides. No mutations associated with constitutive macrolide resistance (rrl) or aminoglycoside resistance (rrs) were detected in the *M. abscessus* complex isolates. The remaining isolates identified by the assay belonged primarily to the *Mycobacterium avium* complex (n=56, 44.1%).

Conclusion: This comprehensive dataset confirms the dominance of the *M. abscessus* complex among clinically relevant NTMs in Brunei. The finding that nearly half of all *M. abscessus* subsp. *abscessus* isolates carry inducible macrolide resistance is a major concern for clinical management, as it predisposes patients to treatment failure with macrolide-based regimens. The successful nationwide implementation of the GenoType NTM-DR assay provides a critical tool for the rapid, molecular-guided therapy of NTM infections, directly impacting public health outcomes in Brunei Darussalam.

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79. **P-37: Selly Erwina** (Faculty of Medicine, Universitas Andalas, Indonesia)

Potency of whole-genome sequencing for mapping lineage and drug resistance of *Mycobacterium tuberculosis* in Indonesia: a systematic review

Full author list: Selly Erwina (1), Muhammad Zaky Innanda (1), Kalaj Nazhiful Haq (1), and SM Rezvi (1)
Faculty of Medicine, Universitas Andalas, Indonesia

Whole-genome sequencing (WGS) has become a transformative method for characterizing lineage diversity and drug resistance in *Mycobacterium tuberculosis* (MTB). Indonesia, as one of the world's highest TB-burden countries, genomic surveillance remains limited and fragmented across regions. This systematic review evaluates the potential of WGS for mapping MTB lineages and drug-resistance mechanisms in Indonesia. A comprehensive search across ScienceDirect, PubMed, and ProQuest identified 233 records, of which 10 studies met inclusion criteria. Extracted data included study characteristics, lineage distribution, resistance-associated mutations, and major findings. Lineage distribution across Indonesia was heterogeneous: Lineage 4 (Euro-American) was predominant, Lineage 2 (Beijing) contributed significantly to transmission and drug resistance, and Lineage 1 (Indo-Oceanic) was enriched in eastern regions such as Papua. WGS reliably detected major resistance-related mutations, with rpoB S450L and H445D being the most frequently reported variants associated with rifampicin resistance. Isoniazid resistance was predominantly linked to katG S315T and *inhA* promoter mutations, while pyrazinamide resistance displayed substantial genetic diversity due to multiple distinct *pncA* variants. Ethambutol resistance was commonly associated with embB M306V/I. Concordance between WGS-predicted and phenotypic results was consistently high for rifampicin and isoniazid, highlighting the reliability of WGS for resistance prediction. Occasional discrepancies were mainly related to the inherent variability of *pncA,* a pattern that aligns with global findings. Several studies also reported region-specific mutations, highlighting the need for locally curated genomic reference databases. Despite its considerable potential, WGS implementation in Indonesia faces challenges, including small sample sizes, unequal regional representation, and limited sequencing capacity. Overall, this review demonstrates that WGS offers substantial advantages for Indonesia's TB control program through precise lineage mapping, accurate and early detection of drug resistance, and enhanced genomic surveillance to monitor transmission and emerging resistance patterns.

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