

Newsletter



IN THIS ISSUE

CONTRIBUTIONS TO WHO GUIDANCE

EXPEDIENTS & TB DRUGS

TRACCOLADES

PUBLICATION HIGHLIGHT

UPCOMING EVENTS

BULLETIN BOARD

RECENT PUBLICATIONS

The World Health Organization (WHO) recently released new recommendations on TB and undernutrition as part of the WHO consolidated guidelines on tuberculosis. Module 6: tuberculosis and comorbidities. TRAC faculty, Peter Cegielski, MD, MPH, served on the Guideline Development Group and played a key role in developing the latest guidelines, which mark a significant step in advancing people-centered care under WHO's End TB Strategy. Key recommendations include 1) nutritional assessment and counseling for all people with TB and their household contacts, 2) provision of nutritional interventions to optimize clinical outcomes in people with TB who have undernutrition, regardless of age, drug resistance, pregnancy, or severity of undernutrition, and 3) provision of food assistance to prevent TB in household contacts of people with TB in food insecure settings. Dr. Cegielski first researched and wrote about nutrition and TB risk for his MPH thesis in 1992-1995 - research at the Master's level can make a difference!

In a recent Call to Action and Consensus Statement, WHO urges for an end to the routine exclusion of pregnant and lactating women from TB research. This landmark initiative outlines a comprehensive framework to ensure equitable access to TB innovations for all, including those most at risk. The consensus statement and call to action are the result of a WHO-led process involving over 80 global experts. TRAC faculty, Lisa Marie Cranmer, MD, MPH, served as co-chair of the TB Vaccine Trials Working Group and co-authored the review on inclusion of pregnant and lactating women in trials. Key actions in the call include 1) closing data gaps on TB in pregnancy and postpartum through improved surveillance and reporting, 2) initiating timely preclinical studies to assess efficacy and safety of novel TB compounds and vaccines in pregnancy, 4) including pregnant and lactating women in all stages of TB drug trials, 5) including pregnant and lactating women in adult TB vaccine research for candidates with a favorable risk-benefit profile and plan for rollout and monitoring, 6) creating enabling environments by addressing legal, ethical, and regulatory barriers, and 7) engaging and empowering affected communities to ensure research is inclusive, respectful, and responsive.

Excipients increase the efficacy of TB drugs

world cand His golini the das de come

Thomas Manning, PhD, MS, is a chemist at Valdosta University working on drug development spanning the treatment of cancer, bacterial and viral infections and neurological diseases. His group has 20 novel complexes that have entered preclinical trials and is also developing an excipient that increases the efficacy of antibiotics for the treatment of TB. An excipient as defined by the World Health Organization (WHO) "...is any component of a drug product other than the active pharmaceutical ingredient". Expedients are often referred to as

pharmaceutical ingredient". Expedients are often referred to as "inactive ingredients" although they serve critical roles in the formulation, stability, delivery, and acceptability of the drug product. In collaboration with the National Institute for Allergy and Infectious Diseases (NIAID) Dr. Manning's group has shown copper (II) markedly increases the efficacy of capreomycin

against drug resistant strains of *Mtb* in vitro, while copper (II) by itself has no efficacy against the bacteria. The international patent which is based on the <u>U.S.</u> patent was

recently approved in the Czech Republic and Slovakia. Copper (II)'s impact on Mtb may involve a range of actions, varying from generating destructive reactive oxygen species to binding amines on proteins and impacting their ability to function. Perhaps the best example of copper (II) as an exipient is how it can synergize with disulfiram to overwhelm Mtb's chemical defense systems (Dalecki et al.). Dr. Manning would like to thank the NIAID, the National Cancer Institute and the National Magnet lab for their collaboration and spectacular work. We look forward to learning more about Dr. Manning's work in the near future.

TRAColades

A huge congrats to TRAC Clinical Core Co-director, Sarita Shah, MD, MPH, on her NIH R01 award titled "Infectiousness and social mixing in asymptomatic TB as a driver of population-level transmission (INSPIRE)". Although asymptomatic TB may account for up to half of bacteriologically confirmed TB globally, there is limited understanding of infectiousness during this stage. Asymptomatic spread is an established paradigm for several infectious diseases but is yet to characterized for TB.



The study will use multiple TB diagnostic tests among close contacts of people with TB to determine the onset of infectiousness and measure social contact patterns along the spectrum of TB disease. These data will be used to model the proportion of TB transmission that occurs during early-stage disease, particularly in community settings. Additional TRAC co-investigators include **Drs. Neel Gandhi, Kristin Nelson, Samuel Jenness, Jeffrey Collins, and David Benkeser.**



Kudos to Terra Riddock, doctoral candidate in the Emory Immunology and Molecular Pathogenesis Graduate Program for being selected as a trainee in the Center for AIDS Research Emory Training Program in HIV Translational Research to End the Epidemic T32 program. Terra is conducting her PhD in TRAC Co-director, Dr. Jyothi Rengarajan's, lab in the Emory Vaccine Center. Her thesis project is titled "Investigating mechanisms of impaired alveolar macrophage responses to Mtb in People with HIV."



The Ethiopia-Emory TB Research Training Program (EETB-RTP) recently launched an Accelerator award (\$4,000) program to support current and former EETB-RTP Fogarty trainees. The award aims to support critical, ongoing TB research and help fill key funding gaps. Congratulations to the first five recipients: Abenezer Dereje Abebe, MD (Investigating the role of matrix metalloproteinase during active Tuberculosis infection and following treatment completion among participants in Addis Ababa, Ethiopia), Fregenet Tesfaye Tegegn, PhD (Immune Dynamics Profiling in Women with TB Infection During Pregnancy and Postpartum), Kelemework Adane Asmare, PhD (Leveraging the Accelerator Award for the Isolation and Drug-susceptibility Testing of Mycobacterium tuberculosis Strains), Meseret Habtamu Mekonnen, PhD (Immune Profiling in Tuberculosis: Revealing Protective Immunity and Disease Dynamics (ImProf-TB), and Tesemma Sileshi Chala, PhD (Evidence Synthesis on Bedaquiline Pharmacokinetics, Pretomanid Drug Resistance, and Laboratory Training).

Congrats to Zaynab Mousavian, PhD, Emory TRAC postdoctoral researcher, working with Drs. Jeffrey Collins and Matthew Magee on her presentation title "Machine learning of plasma multi-omics data distinguishes pulmonary tuberculosis from other respiratory infections" at the 2025 Bay Area TB Science (BATS) Symposium in San Francisco on September 25th. The Symposium was hosted by the University of California San Francisco Center for TB

Publication Highlight

TRAC Bioinformatics and Systems Biology Co-director, Jeffrey Collins, MD, MSc, and Developmental Core Codirector, Russell Kempker, MD, MSc's, viewpoint article titled "A metabolic syndrome: Understanding host factors that drive mortality in tuberculosis meningitis" reflects on an a study published in Cell Press by Nhat et al. titled 'Pre-treatment untargeted cerebrospinal fluid metabolomic profiling in tuberculous meningitis uncovers pathways associated with mortality'.

TB meningitis (TBM) is the most lethal manifestation of TB disease, and the rates of TBM mortality and neurological morbidity among TBM survivors are unacceptably high and have not improved in 30 years. Drs. Collins and Kempker conclude that

Nhat et al. shed light on the important role of novel cutting-edge methods in understanding the underlying pathophysiology of TBM, namely the critical role of energy metabolism in the host response, which offers exciting new avenues to explore potential host-directed therapy targets.

Upcoming Events TB WORKS IN PROGRESS SEMINAR: DEVELOPMENT AND VALIDATION OF TREATMENT DECISION ALGORITHMS FOR PEDIATRIC TUBERCULOSIS

Friday October 17th, 2025, 9–10 am CNR Room 3001 and Zoom [Flyer]

Amyn A. Malik, MPH, PhD, MBBS, is an Assistant Professor of Epidemiology at O'Donnell School of Public Health, UT Southwestern Medical Center, Dallas, Texas, and an infectious disease epidemiologist. Dr. Malik's research portfolio and interests include work on Drug Susceptible and Drug Resistant TB, Pediatric TB, contact tracing, and provision of TB preventive treatment. Dr. Malik has been part of implementing several global

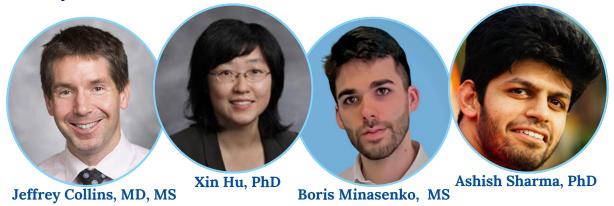
health research and delivery programs including grants from the National Institutes of Health, Bill and Melinda Gates Foundation, The Global Fund, and the Stop TB Partnership.

VOL. 32 OCTOBER 2025

SYSTEMS BIOLOGY VIRTUAL & IN-PERSON OFFICE HOURS



4th Thursday of the month Aug-Oct & Dec 11 10-11am ET, RRR 205 & Zoom



Drop in to receive one-on-one support from informaticists with 'omics' study design and data analysis for tuberculosis research -

including bulk and single cell transcriptomics, metabolomics and lipidomics. For more information please contact:

jeffrey.michael.collins@emory.edu



Bulletin Board



The expected outcomes of the TRAC Bridge Award are to provide support to help mitigate the effects of federal funding cuts on TB investigators through helping investigators complete and publish partially completed aims and sub-aims, pivot to new areas of TBrelated research, develop new collaborations, and generate preliminary data for future grant applications. Please review the full RFA here.



Recent NIH Notices and Updates



- Updated NIH Policy on Foreign Subawards, NOT-OD-25-104, May 1, 2025
- New Application Structure for NIH-Funded International Collaborations, NOT-OD-25-155, September 12, 2025
 - <u>FAQs for Foreign Subawards</u> (applications with foreign subawards will be withdrawn for due dates on or after September 25, 2025.
- <u>Updated NH Processes for No-Cost Extensions</u>, NOT-OD-25-110, May 7, 2025
- Update: No-Cost Extension Functionality in eRA, NOT-OD-25-142, August 7, 2025
- Early Stage Investigator (ESI) Eligibility Extension and Reinstatement. NIH has granted automatic extension of ESI eligibility for those impacted by delays in grant application submissions, peer review, or award processing timelines between January 1 May 1, 2025. See <u>FAQs</u>
- <u>Supporting Fairness and Originality in NIH Research Applications</u>, NOT-OF-25-132, July 15, 2025
 - NIH will only accept six new, renewal or revision applications from a PD/PI for all council rounds in a calendar year. See updated **FAQs**.
- NIH Will Stop Posting Notices of Funding Opportunities in the NIH Guide for Grants and Contracts in FY2026, NOT-0D-25-143, August 14,2015
- NIH Director Statement: Advancing NIH's Mission Through a Unified Strategy NIH Priorities, August 15, 2025

September Publications

Bwambale K, Nakkonde D, Nassanga G, Buregyeya E, **Zalwango S, Sekandi JN**. <u>TB-Related Stigma: A Hidden Obstacle to Adherence Monitoring with Video Directly Observed Treatment Among Patients with Tuberculosis in Uganda</u>. Res Sq. 2025. DOI: 10.21203/rs.3.rs-7447805/v1.

Carpi G, Seifert M, De la Rossa A, Uplekar S, Rodrigues C, **Tukvadze N, Omar SV**, Suresh A, Rodwell TC, Colman RE. <u>Comparative assessment of line probe assays and targeted next-generation sequencing in drug-resistant tuberculosis diagnosis</u>. <u>EBioMedicine</u>. 2025;119:105875. DOI: 10.1016/j.ebiom.2025.105875.

Cherezov D, Dam T, Najjingo I, Mbabazi M, Kisembo H, Kirenga B, Soka G, Ngadaya E, Mfinanga S, Madabhushi A. <u>Opportunistic use of artificial intelligence with X-ray imaging for diagnosis of HIV status in tuberculosis patients in Uganda and Tanzania.</u> PLOS Digit Health. 2025;4(9):e0000988. DOI: 10.1371/journal.pdig.0000988.

Choshi P, Pedretti S, Chimbetete T, Gangula R, Shey M, Stek C, Lai RPJ, Wilkinson R, **Meintjes G**, Phillips E, Peter J. <u>The association of class II HLA alleles with tuberculosis-associated immune reconstitution inflammatory syndrome.</u> PLoS Pathog. 2025;21(9):e1013497. DOI: 10.1371/journal.ppat.1013497.

Collins JM, Bobosha K, Narayanan N, Gandhi NR, Day CL, Rengarajan J, Kempker RR, Lau MSY, Nellis M, Tukvadze N, Shah NS, Brust JCM, Nizam A, Ismail NA, Kauffman KD, Sakai S, Jones DP, Barber DL, Ziegler TR, Ernst JD, Blumberg HM, Wassie L. <u>A Plasma Metabolic Signature to Diagnose Pulmonary Tuberculosis and Monitor Treatment Response.</u> J Infect Dis. 2025;232(3):578-87. DOI: 10.1093/infdis/jiaf240.

Collins JM, Kempker RR. <u>A metabolic syndrome: Understanding host factors that drive mortality in tuberculosis meningitis</u>. Med. 2025;6(9):100705. DOI: 10.1016/j.medj.2025.100705.

de Nooy A, **Omar SV**, Ockhuisen T, Zwerling A, Shrestha S, Suresh A, Khan S, Colman RE, Uplekar S, Rodwell TC, Ismail N, Grantz K, Girdwood S, Nichols BE. <u>Cost-effectiveness of Targeted Next Generation Sequencing for TB drug-resistance testing as an alternative to the standard of care in South Africa. Clin Infect Dis. 2025. DOI: 10.1093/cid/ciaf495.</u>

Esmael A, Mihret A, Abebe T, Mussa D, Neway S, **Ernst J, Rengarajan J, Wassie L**, Howe R. <u>Activation and proliferation profiles of M. tuberculosis specific dual functional CD4+T cells from smear negative pulmonary TB patients.</u> PLoS One. 2025;20(9):e0327243. DOI: 10.1371/journal.pone.0327243.

Grint DJ, Dhillon J, Butcher PD, Adams J, Munshi T, Witney AA, Gould K, Laing K, Cousins C, **Wasserman S**, Fielding K, Harrison T, Jindani A. <u>Xpert MTB/RIF® cycle threshold as a marker of TB disease severity; Implications for TB treatment stratification</u>. Clin Infect Dis. 2025. DOI: 10.1093/cid/ciaf527.

Houben R, Veeken LD, Schwalb A, Grint DJ, **Wasserman S**, van Crevel R, Horton KC. <u>Do no harm - reevaluating the risks of overtreatment in community-wide tuberculosis screening</u>. medRxiv. 2025. DOI: 10.1101/2025.09.18.25335917.

Kendall MA, Hughes MD, Kim S, Aaron LA, Naini L, Suryavanshi N, **Shah NS**, Rouzier V, Hafkin J, Sise T, Beck J, Heckman BE, Haberer JE, Harrington M, Scarsi KK, Hesseling AC, Swindells S, Churchyard GJ, Gupta A. <u>Protecting households on exposure to newly diagnosed index multidrug-resistant tuberculosis patients: Study protocol for the PHOENIx phase 3 clinical trial.</u> Contemp Clin Trials. 2025;158:108084. DOI: 10.1016/j.cct.2025.108084.

Kurbatova EV, Dooley KE, **Carr W**, Stout JE, Nuermberger EL, Phillips PPJ, Scott NA, Upton CM, Ignatius E, Haas M, Walter ND, Traxler RM, Brown NE, Boyd R, Bryant KE, Dixon MG, Savic R, Eichberg C, Hesseling A, Bark C, Benator DA, Muzanyi G, Twycross NS, Fox GJ, Pierre S, Burzynski J, Fitzgerald DW. <u>Phase 2C clinical trial of novel short-course regimens for the treatment of pulmonary tuberculosis: TBTC study 38/CRUSH-TB design. Contemp Clin Trials. 2025;158:108075. DOI: 10.1016/j.cct.2025.108075.</u>

Metcalfe JZ, Weir IR, Scarsi KK, Mendoza-Ticona A, Pierre S, Hall L, Leon-Cruz J, Svensson EM, Koele SE, Samaneka W, Kanyama C, Yohane M, Nevrekar N, Ntsalaze B, Marc JB, Goth M, **Maartens G**, Chaisson R. <u>A 3-month clofazimine-rifapentine-containing regimen for drug-susceptible tuberculosis versus standard of care (Clo-Fast): a randomised, open-label, phase 2c clinical trial</u>. Lancet Infect Dis. 2025. DOI: 10.1016/s1473-3099(25)00436-0.

Rossi-Smith P, Kim J, Skirlo K, Ferris T, Green JP, Stek C, Huse KK, Mortimer PM, Olona A, Wieder C, Moseki R, Silva Dos Santos M, MacRae JI, Sriskandan S, Ebbels TMD, Wilkinson RJ, Denton AE, Matheson NJ, Anand PK, **Meintjes G**, Thomas DC, Lai RPJ. <u>Taurine transport is a critical modulator of ionic fluxes during NLRP3 inflammasome activation</u>. Cell Rep. 2025;44(10):116317. DOI: 10.1016/j.celrep.2025.116317.

Rupasinghe P, Ismail N, Mulders W, Warren RM, Joseph L, Ngcamu D, Gwala T, **Omar SV**, Vereecken J, de Jong BC, Rigouts L, Borroni E, Cirillo DM, Schön T, Miotto P, Köser CU. <u>In vitro exposure to clofazimine can select for delamanid and pretomanid resistance in Mycobacterium tuberculosis.</u>
Antimicrob Agents Chemother. 2025:e0111325. DOI: 10.1128/aac.01113-25.

Selvavinayagam ST, Anusree A, Yong YK, Sankar S, Frederick A, Rajeshkumar M, Kumar MS, Sampath P, Sankar G, Roy CL, Karishma SJ, Murugesan A, Balakrishnan P, Govindaraj S, Byrareddy SN, **Velu V**, Shankar EM, Larsson M, Kannan M, Raju S. <u>Clinical laboratory analytes and platelet-associated parameters as surrogate markers of subclinical inflammation in latent tuberculosis infection.</u> Front Immunol. 2025;16:1662454. DOI: 10.3389/fimmu.2025.1662454.

Sobol R, **Omar SV**, Brown T, Joseph L, Lutchminarian K, Tang L, Lan Y, Willis F, Campbell A, Warren JL, Cohen T, **Brust JCM**, **Naidoo K, Shah NS**, **Gandhi NR**, Mathema B. <u>Transmission of Bedaquiline-resistant Mycobacterium tuberculosis in KwaZulu-Natal, South Africa.</u> Am J Respir Crit Care Med. 2025. DOI: 10.1164/rccm.202506-1489OC.

Sodeke O, **Shah NS**, Pals S, Riabokon S, Samsonova O, Mishara F, Doan I, Hetman L, Barzilay E, Podolchak N, Da Silva J. <u>Lower Tuberculosis Incidence Among People With HIV Who Completed Isoniazid Preventive Therapy in Ukraine, a High-Burden Multidrug-Resistant Tuberculosis Setting: A Retrospective <u>Cohort Study.</u> Clin Infect Dis. 2025;81(2):314-21. DOI: 10.1093/cid/ciaf069.</u>



Have items to include in a future newsletter?
Email:
lisa.sharling@emory.edu

CITE THE TRAC
P30AI168386



WEBSITE TB.EMORY.EDU