A closer look at the Physiologic Biomarker (PhyBM) Preclinical Laboratory

Who we are: We are a joint team of scientists that cooperatively develops and advances new molecular tools for drug evaluation while probing the effect of drugs on bacterial phsiology.

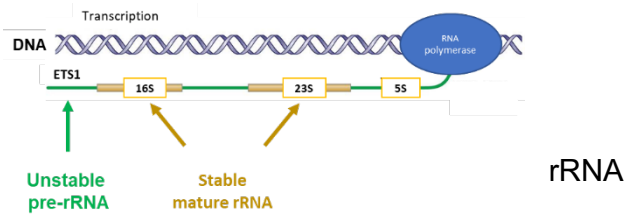
Our novel approach: Our focus is on measurement of pathogen health rather than pathogen burden. Antimicrobials have long been been evaluated based on the degree to which they reduce the burden of bacteria such as *Mycobacterium tuberculosis.* However, because certain antibiotics contribute to cure without reducing burden, we know that antibiotics do more than simply reduce bacterial burden. Evaluating only burden misses these important effects. Our novel approach is harnessing the effect of drugs on the physiologic processes of *M. tuberculosis* for pharmacodynamic evaluation.

Our goal: To develop and bring to practice new tools for antibiotic evaluation that will accelerate antibiotic selection and advancement,

Our tools: Our portfolio of molecular assays includes tools that evalute pathogen health as indicated by bacterial physiologic proceses.

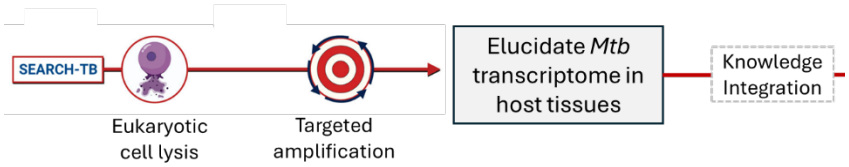
RS RATIO

A digital PCR assay of onging ribosomal RNA synthesis based on abundance of unstable precursor relative to stable mature rRNA.



rRNA

SEARCH-TB



Ongoing methods development: With support from PReDiCTR-TB, we are developing high-throughput methods amenible for drug screening.

Our contributions: Our innovations are further described in the manuscripts below.

- "Mycobacterium Tuberculosis Precursor rRNA as a Measure of Treatment-Shortening Activity of Drugs and Regimens." *Nature Communications* 12 (May 2021): 2899.
- "Combination of Mycobacterium Tuberculosis RS Ratio and CFU Improves the Ability of Murine Efficacy Experiments to Distinguish between Drug Treatments." *Antimicrobial Agents and Chemotherapy* 66, no. 4 (2022): e0231021.
- "Lung Microenvironments Harbor Mycobacterium Tuberculosis Phenotypes with Distinct Treatment Responses." *Antimicrobial Agents and Chemotherapy* 67, no. 9 (2023): e0028423.
- "Deconvoluting Drug Interactions Using M. Tuberculosis Physiologic Processes: Transcriptional Disaggregation of the BPaL Regimen in Vivo." *Antimicrobial Agents and Chemotherapy*, September 18, 2025, e0049225.
- "Emergence of Antibiotic-Specific Mycobacterium Tuberculosis Phenotypes during Prolonged Treatment of Mice." *Antimicrobial Agents and Chemotherapy* 0, no. 0 (2025): e01310-24.
- "Transcriptional Adaptation of Mycobacterium Tuberculosis That Survives Prolonged Multi-Drug Treatment in Mice." *mBio* 14, no. 6 (2023): e0236323.
- "Standardized RS Ratio Metrics to Assess Tuberculosis Antimicrobial Efficacy and Potency." *Antimicrobial Agents and Chemotherapy* 67, no. 1 (2023): e0148322.