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DEFENSE OF THE DOCTORAL
DISSERTATION

**“Development of biomarkers and investigation of host
immune responses in Tuberculosis”**

by

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Tuesday, Aug 23rd, 2022
10:00 AM

Join in person: ICPH Auditorium C109 – Space limited

Join Zoom Presentation:

<https://rutgers.zoom.us/j/92963739869?pwd=bnlCR01zMWpnb0d5TjZ5azlUbXh4dz09>

Meeting ID: 929 6373 9869
Password: 211737

ABSTRACT

Tuberculosis (TB), an ancient disease, continues to be among the leading causes of mortality worldwide, now far worsened by the devastating effects of the COVID-19 pandemic. Exposure to *Mycobacterium tuberculosis* (Mtb) aerosols leads to infection in most individuals. However, a proportion of frequently exposed individuals are resistant to infection. Among infected individuals, outcomes range from latent infection, subclinical disease to active TB disease. Furthermore, individuals with active TB show heterogeneity in transmission. Currently, several questions remain unanswered in the natural history of Mtb exposure, infection and progression to disease: I) Why are some individuals protected from infection while others become infected? II) What host-pathogen factors drive heterogeneity in transmission III) In populations with high TB risk, can a host-based triage test segregate active TB from other respiratory infections with similar symptoms? This thesis leverages peripheral blood specimens and Mtb-strains collected from well-established cohorts of TB patients and their household contacts (HHC) from India and Brazil, and endeavors to address the above questions in three independent investigations. From these three studies: 1) we developed host diagnostic and predictive biomarkers for intended use among TB high-risk groups, using computational tools and the NanoString platform; 2) we identified T-cell mediated IFN- γ -independent resistance to Mtb infection in highly exposed individuals that remain persistently negative to the TST and IGRA screening tests (“resisters”); and 3) we identified two qualitatively distinct neutrophil subsets that contribute to the distinct immunopathologies and heterogeneity in high- and low-transmission Mtb infections, using the Mtb-susceptible C3HeB/FeJ mouse model. These combined approaches enable the development and clinical translation of candidate host biomarkers to screen and stratify individuals by TB risk, identify novel correlates of protection against Mtb infection and provide new strategies that can predict and/or mitigate Mtb transmission.