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UMPA Postdoc Spotlight Series

Spring Edition

Article | Open Access | Published: 18 February 2021

Gastrointestinal microbiota composition predicts peripheral inflammatory state during treatment of human tuberculosis

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Nature Communications **12**, Article number: 1141 (2021) | Cite this article

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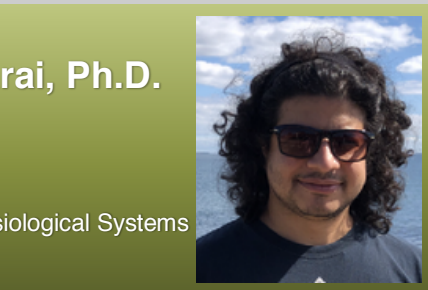
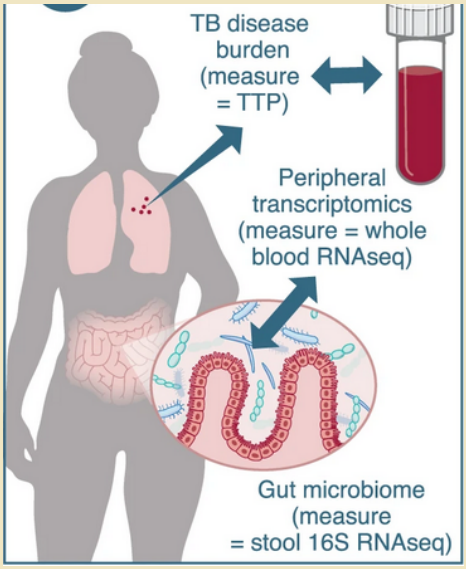
Microbiology and Physiological Systems





I am a postdoctoral researcher in Bucci Lab. I am interested in using machine learning models to increase the biological understanding of omics data associated with clinical phenotypes. During my PhD, I was mainly involved in two projects: i) Understanding the dynamics of gut microbiome and its effect on host inflammatory response during tuberculosis treatment ii) Identifying gut microbial species as a biomarker to differentiate elderly with Alzheimer's disease. In my spare time, I like to program in R and enjoy exploring data visualization techniques.

Active TB disease is one of the leading causes of death worldwide. Individuals infected with Mtb causes heightened expression of inflammatory pathway, mainly, Type I and Type II interferon pathways and resolves with antibiotic therapy (HRZE).

Previous studies have shown that early phase of antibiotic TB treatment rapidly reduces the burden of Mtb but causes shifts in gut microbiota by depleting many Clostridia species which may play a role in host immunomodulation.

In our study, we hypothesized that there might be a relation between microbiome alterations and the resolution of inflammatory responses to TB during treatment. To test the hypothesis, we leveraged two longitudinal studies of TB therapy involving 55 individuals and a cross sectional study from 55 healthy controls where we collected fecal samples(microbiome), sputum (Mtb burden) and peripheral blood (RNA-Seq). One subset of the longitudinal cohort involved an experimental TB treatment (NTZ) which didn't reduce the Mtb load. Comparing standard TB treatment with an experimental treatment, we were able to decouple the microbiome effects on host response from pathogen clearance.

Using random forest regression, we found that the renormalization of TB inflammatory state is associated with clearance of MTb, increased abundance of Clusters IV and XIVa Clostridia and decreased abundance of Bacilli and Proteobacteria. Using healthy controls, we find similar associations of microbial species with peripheral gene expressions. Overall, it suggests that antibiotic-induced reduction in pathogen burden and changes in the microbiome are independently associated with treatment-induced changes of the inflammatory response of active TB, and the response to antibiotic therapy may be a combined effect of pathogen killing and microbiome driven immunomodulation.