

Title: Modulation of gut-associated Immune cells in guanyl cyclase C receptor mutant mice using orally delivered particulates

Brief Summary: Past and ongoing work in the laboratories of Sandhya Visweswariah and Siddharth Jhunjunwala demonstrated that an activating mutation in receptor guanyl cyclase C (GCC) alters the type and numbers of immune cells present in the gut. Our primary goal in this project is to understand what signals lead to the alterations in immune cells, and how this might affect the gut pathology in these mutant mice. Does the microbiome induce such changes? While computational analysis of the omics data shows an increase in certain detrimental microbial species, effects on the immunological cell types remain to be understood. Finally, as a possible therapeutic strategy to prevent the negative consequences of this mutation, we propose to test the efficacy of oral particulate delivery to modulate immune responses in the gut.

Whom would the student work with:

- a. Prof. Sandhya Visweswariah (<https://mrdg.iisc.ac.in/sandhya/index.htm>)
- b. Prof. Siddharth Jhunjunwala (<https://jhunjunwalalab.in/>)

Expected learnings for a student from this project:

1. Become an expert in gut physiology and mucosal immune responses, including microbiome analysis by NGS.
2. Understand cellular signaling pathways and means to perturb them to answer questions on how GCC-receptor signaling and immune cells are linked
3. Develop skills to make particulate therapeutics
4. Work with animal models of research and assess therapeutic outcomes in these models

What should the student be comfortable with to take up this project:

1. Basic expertise in biology and mathematics (undergraduate level would suffice)
2. An interest in learning experimental skills and working with animal models for research
3. An interest in computational analysis techniques and analyzing omics data

Relevant Publications

1. Mishra V., Bose A., Kiran S., Banerjee S., A Shah I., Chaukimath P., M Reshi M., Srinivas S., Barman A., **Visweswariah S.S.** (2021) Gut-associated cGMP mediates colitis and dysbiosis in a mouse model of an activating mutation in GUCY2C. *J. Exp. Med.* e20210479. doi: 10.1084/jem.20210479.
2. Prasad H, Mathew J.K.K and **Visweswariah, S.S.** (2022) Receptor Guanylyl Cyclase C and Cyclic GMP in Health and Disease: Perspectives and Therapeutic Opportunities. *Front Endocrinol (Lausanne)*. 13:911459. doi: 10.3389/fendo.2022.911459.eCollection 2022.
3. Sharma P, Vijaykumar A, Raghavan JV, Rananaware SR, Alakesh A, Bodele J, Rehman JU, Shukla S, Wagde V, Nadig S, Chakrabarti S, **Visweswariah SS**, Nandi D, Gopal B, Jhunjunwala S. (2022) Particle uptake driven phagocytosis in macrophages and neutrophils enhances bacterial clearance. *J Control Release* 343: 131-141