Dr. Brantley Hall is a Postdoctoral Fellow at the Broad Institute of Harvard and MIT and the Center for Computational and Integrative Biology at Massachusetts General Hospital and Harvard Medical School. As a postdoc, he was awarded the Helen Hay Whitney Postdoctoral Fellowship. He currently studies alterations to the gut microbiome in IBD in the laboratory of Dr. Ramnik Xavier, and is developing strategies to culture complex gut communities ex vivo to enable experiments to determine how to rationally manipulate the gut microbiome. He received a B.S. in Biological Sciences and a Ph.D. in Genetics, Bioinformatics, and Computational Biology from Virginia Tech. He was also awarded the NSF Graduate Research Fellowship, and the East Asia and Pacific Summer Institutes Fellowship. As an undergraduate, he developed a novel bioinformatic method to identify the first Y chromosome genes in mosquitoes. Then, as a graduate student knocked-out one of these genes using CRISPR to generate the first sex-reversed mosquitoes and identify the first male-determining factor in any insect. These results have been published in first-author manuscripts in Science and PNAS.

Abstract

Dysbiosis of the human gut microbiome, a taxonomic imbalance in community composition, has been associated with numerous diseases including metabolic syndrome and Inflammatory Bowel Disease (IBD). It is widely hypothesized that dysbiotic gut microbial communities can be rationally remodeled to treat a wide variety of these diseases. To realize these goals, the microbiome field must pivot from observational studies to mechanistic investigations to achieve the ultimate goal of manipulating the gut microbiome to treat disease. Here, I will discuss my work with the Longitudinal Stool Study IBD cohort that unravels the causes of dysbiosis of the gut microbiome in IBD, specifically oxidative stress. In the IBD gut, we found a significantly higher abundance of facultative anaerobes that can tolerate the increased oxidative stress characteristic of the IBD gut. We also detected dramatic, yet transient, blooms of Ruminococcus gnavus in IBD patients, often co-occurring with increased disease activity. We identified two distinct clades of R. gnavus strains, one of which is enriched in IBD patients. We identified 199 IBD-specific R. gnavus genes involved in oxidative stress responses, adhesion, iron-acquisition, and mucus utilization, potentially conferring an adaptive advantage for this R. gnavus clade in the IBD gut. I will also discuss the development of an ex vivo gut model using parallel mini-bioreactors enabling the culture of complex polymicrobial communities that will lay the groundwork for rational manipulation of the gut microbiome. The long-term goal of my research program will be to deliberately modulate the gut microbiome to treat IBD and metabolic disorders such as Type 2 Diabetes.