Deciphering the chemical crosstalk of host-gut microbiome interactions

Pamela V. Chang
Department of Microbiology and Immunology
Cornell University

The gut microbiome comprises trillions of microorganisms that inhabit the mammalian intestines. These microbes regulate myriad aspects of host physiology, including factors that modulate many inflammatory diseases. Despite the abundance and prevalence of the gut microbiota, little is known regarding the pathways and mechanisms by which these microbes affect host health. Emerging evidence suggests that many small-molecule metabolites that are produced by the gut microbiota have the ability to modulate host defense mechanisms in various inflammatory diseases. However, the identities of these metabolites, how these metabolites modulate host processes, including the cell types and pathways that they affect, and how these metabolites are produced by the gut microbiota, including the bacteria that produce them and the enzymes that are responsible for their biosynthesis, remain largely uncharacterized. We describe several amino acid-derived metabolites produced by the gut microbiota that improve morbidity in a mouse model of inflammatory bowel disease (IBD). We have characterized the host targets of these metabolites, including a host receptor and downstream pathways that are modulated by the metabolites in vivo. In complementary work, we have also developed chemical approaches for probing the metabolic activities of biosynthetic enzymes expressed by the gut microbiota that are responsible for producing important classes of small-molecule metabolites whose metabolism is dysregulated in IBD. Together, our findings shed light on important, unanswered questions regarding the molecular mechanisms by which the gut microbiome affects host physiology and provide potential targets for prophylactic and therapeutic treatments for ameliorating morbidity in inflammatory diseases of the gut, such as IBD and colorectal cancer.