Metabolism at the Host-Microbe Interface

Jason M. Crawford, Ph.D.
Professor of Microbial Pathogenesis
Associate Professor, Chemistry and Associate
Yale University

The Crawford laboratory focuses on **Metabolism at the Human-Microbe Interface**. High-throughput genome sequencing of bacteria (and fungi) has revealed many highly unusual "orphan" biosynthetic gene clusters suspected of synthesizing novel, structurally diverse, and biologically active small molecules. These types of naturally produced molecules often regulate complex interactions with their animal hosts, hold a rich history of being utilized as human drugs, and serve as excellent molecular probes for identifying new drug targets for a wide variety of diseases. Additionally, there are still many novel metabolites of functional relevance in well-characterized animals, such as humans and mice. Using a blend of small molecule chemistry, protein biochemistry, cell biology, and microbiology, the lab exploits the natural interactions between bacteria and animals to discover new molecules with signaling, antimicrobial, immunomodulatory, and anticancer activities. The lab also connects these products to their underlying biosynthetic genes, characterizes the biosynthetic enzymes involved in their construction, and investigates their roles in biology and medicine.

In this context, we address two major biological questions at the host-bacteria interface, one from the microbe perspective and one from the host perspective: How do bacterial human/mouse microbiome members regulate host responses, such as inflammation, signal transduction, and DNA damage, at the metabolic level? And how do human and mouse immune cells, such as macrophages, rewire immunometabolism in response to microbial insults? In this lecture, an overview will be presented and then an example from each category will be highlighted further.