BRIGHAM AND WOMEN'S HOSPITAL
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Channing Microbiome Seminar

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Unraveling the links between the gut microbiome and type 1 diabetes

Type 1 diabetes (T1D) is an autoimmune disorder that results from T cell-mediated destruction of the insulin-producing beta cells of the pancreatic islets. Although approximately 70% of T1D cases carry predisposing HLA risk alleles, only 3–7% of children with those alleles develop T1D, indicating a significant non-genetic component to the disease. The thesis of my work is that the gut microbiome, the 100 trillion symbiotic bacteria that inhabit the human intestinal tract, is a critical aspect of this non-heritable component. My work has characterized the developing infant gut microbiome in a longitudinal, frequently-sampled, multi'omic analyses of birth cohorts at risk for T1D. In the first study we found that there is a dramatic shift in the composition of the gut microbiome beginning one year prior to clinical diagnosis of T1D, consisting of an overrepresentation in the gut of pro-inflammatory microbes along with an inflammatory metabolic signature. This microbiota may produce a gut mucosal inflammatory stimulus that moves the systemic immune response towards islet autoimmunity in a genetically-prone individual. In our subsequent study we found that prior to the appearance of this pro-inflammatory microbiota, the gut microbiome of children at highest risk for diabetes is dominated by the genus Bacteroides, members of which produce a unique form of lipopolysaccharide (LPS) that we demonstrate nearly completely antagonizes TLR4. Such a microbiota may hamper immune education in the critical early time window. This work has revealed that the balance of LPS subtypes within the gut microbiota and their differential capacity to stimulate innate immunity via endotoxin tolerance is one mechanism by which the human microbiome might influence immune development and progression to T1D. The goal of my future work is to identify additional mechanisms by which the microbiome impacts T1D. I will bring findings from my human studies to the germ-free non-obese diabetic (NOD) mouse to further define the role of the microbiome in T1D.

Bio: My research combines computational and experimental expertise to probe the relationship between the human microbiome and diseases including type 1 diabetes and colorectal cancer. I strive to generate a high-level understanding of how the molecular interactions between the immune system and the intestinal microbiome regulate human health. My background and training spans computational biology, microbiology, and immunology in equal measure.

Hosted by Yang-Yu Liu