PROJECT SUMMARY/ ABSTRACT: SALOMON PROJECT

The intestinal microbiome plays a significant role in maintenance of health and homeostasis. Many disease states are associated with an altered microbiome, known as dysbiosis, which could exacerbate disease and worsen inflammation. Previous data has shown children with congenital heart disease (CHD) have an abnormal intestinal microbiome with increased amounts of proinflammatory bacteria and reduced numbers of healthy beneficial bacteria. These children also undergo cardiac surgery with cardiopulmonary bypass, which is known to cause significant amounts of systemic inflammation and induce intestinal epithelial barrier dysfunction. The systemic inflammation results in low cardiac output state, which is a major contributor to morbidity and mortality in this patient population.

We hypothesize that pre-operative intestinal dysbiosis in pediatric patients with CHD produces inflammatory metabolites that exacerbate CPB-induced intestinal epithelial barrier dysfunction and systemic inflammation. Our specific aims will map the intestinal microbiome and evaluate intestinal metabolite profiles associated with inflammatory signaling mediated through intestinal barrier dysfunction. We will also implement an established piglet model of bypass to evaluate the influence of the microbiome, barrier function, and metabolites on systemic inflammation. Innovation of this study lies in the concept of studying the microbiome in patients with congenital heart disease, biological innovation in being the first to temporally map the microbiome in a variety of cardiac lesions, and technical in the use of an animal model of cardiopulmonary bypass to evaluate the microbiome.

This proposal will yield novel evidence of the role the intestinal microbiome plays in relation to congenital heart disease and the systemic inflammation and patient outcomes following cardiac surgery with cardiopulmonary bypass. Combined, these results will pave the way for future studies targeting interventions on the microbiome to improve patient outcomes following surgery with cardiopulmonary bypass.