Fuel for Survival: metabolic interventions to prevent neonatal sepsis

Background: Of all children that die in the first 5 years of life, half are newborns. Sepsis, a host response to systemic microbial infection, is a leading cause. While vaccines have eliminated a substantial burden of severe infection among older children, most are not given to neonates, and the time required to mount an adaptive immune make them ineffective for neonatal infection prevention. With this, therapies that broadly enhance host resilience to infection, that could work quickly while being feasible to implement in low-resource settings are most likely to make a difference. Our research identified how boosting the newborn's innate immune system with the Bacille Calmette Guerin (BCG) vaccine against tuberculosis offers protection from neonatal sepsis by stimulating the newborn host to rapidly produce mature neutrophils through a process called "emergency granulopoesis", or EG. Our research was motivated by real-world findings from randomized clinical trials showing that BCG vaccination lowered the risk for newborns to die by half. However, not all newborns benefit from BCG vaccination, and we hypothesize that this is because immune boosters like BCG need "fuel" to work. Robust data from human studies had found that newborns that are not fed colostrum, the first breast milk, within an hour of birth are more likely to die from infectious disease. Given the strong relationship between nutrition and immune responses, we are now investigating how there critical first feeds impact on newborn immunity and the response to BCG.

Project details: You will be joining our team within the Canadian Centre for Vaccinology, and the I3V research cluster at Dalhousie University in Halifax, Canada. This project investigates the relationship between colostrum feeding and BCG vaccination to determine whether BCG is rendered ineffective in metabolically ill-equipped (e.g. colostrum deprived) newborns, and if so, what supplementation strategies are most effective at restoring the protective capacity of BCG vaccination. Independent of BCG vaccination, the mechanism by which colostrum offers protection from neonatal sepsis is also unknown. By investigating the relationship between neonatal nutrition and sepsis outcomes, this project will also help fill this knowledge gap. This project includes the utilization of mouse models, including novel methods such as non-invasive metabolic phenotyping using indirect calorimetry to determine how host metabolic status relates to sepsis outcomes. In parallel, our team is collaborating with partners in Kenya whereby we will have access to colostrum samples from mothers whose newborns were healthy, or who became septic. The multi-omic data generated from these samples will serve as a tool to identify candidate protective molecules associated with good infant outcomes, and to test them for cause-and-effect in preclinical models. The project offers opportunities for learning exchanges to the University of Copenhagen to work with our collaborators using large animal models to study neonatal nutrition and sepsis.

Candidate characteristics: Prior experience in either wet bench/preclinical work, bioinformatics, or both. Individuals with a strong motivation to learn would also be considered. Candidates should be self-driven and take initiative to drive their work forward, while adhering to lab processes for data collection, data analysis using R programming, and record keeping. Animal models used by our team require flexible working hours, including weekends and nights on 1-2 occasions per month. Given the collaborative nature of our work, the individual must be adaptable and motivated to work in diverse team settings. This includes responding well to feedback and being willing to follow or to lead, as the situation demands. Our team has a strong commitment to EDIA and expects all lab members to undertake EDIA training to create an inclusive and welcoming environment where students and staff from low- and high- resource settings can learn together and thrive.

Interested? Get in touch!
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