



PhD. Defence
DEVELOPMENTAL ADAPTATIONS OF IMMUNE AND METABOLIC FUNCTION IN CALVES AND THE INFLUENCE OF THE INTESTINAL MICROBIOTA IN HEALTH AND DISEASE

Lautaro Rostoll Cangiano

Date: January 10th 2023 at 9:30am

The PhD Defence for Lautaro Rostoll Cangiano has been scheduled for January 10th, 2023 at 9:30am. The defence will be held online via Teams and in 141: https://teams.microsoft.com/l/meetup-join/19%3ameeting_MjViZWU5NzYtZjk5Mi00Y2JkLTlkZmltMzk2MDYwOWQ5YTM4%40thread.v2/0?context=%7b%22Tid%22%3a%22be62a12b-2cad-49a1-a5fa-85f4f3156a7d%22%2c%22Oid%22%3a%22fbd28915-dda5-478f-8ecb-a3682dcf0c3a%22%7d

The exam committee will consist of:

Examining Chair: Dr. Elijah Kiarie

Adv. Committee Member: Dr. Ignacio Ipharraguerre

Adv. Committee Member: Dr. Bonnie Mallard

Additional Graduate Member: Dr. Katie Wood

External Examiner: Dr. Michael Ballou

Abstract:

Several components of dairy farm rearing systems are known to affect developmental programming of calves by acting as epigenetic regulators, influencing the trajectory of immune system development. Therefore the objectives of this research were to 1) characterize how systemic and colon tissue-resident B and $\gamma\delta$ T cells develop from birth until weaning, 2) Characterize weaning influences of the intestinal microbiota and immune responses in the colon of Holstein bull calves, 3) Evaluate how supplementation of a *Saccharomyces cerevisiae boulardii* (SCB) probiotic and prophylactic neomycin administration impacts the intestinal microbiota in early life, and how changes in the nascent intestinal bacterial community impact intestinal immunity and systemic metabolism, and lastly 4) Develop a protocol of experimental induction of leaky gut to model and study its detrimental effects on gut tissue function and inflammatory response. Data from chapter 2 demonstrates that ontological adaptations during early life coordinate immune function and development, promoting $\gamma\delta$ T cell expansion possibly to provide early protection and immune tolerance until other branches of the immune system become fully functional. Additionally, microbial interventions in early life can shape microbial colonization and succession in early life. Chapter 3 shows that supplementing a probiotic of SCB increased microbial diversity and species richness which was associated with an increase in secretory Immunoglobulin A production. Furthermore, although the intestinal microbiota plays many beneficial functions in maintaining host health, certain factors within our management systems also impact intestinal health and can derail the normal trajectory of intestinal colonization and succession affecting host metabolic function. As shown in chapter 4, antimicrobial-mediated changes in the microbial composition of key bacterial groups affected the metabolism of bile acids and is possibly linked to changes in metabolic function of adipose tissue. Lastly, chapter 5 describes an experimental leaky gut model using repeated intramuscular injections with indomethacin to study the detrimental effects of failed barrier function on gut tissue function and inflammatory response. In summary, this thesis provides an examination of the ontological adaptations of the calf's adaptive immune system and how the intestinal microbiota influences calf immune and metabolic function in health and disease