PhD DEFENCE – Wednesday, March 23rd, 2016
Student: Alistair Chenery
Title: **REGULATION OF MUCOSAL T CELL RESPONSES BY INTESTINAL HELMINTHS AND RETINOIC ACID METABOLISM**
Time and Location: 12:30 pm, Room 226, Biomedical Research Centre, 2222 Health Sciences Mall, UBC Campus
Supervisor: Dr. Colby Zaph

ABSTRACT

Mucosal immune diseases such as asthma and inflammatory bowel disease are associated with major environmental factors - diet, geography, hygiene, infections - that contribute to disease risk. The mucosal immune system is in direct contact with the external environment and must balance protective immune responses with tolerance to innocuous antigens. Since chronic inflammation at mucosal sites depends on a diverse set of T cell-driven responses, understanding the factors that regulate mucosal T cell differentiation and function is key to developing better treatments to a variety of inflammatory diseases. Further, immunological cross-talk can occur between mucosal organs such as the intestine and the lung, but the role of T cells in this cross-talk is poorly defined.

The work herein investigates the effect of external factors, specifically intestinal infections and dietary immunomodulators, on mucosal T cell responses in the context of inflammation in the intestine and the lungs. Using a mouse model of infection with the intestinal helminth *Trichuris muris*, I show infection-mediated alterations in the lung microenvironment that can protect against murine models of allergic airway inflammation. I further show that intestinal *T. muris* infection has a systemic effect on hematopoiesis in the bone marrow. In other studies, I examine the role of the dietary vitamin A metabolite, retinoic acid, on T cell function during intestinal inflammation. Specifically, I investigate how metabolism of retinoic acid by the enzyme Cyp26b1 modulates T cell differentiation and function and show that Cyp26b1 controls regulatory T cell and T helper 17 differentiation *in vitro*. Further, I posit a role of Cyp26b1 in regulating effector T cell function *in vivo* using a murine model of T cell-driven inflammatory bowel disease.

Thus, the results presented here provide further insight into helminth-mediated immune regulation, intestine-to-lung mucosal immune crosstalk, and dietary immunomodulation that regulate mucosal T cell responses.