The Centre for Blood Research
VIRTUAL SEMINAR SERIES

Wednesday, April 7, 2021
11:00am - 12:00pm PT

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"Tolerance and Autoimmunity to Red Blood Cells"

The immune system has an intricate set of checkpoints to tolerize autoreactive lymphocytes to self-antigens (e.g., deletion or anergy (non-responsiveness)). When checkpoints fail or are incomplete, autoimmune pathology can ensue. Given their abundance (i.e., 20-30 trillion RBCs circulating in an adult human) and their essential functions, one would predict that tolerance to RBCs would be stringent. Unexpectedly, loss of tolerance to RBCs occurs frequently; 0.1% of healthy blood donors have detectable autoantibodies bound to their RBCs and this prevalence increases to ~8% in hospitalized patients. Loss of tolerance may induce pathogenic anti-RBC autoantibodies and result in AIHA, a severe, and sometimes fatal, disease. Patients with AIHA present with pallor, fatigue, hemoglobinuria, decreased hematocrit and splenomegaly. Treatment strategies have variable success and relapse rates can be as high as 50%. Moreover, supportive care using RBC transfusions is challenging because most autoantibodies recognize ubiquitous RBC antigens; thus, virtually all donor units are crossmatch incompatible. The etiology of AIHA is generally unknown; nonetheless, although >50% of AIHA cases are idiopathic, some are associated with lymphoproliferative disorders, infections (e.g., SARS-CoV-2 (COVID-19), HIV) and, more recently, as an adverse event due to cancer immunotherapy. Today, I will discuss our novel murine model of AIHA, identify immune cell subsets and potential pathways and that may be involved in initiation of autoimmune pathology, and share new data on a promising therapeutic.