Research Interests

The innate immune system is an evolutionarily ancient system that depends on key sentinel cells of the mononuclear phagocyte system (e.g., monocytes, macrophages, dendritic cells (DCs), and neutrophils) to provide the first line of defense against pathogenic microbes. Signalling defects within these innate immune cells may result in immunodeficiency characterized by the inability to clear infections, while excessive or inappropriate activation of these cells can lead to devastating acute or chronic inflammatory diseases such as cancer, sepsis, arthritis, asthma, atherosclerosis and inflammatory bowel disease. The mononuclear phagocyte system is also critical for organising appropriate adaptive immune responses against pathogens and cancer cells and for
maintaining immunological tolerance to self-antigens and for limiting potentially self-destructive immune responses.

The long-term goal of the laboratory is to identify the key genes and cellular signalling pathways that guide the development and activity of cells of the mononuclear phagocyte system. We are particularly interested in the role of tyrosine kinase/phosphatase-regulated signalling pathways that control signalling thresholds important for the development and function of DCs and other phagocyte populations. A complementary research theme in the laboratory is centred on the study of cytokine networks that regulate immunosuppressive programs within phagocytes. Our work utilizes mouse models in which the levels and activities of key signaling molecules have been manipulated allowing us to delineate the roles of these gene products in mammalian phagocyte biology and in innate/adaptive immunity at the whole animal level. We are using these mouse models, together with comprehensive immuno-phenotyping platforms such as mass cytometry, to explore how changes in phagocyte signalling thresholds impact immunological diseases such as inflammatory bowel disease, atherosclerosis and cancer. Ultimately, this research program will lead to the identification of critical proteins and pathways that may become targets of future therapeutic strategies to either augment host-pathogen/tumour responses or alleviate pathological immune responses.