## Department of Anatomy & Cell Biology Seminar Series

## Ramesh Shivdasani, MD, PhD

Professor of Medicine Dana-Farber Cancer Institute Harvard University

## Cellular compartments and selforganization of the intestinal stem cell niche

Intestinal stem cells (ISCs) expressing Lgr5 self-renew at the bottom of epithelial crypts, while their progeny proliferate and differentiate in higher crypt tiers. These cell behaviors, originally characterized in the McGill Dept. of Anatomy between the 1950s and 1970s, depend on bone morphogenetic protein (BMP) and canonical Wnt signaling. Although the adjacent mesenchyme was suspected to provide these key signals for epithelial self-renewal, the responsible cells remained unknown, in part because intestinal mesenchyme was long regarded as a loose collection of generic "myofibroblasts." Recent research, however, reveals the mesenchyme as a highly organized tissue with distinct cell types that express multiple Wnt/Rspondin and BMP agonists and antagonists. Cell types that include telocytes, trophocytes, and various smooth muscle populations, combine to produce tight signaling gradients that influence epithelial cell properties over just a few cell diameters. The anatomic arrangements of these distinct mesenchymal cells appear largely self-organized, with a limited number of cell types driving the relative positions of others along the source of the tight signaling gradients. The seminar will describe how high-resolution microscopy, singlecell transcriptomics, and in vitro organoid assays jointly generated a simple model to explain complex tissue physiology.

> Hosted by: Chantal Autexier, PhD, and John Bergeron, PhD





Wednesday, Oct. 11, 2023 11:30am - 12:30pm

