Targeting the nuclear receptor HNF4A for the treatment of gut diseases

Gut diseases have a huge impact on the Canadian health care system cost. Indeed, Canada has among the highest rates of intestinal inflammatory bowel diseases (IBD) in the world with approximately 233 thousands of people that were living with it in 2012. Colorectal cancer (CRC) is the second most commonly diagnosed cancer in Canada, accounting for over 12% of cancer deaths in the population. One commonality of these diseases is the deregulation of intestinal epithelium renewal properties that insure protection against luminal threats as well as preservation of organism digestive functions. Gut epithelial stem cells are responsible for the constant epithelium renewal. Nuclear receptors are proteins that regulate the expression of the cell genome accordingly to cellular specificity. We have identified the protein HNF4A as a regulator of gut epithelial cell proliferation. The gene encoding this protein is altered in both IBD and CRC. We suspect this protein to regulate specific signaling pathways already known to play an important role in the progression of gut diseases. With the use of novel biological systems derived from mice and human tumours, we expect to discover the biological relevance of HNF4A interaction with these signaling pathways. This research will allow the discovery of alternative ways of improving therapeutically targeting strategies against gut diseases.