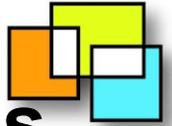
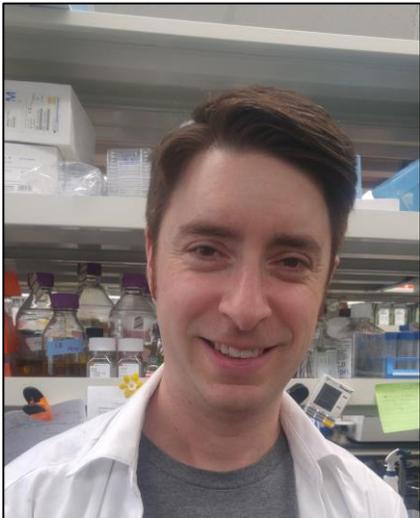


# Donnelly Centre PDF and RA Seminar Series



## Novel biological functions of the Crohn's disease risk factor NOD2



***Dr. Dave Prescott***  
Postdoctoral Fellow  
University of Toronto  
Girardin Lab

**DATE: Monday May 14<sup>th</sup>, 2018**  
**TIME: 12:00 – 1:00 pm**  
**LOCATION: Red Room**

Crohn's disease is a severe, debilitating inflammatory disorder of the gastrointestinal tract that affects approximately 1 in 300 Canadians. The precise etiology of the disease remains unknown, but evidence collected from clinical, epidemiological, and genomic studies suggest that this condition arises as a result of an inappropriate immune response to the intestinal microbiota following the exposure of unknown environmental triggers to a genetically susceptible individual. To date, over 200 risk alleles have been identified that result in an increased susceptibility to developing CD, a number of which are known to be found in genes that are vital to the function of the innate immune system. Of these genes, the greatest risk is conferred by mutations in *Nod2*, which encodes an intracellular receptor that detects fragments of the cell wall of invading bacteria. However, it remains entirely unclear how a loss in function of this gene can ultimately lead to the development of widespread intestinal inflammation. This is in part due to the fact that our understanding of the biology of NOD2 activation is largely incomplete, with the bulk of its known functions being restricted to its effects in peripheral blood leukocytes. With this in mind, we set out to explore new roles for NOD2 activation using the Cre-Lox recombinase system to specifically eliminate *Nod2* gene expression in alternative tissues and cell types. In this talk I will describe 2 novel functions of NOD2 that we have discovered by this approach - modulation of the adaptive immune response via NOD2-dependent alterations in dendritic cell function, and NOD2-dependent maintenance of intestinal epithelial stem cell function. We hope that the identification of these alternative functions of NOD2 will lead to a better understanding of the pathogenesis of Crohn's disease, which is ultimately needed for improved therapies, preventions, or an eventual cure.



**Donnelly Centre**  
for Cellular + Biomolecular Research



UNIVERSITY OF  
**TORONTO**