Supervisor & Project Information Form

Please complete and return via email ONLY to gdip.hres@utoronto.ca by ***Monday September 30, 2019***

Supervisor Information

MUST have unrestricted SGS appointment (appointment to supervise graduate students)

Name: **Greg Fairn**	**Email:** **Greg.fairn@unityhealth.to**
SGS Department: **Biochemistry & the IMS**	**Field of Research:** **Cell Biology, Biochemistry, Immunology**
Research Institution affiliation (if applicable): **KRCBS, St. Michael's Hospital**	**Location of Work:** **KRCBS, St. Michael's Hospital** **209 Victoria St.**
Student contact time (number of hours per week YOU are available to the student for any concerns or to review progress:	**20-30h/week**

Project Information (will be posted on GDipHR website for student access)

TITLE: Characterization of novel NOD1 and NOD2 interacting partners.

DESCRIPTION (MAX 500 WORDS): The cytosolic pattern recognition receptors (PRRs) NOD1 and NOD2 play crucial roles in host defense and survival, primarily by conferring responsiveness to cytosolic bacterial peptidoglycans (γ-D-glutamyl-*meso*-diaminopimelic acid (iE-DAP) and muramyl dipetide (MDP)) shed by bacteria during infection. Dysregulation of NOD1/2 function leads to severe immunologic and inflammatory diseases such as Crohn's disease (CD) and Blau syndrome. Although soluble in the cytosol, NOD1/2 appear to associate with the plasma membrane (PM) and endosomal compartments for the surveillance of bacterial cell wall components and promote activation of the NF-κB and MAPK signaling pathways from endosomal membranes via the RIP2 kinase. Lacking recognizable membrane-targeting domain, NOD1/2 have been suggested to be anchored to membranes indirectly, via cytoskeletal components or membrane-bound proteins or to endosomes by endosomal proteins such as SLC15A3. BirA tagged proteins were generated and used in a BioID proteomics screen to identify potential NOD1- and NOD2-interacting proteins. As expected, a number of plasmalemmal and endomembrane proteins were identified as high-confidence NOD1- and NOD2-proximity interactors. Membrane proteins and membrane-associated polypeptides (as determined by GO enrichment analysis: pantherdb.org GO:0016020) represented >85% (111/129) of the NOD1 and >80% (58/72) of the NOD2 high confidence proximity interactors. This project will follow-up on specific group of interacting partners and determine their role in regulating response to peptidoglycan.

If human subjects are involved, have the appropriate Research Ethics Board approvals been obtained?

☐Yes ☐ **X** No ☐Application Submitted (Date: _____)

Do you expect this work will be published within the 20 months?

☐Yes ☐No ☐ **X** Uncertain / Other

Student Roles & Responsibilities (*please be as specific as possible****)***

Please indicate who will serve as the student's direct report for daily oversight (PI, PhD student, technician, etc…)

The student will be responsible for all aspects of the project, experimental design, completion, data analysis and assembly of manuscripts. Experimentally, the project will rely on co-immunoprecipitation and other assays to investigate protein-protein interactions. We will also use CRISPR or siRNA silencing to examine the impact of loss of the binding partners on the NOD1 and NOD2 dependent signaling.

Daily oversight will be provided by the PI and either a PhD student or post-doctoral fellow working on a related, yet distinct, project related to NOD1 and NOD2.