



COLLEGE of
BIOLOGICAL SCIENCE

DEPARTMENT OF MOLECULAR
AND CELLULAR BIOLOGY

Announcement:

*All interested members of the university community are invited to attend the Final Oral Examination for the degree of **Master of Science** of*

ALYSSA CAMPBELL

On Thursday, August 24, 2023 at 1:30 p.m. (online)

Thesis Title: Investigating nectin-2 in kidney podocytes

Examination Committee:

Dr. Jasmin Lalonde, Dept. of Molecular and Cellular Biology (Exam Chair)
Dr. Nina Jones, Dept. of Molecular and Cellular Biology
Dr. Marc Coppolino, Dept. of Molecular and Cellular Biology
Dr. Jim Uniacke, Dept. of Molecular and Cellular Biology

Advisory Committee:

Dr. Nina Jones (Advisor)
Dr. Marc Coppolino
Dr. Alicia Vilorio-Petit

Abstract: Kidney podocytes are specialized epithelial cells that extend actin-rich projections known as foot processes to envelop the outer surface of glomerular capillaries. Focal adhesions anchor podocytes to the underlying glomerular basement membrane and between adjacent foot processes lies a unique intercellular junction known as the slit diaphragm, which serves as a selective barrier for blood filtration. Both of these adhesion complexes are bridged with the actin cytoskeleton, serving as signalling hubs for actin dynamics that uphold foot process integrity. Understanding the mechanisms that connect podocyte morphology and adhesion is critical to understanding kidney disease involving podocyte injury. Here, we begin to elucidate a novel role for cell adhesion protein nectin-2 in podocyte signalling and function. Nectin-2 is a mediator of cellular junctions and actin cytoskeletal dynamics and we hypothesized that it contributes to these processes in podocytes. To this end, we first characterized nectin-2 expression and localization in immortalized human podocyte cells and mouse glomeruli and demonstrated that its knockdown promotes increased proliferation and impaired adhesion or survival. Furthermore, we showed that nectin-2 clustering promotes its tyrosine phosphorylation which facilitates downstream interactions and actin reorganization. Finally, we identified nectin-2 proximity interactors via BioID and used this data to explore nectin-2 localization and function in podocytes through gene ontology analysis. Taken together, these studies implicate nectin-2 in the signalling events that mediate slit diaphragm and focal adhesion dynamics as they relate to podocyte morphology and adhesion.

Curriculum Vitae: Alyssa completed her Bachelor of Science (Hons.) in Molecular Biology and Genetics at the University of Guelph in December 2020. She began her Master of Science program in Molecular and Cellular Biology in Dr. Jones' lab in September 2021.