



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*

**UNA PANTIC**

**On Wednesday, July 10, 2024 at 9:30 a.m.** (SSC 1511)

**Thesis Title:** Exploring the roles of Dok1/2 adaptor proteins in modulating podocyte adhesion dynamics

**Examination Committee:**

Dr. Stephen Seah, 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. Ray Lu, Dept. of Molecular and Cellular Biology

**Advisory Committee:**

Dr. Nina Jones (Advisor)

Dr. Marc Coppolino

Dr. Todd Gillis

**Abstract:** Podocyte adhesion to the basement membrane is required for glomerular filtration and is partly mediated by dynamic signaling events within focal adhesions (FAs). Integrins are a major component of FAs, and their activity and matrix binding can be negatively regulated by adaptor proteins Dok1 and Dok2. We recently identified Dok1 as a binding partner for Nck1 and Nck2, which we have shown previously are essential regulators of podocyte adhesion and FA remodeling. Herein we investigated the role of Dok1/2 in podocytes. We generated single and double knockout (KO) podocytes for use in functional assays. Dok KO podocytes show more adhesion and impaired spreading compared to controls. In addition, they display higher surface levels of integrin  $\beta$ 1 relative to control along with altered expression of FA proteins p130Cas, Paxillin, and FAK. Lastly, we found that DOK1 and DOK2 are upregulated in human kidney diseases. These findings reveal that Dok1/2 regulate integrin signaling and adhesion dynamics in podocytes, and we speculate that their increased expression may decrease integrin activation leading to podocyte detachment.

**Curriculum Vitae:** Una completed her Bachelor of Science (Honours) with a major in Molecular Biology and Genetics and a minor in Biotechnology at the University of Guelph in 2022. In the Fall of 2022, she entered into the MSc program in Molecular and Cellular Biology at the University of Guelph under the supervision of Dr. Nina Jones.

**Awards:** Excellence in Blitz Presentations - Canadian Kidney Discoveries Network (CKDN) Conference, Montreal (2023)

**Publications:** Una V. Pantic\*, Nikkita T. Dutta\*, Noah J. Phippen\*, Claire E. Martin, Laura A. New, Peihua Lu, Begüm Alural, Lamine Aoudjit, Tomoko Takano, Anne-Claude Gingras, Nina Jones (2024). Dok1/2 adaptor proteins control podocyte adhesion dynamics through negative regulation of integrin signaling. Under review at Journal of American Society of Nephrology.

\*Authors contributed equally