Department of Molecular and Cellular Biology

Graduate Seminar MCB*6500

Friday, March 22, 2024 @ 12:45 p.m.

presented by:

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"ARHGEF10 AS A NOVEL REGULATOR OF PODOCYTE ADHESION "

Podocytes are terminally differentiated cells which encase glomerular capillaries to create a crucial barrier in kidney filtration. Podocyte integrity is sustained by signaling mechanisms which dynamically reorganize their specialized cytoarchitecture and adherence to the underlying glomerular basement membrane under fluctuating filtration requirements. Compromised adhesion is particularly consequential as podocyte loss is permanent and characteristic of progressive kidney disease.

The NCK adaptor proteins, NCK1 and NCK2, are well-established as crucial regulators of podocyte cytoarchitectural signalling, and emerging evidence suggests pivotal roles of NCKs in organizing podocyte adhesion dynamics as well. The NCK paralogues consist of three tandem Src homology (SH) 3 domains followed by a carboxy-terminal SH2 domain which coordinate cytoplasmic signaling through binding PxxP and phosphorylated-YDxV sequences. Using proteomic approaches, several podocyte adhesome components have been identified as NCK interactors, including RhoA exchange factor ARHGEF10 which is differentially expressed in specific podocytopathies in a similar manner to its proposed SH2-dependent binding partner, NCK2. Although ARHGEF10 has been documented to induce adhesion structures in multiple cell types, its functions are still poorly understood. Moreover, it has yet to be characterized in the podocyte.

In this project, I will test the hypothesis that ARHGEF10 is a novel regulator of podocyte adhesion through NCK2 signalling by attempting to deduce the biochemical basis of the ARHGEF10-NCK2 interaction, then characterizing the role of ARHGEF10 in the podocyte. Ultimately, this research will aid in defining the regulatory mechanisms of podocyte adhesion and provide insight into disruptions that are perpetuated in podocytopathy.