UNIVERSITY of GUELPH

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*

MATTHEW HORN

On Wednesday, May 3, 2023 at 1:30 p.m. (SSC 1511)

Thesis Title: **Elucidating the role of Vangl2 and its interactions with Wnt/β-catenin signaling**

Examination Committee:

Dr. Jasmin Lalonde, Dept. of Molecular and Cellular Biology (Exam Chair)
Dr. Terry Van Raay, Dept. of Molecular and Cellular Biology
Dr. Ray Lu, Dept. of Molecular and Cellular Biology
Dr. Angela Scott, Dept. of Molecular and Cellular Biology

Advisory Committee:

Dr. Terry Van Raay (Advisor)
Dr. Ray Lu

Abstract: The Wnt signaling pathway is one of the oldest and conserved pathways in eukaryotic development playing essential roles to control cell patterning, polarity, migration, and stem cell maintenance. Wnt signaling is commonly split into the Wnt/β-catenin pathway, required for cell patterning and proliferation, and the non-canonical or Wnt/Planar cell polarity (Wnt/PCP) pathway, required for cell migration and polarity. These two pathways share common ligands and receptors and the intracellular scaffolding protein Disheveled, but then diverge downstream. In Wnt/β-catenin signaling, β-catenin is a transcriptional co-activator, whereas the transmembrane protein Vangl2 induces cell polarity. It is hypothesized that different mutant alleles of Vangl2 predispose the embryo to different Wnt/β-catenin sensitivities during gastrulation. Vangl2^{m209} and Vangl2^{m747} alleles have premature truncations near the C-terminus, eliminating two putative Dvl binding domains and the C-terminal PDZ binding domain. Both phenotypes were recapitulated with CRISPR induced alleles. My results refute my original hypothesis and demonstrate that the C-terminal domain of Vangl2 does not affect Wnt/β-catenin signaling. Instead, my data supports a model whereby the C-terminal domain of Vangl2 suppresses Wnt/PCP signaling to constrain the Wnt/PCP signal along the dorsal-ventral axis.

Curriculum Vitae: Matthew completed the Advanced Diploma in Biotechnology-Advanced at Seneca College of Applied Arts and Technology in April 2019. He then completed his Bachelor of Science (Hons.) in Molecular Biology and Genetics at the University of Guelph in April 2021. In May 2021, he began his Master of Science program in Molecular and Cellular Biology at the University of Guelph in the lab of Dr. Terry Van Raay.

Publications: Bell IJ, **Horn MS**, Van Raay TJ, 2022. Bridging the gap between non-canonical and canonical Wnt signaling through Vangl2. Semin Cell Dev Biol 125:37-44.