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 ***Doctor of Philosophy*** *of*

HANNAH ROBESON

on Tuesday, September 6, 2022 at 1:30 p.m. (online)

Thesis Title: **Characterization of physiological roles of adaptor protein ShcD in the adult mammalian central nervous system and testes**

Examination Committee:

Dr. Jaideep Mathur, Dept. of Molecular and Cellular Biology (Exam Chair)
Dr. Nina Jones, Dept. of Molecular and Cellular Biology
Dr. Jasmin Lalonde, Dept. of Molecular and Cellular Biology
Dr. Shaun Sanders, Dept. of Molecular and Cellular Biology
Dr. David Kaplan, Program in Neuroscience and Mental Health, Hospital for Sick Children (External Examiner)

Advisory Committee:
Dr. Nina Jones (Advisor)
Dr. Jasmin Lalonde
Dr. John Vessey
Dr. Elena Choleris

Abstract: Cellular signaling is an essential process by which an organism is able to interpret and respond to stimuli, eliciting responses which regulate important cellular functions including proliferation, differentiation, migration, and survival. These signaling cascades are mediated by protein-protein interactions which enable signal transduction, culminating in a biological response. Adaptor proteins, including those in the Shc (Src homology and collagen) family, are an important class of molecules involved in these pathways, functioning as scaffolds in the formation of signaling complexes. The Shc family constitutes four members – ShcA, -B, -C and -D – which share a similar general architecture but diverge in their expression profiles and specific functions. ShcD, the most recently identified Shc family member, remains the least well characterized. Though advancements have been made in identifying roles for ShcD in cancer pathology with links to metastasis, little remains known as to its roles in normal physiological signaling.

Through a combination of *in vitro*, *in vivo* and *in silico* approaches, and the use of both cell-based and animal models, we provide a characterization of ShcD expression and function in two distinct organ systems with high ShcD expression – the brain and the testes. We first show that ShcD is expressed in both neural progenitor cells and mature neurons. We further demonstrate that knockout of ShcD in mice results in brain abnormalities including altered olfactory bulb morphology and function, as well as changes in biochemical signaling molecules associated with neuronal differentiation. This loss of ShcD results in alterations in cell populations in neurogenic niches, identifying a putative role for ShcD in neurogenesis. We also expanded our investigation to profile ShcD expression in the testes and identified marked ShcD expression in Sertoli cells. We demonstrate that overexpression of ShcD results in dysregulation of MAPK signaling pathways as well as alterations in proliferation. Finally, we show that overexpression of ShcD results in increased cellular outgrowth from a spheroid, suggesting ShcD may increase propensity for

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migration or alter cell-cell attachment. Together, these findings explore ShcD expression and function in a previously overlooked capacity and provide additional context for our understanding of this elusive molecule.

Curriculum Vitae: Hannah obtained her B.Sc. (Hons), Biological Sciences at the University of Guelph. In the Fall of 2016, she began her M.Sc. in Molecular and Cellular Biology with a collaborative specialization in Neuroscience under the supervision of Dr. Nina Jones and in the Fall of 2017, transferred to the Ph.D. program.

Awards: Ontario Graduate Scholarship (2019).

Publications: Robeson HN, Lau HR, New LA, Lalonde J, Armstrong JN, Jones N. 2019. Localization of the phosphotyrosine adaptor protein ShcD/SHC4 in the adult rat nervous system. *BMC Neuroscience.* 20:57.

Prowse N, Dwyer Z, Thompson, A, Fortin T, Elson K, Robeson HN, Fenner B, Hayley S. 2019. Early life selective knockdown of the TrkB receptor modulates adult stress phenotype. Behavioral Brian Research 378:112260.