



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*

**JULIA BROTT**

**on Wednesday, April 15, 2020 at 9:30 a.m.**

**Thesis Title:** The RNA-binding protein heterogeneous nuclear ribonucleoprotein K is responsible for regulating the fate decisions of neural precursor cells of the developing cerebral cortex

**Examination Committee:**

Dr. G. van der Merwe, Dept. of Molecular and Cellular Biology (Exam Chair)

Dr. J. Vessey, Dept. of Molecular and Cellular Biology

Dr. T. Van Raay, Dept. of Molecular and Cellular Biology

Dr. S. Ryan, Dept. of Molecular and Cellular Biology

**Advisory Committee:**

Dr. J. Vessey (Adv)

Dr. J. Lalonde

Dr. T. Van Raay

**Abstract:** Neurogenesis within the developing cortex occurs as a result of the controlled differentiation of neural precursor cells (NPCs), achieved by tightly regulated gene expression. Many RNA-binding proteins have been implicated in regulating gene expression throughout development, such as the heterogeneous nuclear ribonucleoproteins (hnRNPs). Specifically, aberrant hnRNP-K expression has been identified in Kabuki syndrome, a neurological disorder characterized by cortical atrophy, ventriculomegaly, and periventricular nodular heterotopia. This research validates hnRNP-K expression within the murine cerebral cortex during the neurogenic period and demonstrates a critical role for hnRNP-K in the cell fate decisions of NPCs. Lentiviral shRNA mediated knockdown of hnRNP-K *in vitro* resulted in a significant increase in the proportion of post-mitotic neuronal B3T<sup>+</sup> cells and a significant decrease in the proportion of Nestin<sup>+</sup> NPCs compared to control. Immunoprecipitation (IP) followed by mass spectrometry revealed hnRNP-K maintains many RNA-based interactions with the nuclear matrix and other proteins known to regulate gene expression, proliferation and differentiation. Interactions validated through the use of reverse IPs revealed hnRNP-K maintains RNA based interactions with nuclear matrix proteins Matrin3 and hnRNP-U. These interactions, in addition to GO analysis, revealed enrichment of hnRNP-K in regulatory processes of gene expression. Specifically supporting a role for hnRNP-K in the negative regulation of gene expression through previously established interactions with PRC2. Overall, our data supports a critical role for hnRNP-K in the cell fating of NPCs in the developing murine cerebral cortex, likely through the control of proneural gene expression.

**Curriculum Vitae:** Julia received her Bachelor of Science (Hons.) at the University of Guelph in early 2018, and then began her M.Sc. in the lab of Dr. John Vessey in May of the same year.

**Awards:** Ontario Graduate Scholarship 2018-2019; Canadian Graduate Scholarship – Masters 2019-2020