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*

# NATALIE PORTE-TRACHSEL

**On Thursday, December 8, 2022 at 9:30 a.m.** (SSC 2315)

**Thesis Title**: **Investigating the role of LC3B in the seeding of Alpha-synuclein in Parkinson's Disease Model Systems**

**Examination Committee:**

Dr. John Vessey, Dept. of Molecular and Cellular Biology (Exam Chair)
Dr. Scott Ryan, Dept. of Molecular and Cellular Biology
Dr. Shaun Sanders, Dept. of Molecular and Cellular Biology
Dr. Nina Jones, Dept. of Molecular and Cellular Biology

**Advisory Committee:**

Dr. Scott Ryan (Advisor)
Dr. Jasmin Lalonde
Dr. Shaun Sanders

**Abstract:** Parkinson's disease is the second most prevalent neurodegenerative disease, presenting in approximately 1% of the population over the age of 60. Despite the prevalence of PD in the aging population, and the significant impact this disease has on the quality of life of patients, there are still no effective treatments to halt the progression of the disease. As more evidence emerges regarding the behaviour of α-syn as a prion-like protein, more research is needed to investigate the mechanism behind how α-syn is seeding cell-to-cell, in order to eventually attempt to halt this transmission. Here, I show that *SNCA* mutant dopaminergic neurons transmit PD pathology (PS129) to the striatum of nod-scid gamma mice via cell engraftment. I also show that PD pathology (aggregated α-syn) and paired helical filaments of tau can seed via exosomes isolated from A53T hiPSCs to primary rat neurons *in vitro*, thereby activating LC3B and decreasing neurite length, maturity, and firing. Finally, I confirm that a partial C-terminal and N-terminal truncation of α-syn disrupts the binding of α-syn and LC3B, thereby reducing the rate of seeding of aggregated and total α-syn via these exosomes. Overall, these findings suggest a potential mechanism for the seeding of α-syn between cells, via the interaction with LC3B. I also suggest a potential preventative mechanism to decrease the seeding of α-syn via exosomes and restore the canonical process of macro autophagy.

**Curriculum Vitae:** Natalie completed her Bachelor of Science (Hons.) in Molecular Biology and Genetics at the University of Guelph in April 2020, where she completed an undergraduate research project with Dr. Scott Ryan. In September of 2020, she began her Master of Science in Molecular and Cellular Biology under the supervision of Dr. Scott Ryan.

**Awards:** Parkinson's Society of Southwestern Ontario Graduate Student Scholarship (2020); Ontario Graduate Scholarship (2021).

Continued…

**Publications:** Stykel, M. G., Humphries, K. M., Kamski-Hennekam, E., Buchner-Duby, B., **Porte-Trachsel, N**., Ryan, T., Coackley, C. L., Bamm, V. V., Harauz, G., & Ryan, S. D. (2021). α-Synuclein mutation impairs processing of endomembrane compartments and promotes exocytosis and seeding of α-synuclein pathology. *Cell reports*, *35*(6), 109099.