



**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*

**SARAH KIRSH**

**On Tuesday, July 12, 2022 at 1:30 p.m.** (online)

**Thesis Title:** **The pharmacological inhibition of the neuropeptide Y1 and Y5 receptors on proliferation, migration, and cell signaling in hypoxic breast carcinomas**

**Examination Committee:**

Dr. Michael Emes, Dept. of Molecular and Cellular Biology (Exam Chair)

Dr. Jim Uniacke, Dept. of Molecular and Cellular Biology

Dr. Shaun Sanders, Dept. of Molecular and Cellular Biology

Dr. Jasmin Lalonde, Dept. of Molecular and Cellular Biology

**Advisory Committee:**

Dr. Jim Uniacke (Advisor)

Dr. Ray Lu

Dr. Shaun Sanders

**Abstract:** Neuropeptide Y (NPY) has been linked to the initiation and progression of breast cancer. NPY activates six G-protein coupled receptors (GPCRs) in breast cancer, of which, NPY1R and NPY5R are the most biologically significant. Activation of these receptors by peptide binding impacts tumour proliferation, migration, invasion, and angiogenesis, especially in hypoxia. Here we show that the use of NPY1R and NPY5R antagonists in MDA-MB-231 and MCF7 breast cancer lines can inhibit hallmarks of cancer and that NPYRs are associated with hypoxic regions in tumour samples. These overlaps correlated with adverse outcomes. Breast cancer is the second most common cancer, with more than 1.3 million people diagnosed each year. Therefore, a greater understanding of how NPY1R and NPY5R antagonists impact breast cancer cell migration, proliferation, invasion, and formation, with a focus on hypoxia, will be an asset in the development of novel therapeutics for breast carcinomas.

**Curriculum Vitae:** Sarah completed her B.Sc. (Hons.) in Biochemistry (Co-op) at the University of Guelph in Fall 2019. She then began her M.Sc in Molecular and Cellular Biology in Fall 2020 under the supervision of Dr. Jim Uniacke.

**Awards:** Graduate Tuition Scholarship (2020) & Ontario Graduate Scholarship (2021).

**Publications:** Medeiros, P.J., Pascetta, S.A., **Kirsh, S.M.**, Al-Khazraji, B.K., and Uniacke, J. (2022). Expression of hypoxia inducible factor-dependent neuropeptide Y receptors Y1 and Y5 sensitizes hypoxic cells to NPY stimulation. *J. Biol. Chem.* 298, 101645.

**Kirsh, S.M.**, Pascetta, S.A., and Uniacke, J. (2022). Spheroids as a 3D model of the hypoxic tumor microenvironment [Manuscript submitted for publication]. In *The Tumor Microenvironment: Methods and Protocols*, (Springer Nature).