



**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*

MARGUERITE CLARKE

On Wednesday, December 7, 2022 at 9:30 a.m. (SSC 2315)

Thesis Title: Elucidating the role of cortactin in invadopodium-based ECM degradation

Examination Committee:

Dr. Jasmin Lalonde, Dept. of Molecular and Cellular Biology (Exam Chair)
Dr. Marc Coppelino, Dept. of Molecular and Cellular Biology
Dr. Steffen Graether, Dept. of Molecular and Cellular Biology
Dr. Jim Uniacke, Dept. of Molecular and Cellular Biology

Advisory Committee:

Dr. Marc Coppelino (Advisor)
Dr. Steffen Graether

Abstract: Cortactin is a key player in the invasion of breast cancer cells due to its involvement in actin polymerization, activation of the Arp2/3 complex, and trafficking of the extracellular matrix degrading protein membrane-type-1 matrix metalloproteinase (MT1-MMP).

The goal of this study was to assess how particular residues of cortactin, tryptophan 22 (W22), lysine 309 (K309), and tyrosine 421 (Y421), are important in invadopodia formation and ECM degradation. We used quick-change mutagenesis to produce cortactin with mutations at these sites and transfected them into MDA-MB-231 cells to assess their effects on this already invasive, immortalized breast cancer cell line. We found that each mutant expressed a dominant negative effect on these cells, impeding actin polymerization, limiting the cell's capacity to degrade gelatin (an ECM analogue), and reducing MT1-MMP cell surface expression. Together, these results indicate that cortactin has extensive protein interactions and has a powerful role in invadopodia function.

Curriculum Vitae: Marguerite completed her Bachelor of Science (Hons.) in Molecular Biology and Genetics at the University of Guelph. She graduated with distinction in April 2019 after spending a semester studying in Scotland at the University of Aberdeen as well. Marguerite began her Master of Science program in Fall 2020 in the lab of Dr. Marc Coppelino.