



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

ARIANNE BERMAS

on Friday, September 24, 2021 at 1:30 p.m. (online)

Thesis Title: Defining mechanisms of antifungal resistance in *Cryptococcus neoformans* by quantitative proteomics

Examination Committee:

Dr. John Vessey, Dept. of Molecular and Cellular Biology (Exam Chair)
Dr. Jennifer Geddes-McAlister, Dept. of Molecular and Cellular Biology
Dr. Rebecca Shapiro, Dept. of Molecular and Cellular Biology
Dr. Cezar Khursigara, Dept. of Molecular and Cellular Biology

Advisory Committee:

Dr. Jennifer Geddes-McAlister
(Advisor)
Dr. Rebecca Shapiro

Abstract: *Cryptococcus neoformans*, an opportunistic yeast-like fungal pathogen, has demonstrated resistance to all major classes of antifungal drugs, including fluconazole – the mainstay treatment of cryptococcosis. To provide mechanistic insight into fluconazole resistance, this study utilized quantitative proteomics to identify significant differences in protein abundance between fluconazole-resistant and fluconazole-susceptible strains of *C. neoformans*. From this data, the gene encoding a protein of interest, ClpX, was identified and further explored. Biolistic transformation combined with double joint homologous recombination was used to construct *clpX* Δ (CNAG_01343) knockouts. Mutant strains were phenotypically characterized to determine a role for ClpX in fungal virulence and involvement in antifungal resistance. Our results reveal that ClpX has an influence on the expression of key virulence factors. Additionally, we demonstrated that ClpX inhibition displays a synergistic effect with fluconazole and could act as a novel therapeutic strategy to reintroduce antifungal susceptibility in resistant *C. neoformans* strains. Overall, this work shows how ClpX, a previously uncharacterized protein in *C. neoformans*, contributes to virulence factor expression and antifungal resistance to fluconazole.

Curriculum Vitae: Arianne completed her Bachelor of Science (Hons.) at Queen's University in Winter 2019 and began her MSc in the lab of Dr. Jennifer Geddes-McAlister in the fall of the same year.