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*

MICHELLE AGYARE-TABBI

On Friday, March 31, 2023 at 1:30 p.m. (SSC 3317)

Thesis Title: **Characterization of the error-prone polymerase *REV1* in DNA damage and antifungal drug resistance in *Candida albicans***

Examination Committee:

Dr. Jasmin Lalonde, Dept. of Molecular and Cellular Biology (Exam Chair)
Dr. Rebecca Shapiro, Dept. of Molecular and Cellular Biology
Dr. Georgina Cox, Dept. of Molecular and Cellular Biology
Dr. Stephen Seah, Dept. of Molecular and Cellular Biology

Advisory Committee:

Dr. Rebecca Shapiro (Advisor)
Dr. Georgina Cox
Dr. George van der Merwe

Abstract: *Candida albicans* is a commensal yeast that exists naturally on human skin and mucosal surfaces. Despite its ability to exist harmlessly in human hosts, it is considered an opportunistic pathogen and can cause severe and life-threatening disease in immunocompromised individuals. It is the fourth most common cause for nosocomial bloodstream infections and is the leading cause of deaths associated with invasive fungal infections. The lack of effective antifungal therapies coupled with the rising incidence of antifungal drug resistance has established this organism as a significant threat to human health. Advancements in gene editing technologies, such as CRISPR, have provided efficient means by which *C. albicans* can be studied to help identify novel antifungal drug targets and explore possible avenues for slowing antifungal drug resistance. In bacteria, there is a well-established phenomenon linking treatment with antibiotics to increased rates of mutagenesis and drug resistance, mediated by error-prone polymerases. These polymerases are upregulated upon stress-induced DNA damage. They facilitate rapid DNA repair and confer tolerance to DNA damage while introducing mutations into the genome, ultimately driving drug resistance. Although error-prone polymerases have been identified and researched in the model yeast organism *Saccharomyces cerevisiae*, they have yet to be characterized in pathogenic yeast such as *C. albicans*. Based on known orthologs in *S. cerevisiae*, six genes encoding error-prone polymerases were knocked out in *C. albicans*. The expression of these factors was assessed to monitor their upregulation in DNA damaging conditions. I focused on REV1 and characterized its role as an important factor in the DNA damage pathway, mutagenesis, and in modulating antifungal drug resistance.

Curriculum Vitae: Michelle completed her Bachelor of Science (Hons.) in Biological Science with a minor in French Studies at the University of Guelph in June 2020. In September of the same year, she began her Master of Science program in Molecular and Cellular Biology at the University of Guelph in the lab of Dr. Rebecca Shapiro.

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Awards: EvoFunPath Fellowship, NSERC CREATE (2021-2022); CanFunNet Presentation Award (2022).

Publications: Cochrane RR, Shrestha A, Severo de Almeida MM, **Agyare-Tabbi M**, Brumwell SL, Hamadache S, Meaney JS, Nucifora DP, Say HH, Sharma J, Soltysiak MPM, Tong C, Van Belois K, Walker EJL, Lachance M-A, Gloor GB, Edgell DR, Shapiro RS, Karas BJ. 2022. Superior conjugative plasmids delivered by bacteria to diverse fungi. Biodes Res 2022:1–15.

Razzaq I, Berg MD, Jiang Y, Genereaux J, Uthayakumar D, Kim GH, **Agyare-Tabbi M**, Halder V, Brandl CJ, Lajoie P, Shapiro RS. 2021. The SAGA and NuA4 component Tra1 regulates *Candida albicans* drug resistance and pathogenesis. Genetics 219.

Spina CJ, Goodall C, Halder V, **Agyare-Tabbi M**, Notarandrea-Alfonzo J, López DG, Shapiro RS, Bohle DS, Khursigara C, Precht R. 2021. In-vitro activity of a novel hypervalent complex against drug-resistant pathogens and bacterial biofilm: Tribasic silver bisperiodate. Under Preparation.