Department of Molecular and Cellular Biology

Graduate Seminar MCB*6500

Friday, January 19, 2024 @ 12:45 p.m.

presented by:

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(Advisor: Dr. Rebecca Shapiro)

"Discovery, Characterization and Mechanistic Study of Novel Antifungal Drugs Proposed by Machine Learning Models "

Fungal pathogens are a significant threat to human health, causing over 300 million serious infections and 1.6 million deaths every year. These infections are very challenging to treat, as only four classes of antifungal medications have been clinically approved, and resistance to these drugs presents a growing threat. Development of new antifungals is difficult because drug targets are limited by the close evolutionary relationship between humans and fungi, and drug discovery screens are not typically optimized for fungal pathogens. Recently, machine learning models have been applied to address similar challenges in antibiotic discovery and have successfully identified both broad- and narrow-spectrum antibiotics. Despite this, the application of machine learning towards antifungal discovery has remained extremely limited. In collaboration with the Stokes lab at McMaster University, we aim to develop a machine learning algorithm capable of generating novel small molecule antifungal drugs against the common fungal pathogen Candida albicans. These drug candidates will be tested for activity in vitro, and the most promising molecules will be further characterized to determine efficacy, spectrum, rate of activity and biofilm penetration. Based on these results, the most promising compound will be chosen for mechanistic study. Overall, this project will leverage machine learning to create highly novel antifungal compounds and characterize their activity in vitro. This represents a powerful new approach to antifungal drug development, which is crucial to decrease the burden of fungal pathogens on human health.