

BIOMEDICAL & VETERINARY SCIENCES

GRADUATE PROGRAM



ANNOUNCES

The Master of Science Seminar and Examination of

Nicolas D. Burns

“Remanding Aspergillus Resistance through Reduction, Re-Sensitization and Repurposing”

Friday, December 8th, 2023

10:00am

Classroom 100



## **Bio**

Nicolas Burns is a graduate of Rochester Institute of Technology. Post graduation he worked in Peixuan Guo's lab as an associate researcher on nanopore technology. From there he came to work in Dr. Seleem's lab in fungal biology and antifungal resistance. His work consisted of evaluating the MCE Drug Repurposing Library to identify compounds capable of inhibiting fungal growth with itraconazole at sub effective doses.

## **Funded by**

VMCVM Office of Research and Graduate Studies

## Lay Language Abstract

*Aspergillus fumigatus* is a diverse fungal organism capable of predating upon immunocompromised individuals. Infections primarily occur through breathing spores that remain dormant until the person's immune system is weakened, via disease, cancer, or transplantation when the spores are able to colonize the lungs. Treatment options for *Aspergillus fumigatus* infections are voriconazole (VRC), itraconazole (ITC), and posaconazole (POS). In the past two decades, we have globally witnessed the emergence of resistance to azoles necessitating the use of amphotericin B (AmB), a severe treatment option.

We challenged *A. fumigatus* CDC isolate #738 with compounds from the MedChem Express (MCE) Drug Repurposing Compound Library (4226 compounds) with itraconazole at 0.06 µg/mL, an ineffective dose. Combinations and compounds that negated 90% of fungal growth were selected and evaluated through published literature. Six compounds, cobicistat, elvitegravir, lopinavir, penfluridol, rilapladib, and rolapitant; were selected due to favorable properties. The combination of ITC, POS, and VRC with the identified compounds demonstrated antifungal enhancement in resistant and susceptible isolates.

We observed the reversal of several resistant strains to POS, ITC, and VRC when our selected drugs were co-applied. This demonstrates the importance of evaluating approved and under current review drugs to identify novel properties to aid our dwindling antifungal supply. This study provides promising combinational therapies for further evaluation in combating resistant *A. fumigatus* infections.

### Publications

Synergistic potential of lopinavir and azole combinational therapy against clinically important *Aspergillus* species. 2023 (Under Review)

### Presentations

- CeZap 2022
- VCOM 2023
- BMVS Symposium 2023
- GPSS 2023,
- VTCDD 2023
- BMVS Seminar 2023

## **Examination Graduate Committee**

### **Major Advisor/Chair:**

Mohamed Seleem, DVM, MS, PhD  
Professor  
DBSP

### **Graduate Advising Committee Members:**

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