Department of Molecular and Cellular Biology

Graduate Seminar MCB*6500

Friday, September 29, 2023 @12:00 p.m.

presented by:

Mary Adofo

(Advisor: Dr. Jennifer Geddes-McAlister)

"Exploring the involvement of specific proteins in the virulence mechanisms of *Cryptococcus neoformans* and their influence on the fluconazole resistance"

Over the past decade, there has been a noticeable increase in the frequency of fungal infections, affecting individuals with compromised immune systems. One of these fungal infections is cryptococcosis, primarily caused by the common fungus Cryptococcus neoformans. This encapsulated yeast is well-known for causing cryptococcal meningitis in HIV/AIDS patients, resulting in hundreds of deaths each year. Throughout the years, research into Cryptococcus pathogenesis has unveiled the significance of its inherent phenotypic traits, which enhance virulence within the host and shield the fungus from antifungal treatments. Examples of these virulence factors include capsule formation and melanin synthesis, both of which play a crucial role in protecting the yeast from environmental stressors like chemicals and radiation, as well as defending against threats posed by the host's immune cells. Furthermore, additional virulence factors, such as mannitol production, and the secretion of extracellular enzymes like urease and superoxide dismutase, along with the fungus' ability to withstand the mammalian body's temperature range, collectively determine its survival within the host and ultimately influence the onset and persistence of the disease. Recent research has identified 13 proteins with significantly high abundance in two fluconazole-resistant strains of C. neoformans. Notably, among these proteins, Prenylated Rab Acceptor 1(Pra1), Xylitol dehydrogenase, and MARVEL (MAL and related proteins for vesicle trafficking and membrane link) domain-containing protein exhibited substantial abundance. Although these proteins have been recognized for their roles in the pathogenicity of other organisms, their potential contributions to building essential cell components that promote antifungal tolerance and how they are involved in the virulence of C. neoformans have not been explored until now.

This research aims to significantly advance the development of more effective therapeutic approaches for combating infections caused by C. neoformans by attaining a deeper comprehension of the roles played by these specific proteins in the intricate interplay between fluconazole resistance and virulence.