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DISSERTATION

Defining Lipid Flippase Function In *Cryptococcus neoformans*  
Pathogenesis and Host Immunity

By

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Infection, Immunity and Inflammation Track,  
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Thursday, April 9<sup>th</sup> 2026  
11:00 AM  
PHRI Auditorium

**Join Zoom Meeting**

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## ABSTRACT

*Cryptococcus neoformans* (Cn) is a major opportunistic fungal pathogen and a leading cause of fungal meningitis in immunocompromised individuals, accounting for ~15% HIV-related deaths globally. Because the infection is initiated in lungs, early interactions between the fungus and host are critical in determining disease outcome. Our previous study has shown that deletion of *Cdc50* increases macrophage phagocytosis and killing, and renders *C. neoformans* avirulent in animal model. However, how fungal flippase dysfunction modulates *Cryptococcus*-host interactions remains unknown. In this study, we show that loss of *Cdc50* disrupts membrane lipid homeostasis, alters extracellular vesicle production and composition, and enhances fungal recognition and killing by macrophages in vitro. In murine model of pulmonary cryptococcosis, the *cdc50* $\Delta$  mutant cells display reduced fungal burden in the lungs and no dissemination to extrapulmonary organs. This is associated with a distinct immune response marked by reduced innate cell recruitment and enhanced secretion of IL-17 and IFN- $\gamma$  cytokines. Together, these findings identify *Cdc50*-dependent lipid homeostasis as a key regulator of early infection dynamics in host-pathogen interactions during pulmonary cryptococcosis.