Proposal

Title – Characterization of pH-responsive genes in *Cryptococcus neoformans*

Program of Study – Cell & Molecular Biology

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Subtype - Basic

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Abstract:

Cryptococcus neoformans is a fungal pathogen that infects many immunocompromised individuals, especially those suffering from HIV/AIDS. *C. neoformans* first infects the lungs, and if not treated can travel to the central nervous system, where it causes a deadly meningitis. What makes *C. neoformans* so deadly is that it is particularly skilled at adapting to the human host in order to avoid being cleared by the immune system. An important aspect of host immune function involves changes in pH; in fungi, pH adaptation occurs via the Rim pathway. The Rim pathway senses the extracellular pH fluctuation when the pathogen enters the neutral/alkaline environment of the human host, and induces production of alkaline proteins in order to survive the pH change. Four specific *C. neoformans* genes, CNAG_01580, CNAG_02291, CNAG_05866, and CNAG_06473, were recently identified in a screen of Rim pathway-related mutants by collaborators at Duke University. In order to characterize these mutants, knockout *C. neoformans* strains were created using In-Fusion cloning and biolistics transformation. The knockout strains will be assessed for alterations in virulence-related phenotypes as well as an infection model in mice to characterize the function of these genes within pH regulation. Potentially, if these specific genes are shown to have a significant effect on virulence and

infection, then they may serve as targets for antifungal therapy and lead to new treatments and help those afflicted with this and other fungal diseases.