

**Title** - Determination of the Impact of pyk1 Deletion on Interactions of *C. neoformans* with the Host Immune System

**Program of Study** – Microbiology

**Presentation Type** – **Choose one of the following:** PowerPoint

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**Category** – **Choose one of the following:** Experimental (Applied)

**Abstract:**

*Cryptococcus neoformans* is an important fungal pathogen of immunocompromised individuals. During initial infection, *C. neoformans* colonizes the airspaces of the lungs, resulting in pneumonia, and subsequently migrates to the central nervous system (CNS). There is also epidemiological evidence for dormancy of cryptococcal infections.

To greater understand fungal carbon utilization (particularly gluconeogenesis and glycolysis) during colonization of these fundamentally different niches within the host, mutants were created at key points in these carbon metabolic pathways. Our objective is to develop a model that will allow for the effective studying of dormancy in this important human pathogen by quantifying cytokine expression in macrophages exposed to these pyruvate kinase mutants that fail to elicit inflammation in the lung. In the course of our study, we seek to identify the factors responsible for the lack of recognition of mutated *Cryptococcus neoformans* by the immune system. The study of cytokine production and immune signaling in host immune cells following exposure to the yeast and subsequent capsule production will hopefully broaden our understanding of dormancy in a pathogen that kills 675,000 people per year in sub-Saharan Africa.

To accomplish this, collected *C. neoformans* mutants (with a deletion of the Pyk gene) will be co-incubated with the harvested macrophages in conditions that simulate the interior of human subjects. Subsequently, the culture broth from this incubation will be saved for later analysis of macrophage cytokine production. The macrophages themselves will also be collected for further analysis of gene expression in loci that regulate immune response to *C. neoformans*.

### **Christian Worldview Integration:**

As Christians we believe that there is value in life, and it is that intrinsic value that moves us to understand the very illnesses that affect it. When we do our research, we do so with a mentality that is fully aware of how intricate and ordered our Lord's handiwork is. When we dissect the femur, extract its bone marrow, and harvest its macrophages, we do so with a growing desire to understand how this intelligent design interacts and communicates with other areas of our body. Colossians 3:23 has fueled our motivation for this project tremendously. We understand that as Christ's ambassadors, whatever we do, we do wholeheartedly as unto the Lord and not for men. This worldview is foundational, and is what compels us to be excellent in our field of study. We want to be ready to give an answer at all times, as it says we should in Peter 3:15. At times this has required long hours of nonstop research, and the reading of endless paper reviews. However, because we understand that this is for the glory of our heavenly Father, we remain determined to present a project that does just that. When we communicate our findings, we want to do so in a way that draws the scientific community closer to the maker of it all. We want nothing more but for our discoveries to be presented in a way that leaves fellow researchers (statewide) in awe of our Creator's masterwork.

The research we are conducting will impact countless communities that are currently suffering from a deadly pathogenic fungus that is under researched. A clearer understanding of how *Cryptococcus* is able to remain latent within the human body for years, bypassing the immune system almost entirely, will pave a road for research that is geared toward influencing dormancy upon active pathogens- a breakthrough discovery. We pray that through our research, lives are saved, knowledge is deepened, and God is exalted.