

Proposal

Title - Characterization by Deletion of Genes Related to Carbon Metabolism in *Cryptococcus neoformans*

Program of Study – Biology

Presentation Type – Choose one of the following: PowerPoint

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

Abstract: *Cryptococcus neoformans* is a fungal pathogen that affects immunocompromised individuals such as AIDS patients. With the high prevalence of HIV in Africa, *C. neoformans* and the closely related *C. gattii* cause over 600,000 deaths annually in Sub-Saharan Africa. Unlike many fungal pathogens, *Cryptococcus* migrates from the lungs to the central nervous system (CNS). Once in the CNS, it causes meningoencephalitis which are life threatening diseases. Carbon utilization is an important part of the persistence of *C. neoformans* because glucose utilization is required for CNS disease, and deletion of pyruvate kinase (PYK1) inhibits glucose utilization and CNS disease. *pyk1* Δ rescue mutants have been identified that are able to grow on glucose.

The mechanism by which *Crypto* recovers glucose metabolism is currently unknown. The goal of the presented project is to identify genes that show increased activity in the rescue mutant compared to the *pyk1* mutant. Objectives include creating successful transformants with deletions in the genes of interest and characterization of those transformants.

Three genes that have been identified as putatively responsible for this phenotype rescue, which appears to be correlated with increased hyphal growth likely due to upregulation of the MAT locus located on Chromosome 5 will be characterized by deletion. Our approach will be in two parts, one to make a series of knockout mutants to identify certain unknown genes role in our species, and the second to sequence the cDNA from both the rescue and original mutant strains to identify differences in expression that are correlated with growth on glucose.

The discovery of the genes related to recovery of phenotype in the rescue mutant would elucidate the carbon cycle regulation in *Crypto*. Because *Crypto* preferentially uses glucose in CSF in vivo, control of glucose utilization could lead to new treatment options for *Crypto* infections.

Christian worldview integration:

Medical ministry also allows Christians to fulfill the biblical command to love one another. The bible talks about this in multiple places, but one example is Galatians 6:2 says to “Carry each other's burdens, and in this way you will fulfill the law of Christ.” Christianity has a long history of supporting community outreach via medical clinics and hospitals in recent years, and monasteries and convents that fulfilled similar roles in the past. Illness gives the Church an unparalleled opportunity to speak into people’s lives and to demonstrate God’s love.

Christ himself set the example of caring for the sick and wounded. As the Bible says in Matthew 9:35: “And Jesus went throughout all the cities and villages, teaching in their synagogues and proclaiming the gospel of the kingdom and healing every disease and every affliction.” Caring for the downtrodden is one of the hallmarks of God’s people. As God’s agents on earth, Christians are responsible to make sure that the world can recognize us by our love for others. What better way to demonstrate God’s love than by saving or a life or making it more liveable?

The overall goal of this research project is to help treat a deadly disease in accordance with the principles displayed by Jesus. This research can impact culture by saving lives and increasing overall quality of life in the lives of those suffering with a *Cryptococcus neoformans* infection as well as their loved ones. Caring for the poor and sick is part of fulfilling the Great Commission.