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). Previously, research has been centrally looking at the fungal carbon metabolic pathway in communication with the host system. In seeking to greater understand fungal carbon utilization in C. neoformans, a mutant strain for the pyruvate kinase gene was created. This mutant strain (Δpyk1) was shown from previous experiments to be avirulent. We propose inserting a gene into this strain that would produce the cytokine interferon-gamma, thus functioning to prevent infection by C. neoformans. Logically, if the addition of a gene producing the cytokine interferon-gamma can be properly inserted to the genome of the Δpyk1 mutant, then the mutant strain could be used as a basis for a vaccine preventing immunocompromised individuals from developing cryptococcosis. Previous studies have shown that insertion of the gene for interferon-gamma into the genome of wild-type C. neoformans created a strain that was able to provide immunity for cryptococcosis in mice. We plan to use this model, but improve upon it by inserting the gene into the attenuated Δpyk1 mutant. In order to do this, a plasmid containing the interferon-gamma gene will be used to eventually transform the C. neoformans Δpyk1 strain. We will create this plasmid containing the interferon gamma gene. Primers were constructed for the amplification of the desired DNA. Infusion technique will then allow us to create the plasmid. Once the plasmid is created, we will move forward in the creation of the vaccine strain.