



Medical Education and Research Grant Outcome Report

Name: Investigating Fungal Infection: Analysis of Spores from the Human Fungal Pathogen *Cryptococcus neoformans*

Principal Investigator: Christina M. Hull

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Department: Biomolecular Chemistry

Program: New Investigator Program

Grant Duration: 08-01-2005 to 7-31-2008 (36 months)

Expenditures: \$100,000 (100%)

Use of Funds (Taxonomy): Basic Research

Research Keywords: infectious disease, medical mycology, eukaryotic development, gene regulation, spore characterization

► **Description:** The goal of the project was to better understand the properties of fungal spores that allow them to infect humans and cause disease. Using the soil fungus *Cryptococcus neoformans* as a model for spore development, the work primarily focused on determining the basic chemical and biological features of spores and assessing the ability of spores to interact with the mammalian immune system and cause disease.

► **Contributions/Results:** The investigators made significant progress in describing the properties of the spores and determining the conditions that lead to rapid germination. They discovered that *C. neoformans* spores are resistant to an array of environmental conditions that would be required for persistence in nature. In addition, spores rapidly germinate in response to nutrient-rich conditions, but are stable in low nutrient conditions for at least several months.

After developing methods to recover RNA from spores during germination, the team discovered genes that are expressed only in spores or during germination. These genes are good candidates for studies to determine what genes are important for growth in response to mammalian lung conditions.

The investigators also started working with mammals by testing the response of mouse alveolar macrophages to spores in culture and the virulence of spores in a mouse respiratory model of infection.

These experiments demonstrated for the first time that *C. neoformans* spores can cause mammalian disease. This finding suggests that spores can play a role in human disease, a finding that merits future study.

► **Met Objectives:** Project completed

► **Timeline for Application of Results:** Unknown

► **New Partnerships or Collaborations:** This project helped form collaborations between Dr. Hull's laboratory and researchers on and off campus. In addition, she recruited an experienced post-doctoral fellow for the expressed purpose of working on the immunological aspects of host-cell interaction. Ongoing studies continue to be supported by researchers in the Department of Animal Sciences and the Department of Pathobiological Sciences.

► **Matched Dollars (cash or in-kind):** None

► **Dissemination:** Articles from this project were published in *Eukaryotic Cell* and *Infection and Immunity*. A third article is in preparation.

► **Additional Funding:** Data from this project were used as Preliminary Studies for a National Institutes of Health R01 grant that was funded through National Institute of Allergy and Infectious Disease in spring of 2010 (\$250K/year, 5/1/2010-4/30/2015).