# THE HARTWELL FOUNDATION

## 2014 Individual Biomedical Research Award

**Christina M. Hull, Ph.D.**

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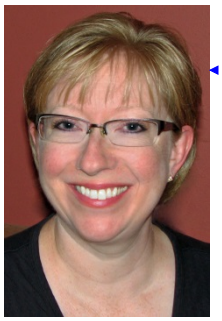

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### Prevention and Treatment of Deadly Fungal Diseases by Targeting Spores

Fungi are neither plants nor animals; they form their own branch in the tree of life. They use two distinct modes of reproduction – vegetative growth (i.e. simple cell growth such as budding) and developmental growth (i.e. complex cell structures resulting in spores). There are many kinds of fungi that infect humans and cause severe illnesses such as systemic blood infections, respiratory infections, allergic asthma, and even meningitis. The incidence of these fungal infections in children is increasing at an alarming rate, due in part to various climate changes that have contributed to the spread of fungi to new environments. This is important because fungal disease typically starts upon exposure to spores present in the soil or in the air, causing infections on the skin, within the lungs or in the blood. Fortunately, most infections are rarely serious unless there is already weakened immunity from other illness, including intensive chemotherapy or from immunosuppressive drugs. It is troubling in the United States that fungal diseases (caused primarily by yeasts and molds) claim thousands of lives on an annual basis and the rates of death are so high (up to 90% for some fungi and ~50% overall). The fundamental clinical challenge is that currently available antifungal drugs are inadequate, because either they are only moderately effective in killing fungi or at the effective dose are highly toxic to the individual. Antifungal drug development is difficult because human and fungal cells (unlike bacteria) are very similar in cell structure and function, making it very difficult to find drugs that will kill fungi without killing the human host. To address this challenge, she proposes to overcome the limited number of druggable targets unique to fungi by implementing a new strategy for antifungal drug development, one that specifically targets spores. Her working hypothesis is that the spore-specific process of germination is distinct from normal human cell growth, and as a result, represents an untapped source of vulnerable drug targets. As a model system, she will use the meningitis-causing yeast *Cryptococcus neoformans*, which has known virulence factors and a reproduction cycle that is susceptible to manipulation. Unlike most fungal pathogens, *C. neoformans* provides advantages because many molecular, genetic, and animal tools exist for characterizing its pathogenicity. If Christina is successful, new and effective interventions for prevention and treatment of severe fungal disease will be possible, benefitting the health and well-being of tens of thousands of affected children.