A potential drug screen for the histidine kinases of Candida albicans

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The yeast *Candida albicans* is the most common human pathogenic fungus. In any given human population 30-50% of all individuals will carry *C. albicans* in their natural skin and intestinal flora. Normal healthy individuals will stay asymptomatic and healthy as the normal human immune system can fight off the invading *C. albicans* cells. In addition, the bacteria of the normal human flora outcompete *C. albicans* and prevent overgrowth. However during severe sickness, use of immune inhibiting drugs or strong antibiotics, that drastically disturb the normal bacterial flora, the opportunistic yeast *C. albicans* can invade its host's tissues and infect. *C. albicans* is responsible for roughly 5% of all hospital acquired bloodstream infections and has a systemic infection mortality rate of approximately 40%. All anti-fungal drugs that are available today have serious side effects, as fungi are eukaryotes, like humans and animals. Many anti-fungal drugs consequently attack both the fungi and the patient, only to different extents. The need for new anti-fungal drugs is therefore paramount. In the past 30 years the frequency of most human fungal infections has decreased while the frequency of *C. albicans* infections have remained stable. This could arguably be attributed to *C. albicans* complex lifecycle and complex host interaction as well as its resilient ability to evade and even escape the human immune system.

C. albicans has 3 different growth forms and all 3 growth forms are used for successful human tissue penetration and subsequent infection. The switch between the different growth forms is highly regulated and essential for successful infection. In order to determine when to switch between the different growth forms *C. albicans* uses 3 environmental sensory proteins called histidine kinases. These proteins are highly important during the early stages of a *C. albicans* infection and if they are disrupted or knocked-out the virulence and mortality rate of a *C. albicans* infection is severely diminished. As histidine kinases are essential for successful infection, and because there are no similar human proteins, they are very attractive potential drug targets.

This project has investigated the possibility to set up a high-throughput drug screen for the 3 histidine kinases of *C. albicans* using the non-pathogenic fission yeast *Schizosaccharomyces pombe* as a model system.

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