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"INVESTIGATING FUNGAL FACTORS SHAPING THE IMMUNOGENICITY OF A NOVEL *CRYPTOCOCCUS* VACCINATION MODEL"

By

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Friday, March 14th, 2025
ICPH Auditorium
11:00 A.M.

Join Zoom presentation
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Meeting ID: 987 4662 6470
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ABSTRACT

Currently, no fungal vaccine exists for clinical use while fungal infections are responsible for over 1.5 million deaths every year. Although anti-fungal drugs are available, they are limited in their applications. As populations susceptible to fungal infections continue to increase combined with the rise of anti-fungal resistance, an effective anti-fungal vaccine is highly desired. Our previous studies identified a *Cryptococcus neoformans* mutant strain *fbp1Δ* as a potential vaccine candidate. This mutant strain contains a deletion of the F-box protein Fbp1, a key subunit of the SCF E3 ligase complex necessary for ubiquitin-mediated proteolysis. Vaccination with heat-killed *fbp1Δ* (HK-*fbp1*) can elicit protection against *C. neoformans* parental strain and its sibling species C. gattii in an interferon gamma (IFN-γ) dependent Type 1 immune response. The protection is preserved in $CD4^+$ T cell depleted animals, indicating that this vaccination approach may work in both immunocompetent and immunocompromised hosts, e.g., HIV/AIDS. However, we have yet to decipher the immunogenic factor(s) expressed by the *fbp1*Δ mutant that are responsible for the induction of the protective immune response. In this study, we have identified that capsule plays an important role in HK-*fbp1* vaccine mediated protection, as acapsular HK-*fbp1* cells showed diminished protection against wild type challenge. Additionally, our studies have shown that Cytokine Inducing Glycoprotein 1 (Cig1), a GPI anchored mannoprotein, is upregulated in *fbp1Δ* and contributes to the immunogenicity of HK-*fbp1*. Deletion of Cig1 in the *fbp1Δ* background resulted in decreased recruitment of anti-fungal effector T cells and diminished production of protective inflammatory cytokines by the host. Furthermore, loss of Cig1 in the *fbp1Δ* mutant resulted in reduced protection in vaccination survival studies at lower vaccine inoculum doses compared to HK-*fbp1*. In aggregate, these findings demonstrate Cig1 is an antigen that contributes to the immunogenicity of HK-*fbp1* that may be utilized to further optimize the HK-*fbp1* fungal vaccine as a tool in the arsenal against invasive fungal infections.