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CpG Adjuvantation Enables Intramuscular Heat-Killed fbp1
Vaccination and Sterilizing Protection Against Cryptococcosis

By

Yu Zhang

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Shihezi University, China, B.S 2016

Thesis Advisor: Chaoyang Xue, Ph.D
Associate Professor
Rutgers New Jersey Medical School
Department of Microbiology, Biochemistry and Molecular Genetics

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PHRI 1st Floor Room W140B

Join Zoom Meeting

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Meeting ID: 916 6542 3551
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ABSTRACT

Despite the rising burden of invasive fungal disease, no fungal vaccine is currently available for clinical use. *Cryptococcus neoformans* is an opportunistic fungal pathogen that initiates pulmonary infection and can disseminate to cause fatal meningoencephalitis. We previously identified HK-fbp1, a heat-killed *C. neoformans* mutant lacking the F-box protein Fbp1, as an intranasal vaccine that confers durable protection. Here, we show that incorporation of the type-C CpG adjuvant ODN2395 transforms this platform into an effective intramuscular vaccine. This combinatorial vaccine enabled effective intramuscular immunization to provide sterilizing immune protection against pulmonary challenge, with mostly complete clearance of fungal burden and blockade of extrapulmonary dissemination. Protection correlated with strong recruitment of innate immune cells to the lung and a coordinated CD4⁺ T-cell response. *Cryptococcus*-specific CD4⁺ T cells produced substantial levels of IFN- γ and IL-17A in lung-draining lymph nodes, whereas muscle-draining nodes exhibited strong IL-2, consistent with coordinated priming and Th1/Th17 effector programming. Protection required IFN- γ , but not other interferons, and persisted in CD4⁺ T-cell- or B-cell-deficient mice, supporting development for immunocompromised hosts. IL-17A also contributed to the protective immunity, but only in a reduced strength regimen. Together, these findings establish CpG-adjuvanted intramuscular HK-fbp1 vaccination as a clinically tractable strategy that can elicit sterilizing antifungal immunity and provide a foundation for advancing HK-fbp1-based antifungal vaccines.