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Candidalysin Drives C. albicans-Induced Allergic Airway Disease Through Platelets

Yifan Wu is currently a postdoctoral associate dividing his time between the labs of Dr. David Corry and Dr. Jill Weatherhead. He completed his medical degree at Shanghai Jiao Tong University School of Medicine and obtained his PhD from Baylor College of Medicine. Dr. Wu's research focuses on the host immune response to the fungi Candida albicans, specifically on the response to cerebral and pulmonary infection. He has discovered novel infectious mechanisms, pathologies, and immune pathways involved in C. albicans mediated cerebritis and allergic airway diseases.

Abstract: Background: The commensal yeast *Candida albicans* promotes allergic responses and is implicated as a cause of asthma, with mechanisms remains unknown. Candidalysin is a cytolytic peptide secreted by *C. albicans* and is a potent immune activator. Dickkopf-1 (Dkk-1) is a platelet-derived WNT pathway antagonist peptide that drives allergen-induced TH2 responses.

Hypothesis: Candidalysin promotes TH2-predominant allergic airway disease by stimulating the secretion of Dkk-1 from platelets in mice.

Methods: C57B6 mice were challenged intranasally with either viable *C. albicans* or synthetic candidalysin every other day for 8 challenges and assessed for induced airway hyperresponsiveness (AHR). Recombinant Dkk-1 or DKK-1 inhibitors were administered i.p. in similarly challenged mice. For *in vitro* studies, human platelets were incubated with *C. albicans* or candidalysin and Dkk-1 release was quantified by ELISA. Flow cytometric analysis of platelets for activation markers was also performed.

Results: Wild type *C. albicans* strongly induced AHR and TH2 responses in wildtype mice, but both parameters were significantly reduced or abrogated when a Dkk-1 inhibitor was given. In contrast, candidalysin-deficient *C. albicans* failed to induce AHR, but AHR was restored by administering exogenous Dkk-1. Candidalysin alone was sufficient to induce AHR and mild eosinophilia and induced both Dkk-1 release and activation of human platelets.

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Conclusion: Candidalysin is both necessary and sufficient for *C. albicans*-induced allergic airway diseases, suggesting the crucial role that candidalysin and platelets play in driving a fungus-dependent allergic disorder.