

Human neutrophils produce antifungal extracellular vesicles against *Aspergillus fumigatus*.

Shopova IA, Belyaev I, Dasari P, Jahreis S, Stroe MC, Cseresnyés Z, Zimmermann AK, Medyukhina A, Svensson C-M, Krüger T, Szeifert V, Nietzsche S, Conrad T, Blango MG, Kniemeyer O, von Lilienfeld-Toal M, Zipfel PF, Ligeti E, Figge MT, Brakhage AA (2020) Human neutrophils produce antifungal extracellular vesicles against *Aspergillus fumigatus*. *mBio* 11(2), e00596-20.

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Abstract

Polymorphonuclear granulocytes (PMNs) are indispensable for controlling life-threatening fungal infections. In addition to various effector mechanisms, PMNs also produce extracellular vesicles (EVs). Their contribution to antifungal defense has remained unexplored. We reveal that the clinically important human pathogenic fungus *Aspergillus fumigatus* triggers PMNs to release a distinct set of antifungal EVs (afEVs). Proteome analyses indicated that afEVs are enriched in antimicrobial proteins. The cargo and release kinetics of afEVs are modulated by the fungal strain confronted. Tracking of produced afEVs indicated that they associated with fungal cells and even

entered fungal hyphae, resulting in alterations in the morphology of the fungal cell wall, and imparted antifungal effects dose-dependently. Two identified human proteins of afEVs, cathepsin G and azurocidin, were heterologously expressed in fungal hyphae, which led to reduced fungal growth. In conclusion, the production of afEVs by PMNs offers an intriguing, previously overlooked mechanism of antifungal defense against *A. fumigatus*.

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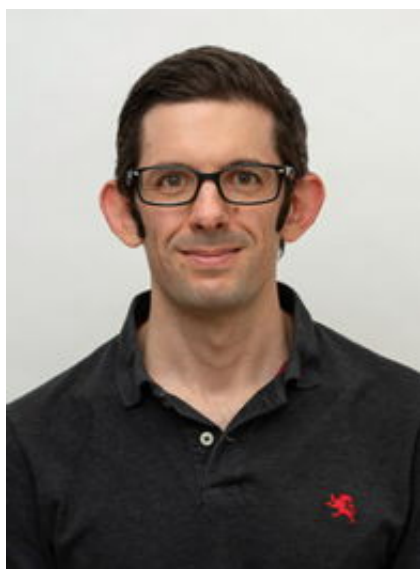
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