

Conidial dihydroxynaphthalene melanin of the human pathogenic fungus *Aspergillus fumigatus* interferes with the host endocytosis pathway.

Thywißen A, Heinekamp T, Dahse HM, Schmalzer-Ripcke J, Nietzsche S, Zipfel PF, Brakhage AA (2011) Conidial dihydroxynaphthalene melanin of the human pathogenic fungus *Aspergillus fumigatus* interferes with the host endocytosis pathway. *Front Microbiol / Fungi and their interactions* 2, 96.

[Details](#)



Abstract

Aspergillus fumigatus is the most important air-borne fungal pathogen of humans. The interaction of the pathogen with the host's immune system represents a key process to understand pathogenicity. For elimination of invading microorganisms, they need to be efficiently phagocytosed and located in acidified phagolysosomes. However, as shown previously, *A. fumigatus* is able to manipulate the formation of functional phagolysosomes. Here, we demonstrate that in contrast to pigmentless pksP mutant conidia of *A. fumigatus*, the gray-green wild-type conidia inhibit the acidification of phagolysosomes of alveolar macrophages, monocyte-derived macrophages, and human neutrophil granulocytes. Therefore, this inhibition is independent of the cell type and applies to the major immune effector cells required for defense against *A. fumigatus*. Studies with melanin ghosts indicate that the inhibitory effect of wild-type conidia is due to their dihydroxynaphthalene (DHN)-melanin covering the conidia, whereas the hydrophobin RodA rodlet

layer plays no role in this process. This is also supported by the observation that pksP conidia still exhibit the RodA hydrophobin layer, as shown by scanning electron microscopy. Mutants defective in different steps of the DHN-melanin biosynthesis showed stronger inhibition than pksP mutant conidia but lower inhibition than wild-type conidia. Moreover, *A. fumigatus* and *A. flavus* led to a stronger inhibition of phagolysosomal acidification than *A. nidulans* and *A. terreus*. These data indicate that a certain type of DHN-melanin that is different in the various *Aspergillus* species, is required for maximal inhibition of phagolysosomal acidification. Finally, we identified the vacuolar ATPase (vATPase) as potential target for *A. fumigatus* based on the finding that addition of bafilomycin which inhibits vATPase, led to complete inhibition of the acidification whereas the fusion of phagosomes containing wild-type conidia and lysosomes was not affected.

Beteiligte Forschungseinheiten

[Infektionsbiologie Peter F. Zipfel](#) [Mehr erfahren](#)

[Molekulare und Angewandte Mikrobiologie Axel Brakhage](#) [Mehr erfahren](#)

[International Leibniz Research School Peter F. Zipfel](#) [Mehr erfahren](#)

Leibniz-HKI-Autor*innen



Axel A. Brakhage

[Details](#)



Hans-Martin Dahse

[Details](#)



Thorsten Heinekamp

[Details](#)



Jeannette Schmalzer-Ripcke

[Details](#)



Andreas Thywißen

[Details](#)



Peter F. Zipfel

[Details](#)

Identifier

doi: 10.3389/fmicb.2011.00096

PMID: 21747802