The hypoxia-induced dehydrogenase HorA is required for coenzyme Q10 biosynthesis, azole sensitivity and virulence of *Aspergillus fumigatus*

Kroll K, Shekhova E, Mattern DJ, Thywissen A, Jacobsen ID, Strassburger M, Heinekamp T, Shelest E, Brakhage AA, Kniemeyer O (2016) The hypoxia-induced dehydrogenase HorA is required for coenzyme Q10 biosynthesis, azole sensitivity and virulence of *Aspergillus fumigatus* *Mol Microbiol* 101(1), 92-108.

Details

PubMed

Abstract

Aspergillus fumigatus is the predominant airborne pathogenic fungus causing invasive aspergillosis in immunocompromised patients. During infection *A. fumigatus* has to adapt to oxygen-limiting conditions in inflammatory or necrotic tissue. Previously, we identified a mitochondrial protein to be highly up-regulated during hypoxic adaptation. Here, this protein was found to represent the novel oxidoreductase HorA. In *Saccharomyces cerevisiae* a homologue was shown to play a role in biosynthesis of coenzyme Q. Consistently, reduced coenzyme Q content in the generated ΔhorA mutant indicated a respective function in *A. fumigatus*. Since coenzyme Q is involved in cellular respiration and maintaining cellular redox homeostasis, the strain ΔhorA displayed an impaired response to both oxidative and reductive stress, a delay in germination and an accumulation of NADH. Moreover, an increased resistance against antifungal drugs was observed. All phenotypes were completely reversed by the addition of the synthetic

electron carrier menadione. The deletion strain ΔhorA showed significantly attenuated virulence in two murine infection models of invasive pulmonary aspergillosis. Therefore, the biosynthesis of coenzyme Q and, particularly, the fungal-specific protein HorA play a crucial role in virulence of *A. fumigatus*. Due to its absence in mammals, HorA might represent a novel therapeutic target against fungal infections. This article is protected by copyright. All rights reserved.

Beteiligte Forschungseinheiten

Molekulare und Angewandte Mikrobiologie Axel Brakhage Mehr erfahren

Mikrobielle Immunologie Ilse Jacobsen Mehr erfahren

Microbiome Dynamics Gianni Panagiotou Mehr erfahren

Leibniz-HKI-Autor*innen



Axel A. Brakhage

Details



Thorsten Heinekamp

Details



Ilse Denise Jacobsen

Details



Olaf Kniemeyer

Details



Kristin Kroll

Details



Derek J. Mattern

Details



Elena Shekhova

Details



Ekaterina Shelest

Details



Maria Straßburger

Details



Andreas Thywißen

Details

Identifier

doi: 10.1111/mmi.13377

PMID: 26991818