Analysis of the *Aspergillus fumigatus* proteome reveals metabolic changes and the activation of the pseurotin A biosynthesis gene cluster in response to hypoxia.

Vödisch M, Scherlach K, Winkler R, Hertweck C, Braun HP, Roth M, Haas H, Werner ER, Brakhage AA, Kniemeyer O (2011) Analysis of the *Aspergillus fumigatus* proteome reveals metabolic changes and the activation of the pseurotin A biosynthesis gene cluster in response to hypoxia. *J Proteome Res* 10(5), 2508-2524.

Abstract

The mold Aspergillus fumigatus is the most important airborne fungal pathogen. Adaptation to hypoxia represents an important virulence attribute for A. fumigatus. Therefore, we aimed at obtaining a comprehensive overview about this process on the proteome level. To ensure highly reproducible growth conditions, an oxygen-controlled, glucose-limited chemostat cultivation was established. Two-dimensional gel electrophoresis analysis of mycelial and mitochondrial proteins as well as two-dimensional Blue Native/SDS-gel separation of mitochondrial membrane proteins led to the identification of 117 proteins with an altered abundance under hypoxic in comparison to normoxic conditions. Hypoxia induced an increased activity of glycolysis, the TCA-cycle, respiration, and amino acid metabolism. Consistently, the cellular contents in heme, iron, copper, and zinc increased. Furthermore, hypoxia induced biosynthesis of the secondary metabolite pseurotin A as demonstrated at proteomic, transcriptional, and metabolite levels. The observed

and so far not reported stimulation of the biosynthesis of a secondary metabolite by oxygen depletion may also affect the survival of A. fumigatus in hypoxic niches of the human host. Among the proteins so far not implicated in hypoxia adaptation, an NO-detoxifying flavohemoprotein was one of the most highly up-regulated proteins which indicates a link between hypoxia and the generation of nitrosative stress in A. fumigatus.

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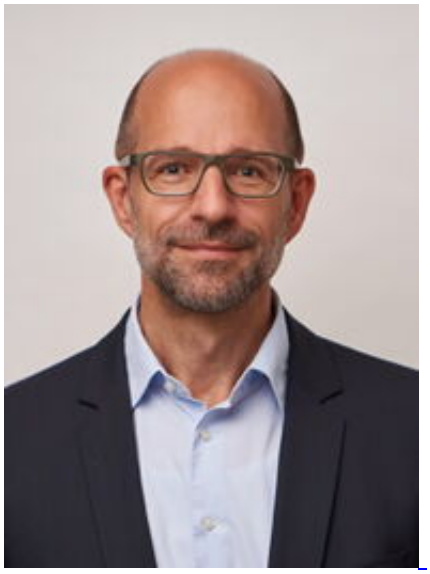

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doi: 10.1021/pr1012812

PMID: 21388144