

Redox proteomic analysis reveals oxidative modifications of proteins by increased levels of intracellular reactive oxygen species during hypoxia adaptation of *Aspergillus fumigatus*.

Shekhova E, Ivanova L, Krüger T, Stroe MC, Macheleidt J, Kniemeyer O, Brakhage AA (2019) Redox proteomic analysis reveals oxidative modifications of proteins by increased levels of intracellular reactive oxygen species during hypoxia adaptation of *Aspergillus fumigatus*. *Proteomics* 19(5), e1800339.

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Abstract

At the site of infection, the human fungal pathogen *Aspergillus fumigatus* faces abrupt changes in oxygen concentrations. An increasing number of studies have demonstrated that elevated production of intracellular reactive oxygen species (ROS) under low oxygen conditions plays a regulatory role in modulating cellular responses for adaptation to hypoxia. To learn more about this process in *A. fumigatus*, we determined intracellular ROS production during hypoxia. Our results confirmed increased amounts of intracellular ROS in *A. fumigatus* exposed to decreased oxygen levels. Moreover, nuclear accumulation of the major oxidative stress regulator AfYap1 was observed after low oxygen cultivation. For further analysis, we applied iodoTMT labelling of redox-sensitive cysteine residues to identify proteins that are reversibly oxidised. This analysis revealed

that proteins with important roles in maintaining redox balance and protein folding, such as the thioredoxin Asp f 29 and the protein disulphide PdiA, underwent substantial thiol modification under hypoxia. Our data also showed that the mitochondrial respiratory complex IV assembly protein Coa6 was significantly oxidised by hypoxic ROS. Deletion of the corresponding gene resulted in a complete absence of hypoxic growth, indicating the importance of complex IV during adaptation of *A. fumigatus* to oxygen-limiting conditions. This article is protected by copyright. All rights reserved.

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Identifier

doi: 10.1002/pmic.201800339

PMID: 30632700