

Additional oxidative stress reroutes the global response of *Aspergillus fumigatus* to iron depletion.

Kurucz V, Krüger T, Antal K, Dietl AM, Haas H, Pócsi I, Kniemeyer O, Emri T (2018) Additional oxidative stress reroutes the global response of *Aspergillus fumigatus* to iron depletion. *BMC Genomics* 19(1), 357.

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Abstract

BACKGROUND: *Aspergillus fumigatus* has to cope with a combination of several stress types while colonizing the human body. A functional interplay between these different stress responses can increase the chances of survival for this opportunistic human pathogen during the invasion of its host. In this study, we shed light on how the H₂O₂-induced oxidative stress response depends on the iron available to this filamentous fungus, using transcriptomic analysis, proteomic profiles, and growth assays.

RESULTS: The applied H₂O₂ treatment, which induced only a negligible stress response in iron-replete cultures, deleteriously affected the fungus under iron deprivation. The majority of stress-induced changes in gene and protein expression was not predictable from data coming from individual stress exposure and was only characteristic for the combination of oxidative stress plus iron deprivation. Our experimental data suggest that the physiological effects of combined stresses

and the survival of the fungus highly depend on fragile balances between economization of iron and production of essential iron-containing proteins. One observed strategy was the overproduction of iron-independent antioxidant proteins to combat oxidative stress during iron deprivation, e.g. the upregulation of superoxide dismutase Sod1, the thioredoxin reductase Trr1, and the thioredoxin orthologue Afu5g11320. On the other hand, oxidative stress induction overruled iron deprivation-mediated repression of several genes. In agreement with the gene expression data, growth studies underlined that in *A. fumigatus* iron deprivation aggravates oxidative stress susceptibility.

CONCLUSIONS: Our data demonstrate that studying stress responses under separate single stress conditions is not sufficient to understand how *A. fumigatus* adapts in a complex and hostile habitat like the human body. The combinatorial stress of iron depletion and hydrogen peroxide caused clear non-additive effects upon the stress response of *A. fumigatus*. Our data further supported the view that the ability of *A. fumigatus* to cause diseases in humans strongly depends on its fitness attributes and less on specific virulence factors. In summary, *A. fumigatus* is able to mount and coordinate complex and efficient responses to combined stresses like iron deprivation plus H₂O₂-induced oxidative stress, which are exploited by immune cells to kill fungal pathogens.

Beteiligte Forschungseinheiten

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Identifier

doi: 10.1186/s12864-018-4730-x

PMID: 29747589