

The novel globin protein fungoglobin is involved in low oxygen adaptation of *Aspergillus fumigatus*.

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Abstract

The human pathogenic fungus *Aspergillus fumigatus* normally lives as a soil saprophyte. Its environment includes poorly oxygenated substrates that also occur during tissue invasive growth of the fungus in the human host. Up to now, few cellular factors have been identified that allow the fungus to efficiently adapt its energy metabolism to hypoxia. Here, we cultivated *A. fumigatus* in an O₂-controlled fermenter and analysed its responses to O₂ limitation on a minute timescale. Transcriptome sequencing revealed several genes displaying a rapid and highly dynamic regulation. One of these genes was analysed in detail and found to encode fungoglobin, a previously uncharacterized member of the sensor globin protein family widely conserved in filamentous fungi. Besides low O₂, iron limitation also induced transcription, but regulation was not entirely dependent on the two major transcription factors involved in adaptation to iron starvation and hypoxia, HapX and SrbA respectively. The protein was identified as a functional haemoglobin, as binding of this cofactor was detected for the recombinant protein. Gene deletion in *A. fumigatus* confirmed that haem-binding fungoglobins are important for growth in microaerobic

environments with O₂ levels far lower than in hypoxic human tissue.

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