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Novel molecular mechanisms of iron sensing and homeostasis in *Aspergillus fumigatus*

Aspergillus fumigatus is a ubiquitous saprophytic mould with clinical relevance, since this fungus is capable to cause life-threatening diseases in immunocompromised patients. During infection, sufficient iron supply is crucial for fungal growth. Iron is an essential nutrient involved in a variety of cellular processes, e.g. electron transport, DNA and amino acid biosynthesis. However, iron excess can be harmful by triggering the formation of cell damaging reactive oxygen species. As a result, *A. fumigatus* has evolved fine-tuned mechanisms to maintain iron equilibrium.

The key regulators of iron homeostasis in *A. fumigatus* are the transcription factors SreA and HapX, which are interconnected by a negative transcriptional feedback loop. SreA represses iron acquisition (e.g. siderophore biosynthesis and reductive iron assimilation) during iron sufficiency to prevent the fungus from iron toxicity. In contrast, during iron limitation, HapX represses iron consuming pathways (including respiration, heme biosynthesis) and activates iron uptake by siderophores via interaction with the heterotrimeric CCAAT-binding complex. Recent findings revealed the contribution of HapX to resistance against iron excess by activation of vacuolar iron storage.

Currently little is known about how SreA and HapX sense the iron status of the cell and which mechanisms are involved in this process. The major aim of this project is to gain new insights into the mode and

regulation of iron sensing by SreA and HapX in *A. fumigatus*.

Publications

Misslinger M, Scheven MT, Hortschansky P, López-Berges MS, Heiss K, Beckmann N, Heigl T, Hermann M, Krüger T, Kniemeyer O, Brakhage AA, Haas H (2019) The monothiol glutaredoxin GrxD is essential for sensing iron starvation in *Aspergillus fumigatus*. *PLoS Genet* 15(9), e1008379. Details PubMed

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