Comparative proteomics of a tor inducible *Aspergillus fumigatus* mutant reveals involvement of the Tor kinase in iron regulation.

Baldin C, Valiante V, Krüger T, Schafferer L, Haas H, Kniemeyer O, Brakhage AA (2015) Comparative proteomics of a tor inducible *Aspergillus fumigatus* mutant reveals involvement of the Tor kinase in iron regulation. *Proteomics* 15(13), 2230-2243.

Abstract

The Tor (Target of Rapamycin) kinase is one of the major regulatory nodes in eukaryotes. Here, we analysed the Tor kinase in *Aspergillus fumigatus*, which is the most important airborne fungal pathogen of humans. Because deletion of the single tor gene was apparently lethal, we generated a conditional lethal tor mutant by replacing the endogenous tor gene by the inducible xylp-tor gene cassette. By both 2D-gel electrophoresis and gel-free LC-MS/MS, we found that Tor controls a variety of proteins involved in nutrient sensing, stress response, cell cycle progression, protein biosynthesis and degradation, but also processes in mitochondria, such as respiration and ornithine metabolism, which is required for siderophore formation. qRT-PCR analyses indicated that mRNA levels of ornithine biosynthesis genes were increased under iron limitation. When tor was repressed, iron regulation was lost. In a deletion mutant of the iron regulator HapX also carrying the xylp-tor cassette, the regulation upon iron deprivation was similar to that of the single tor inducible mutant strain. In line, hapX expression was significantly reduced when tor was

repressed. Thus, Tor acts either upstream of HapX or independently of HapX as a repressor of the ornithine biosynthesis genes and thereby regulates the production of siderophores.

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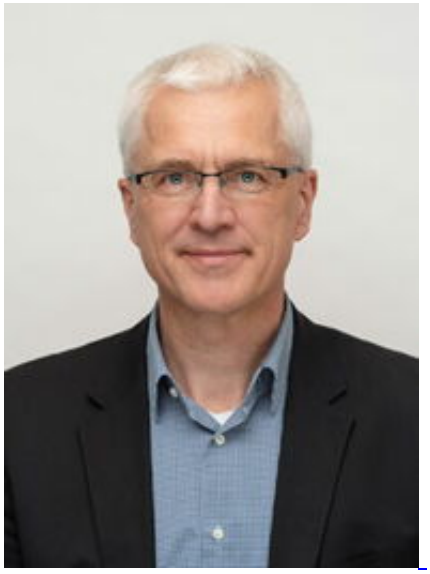

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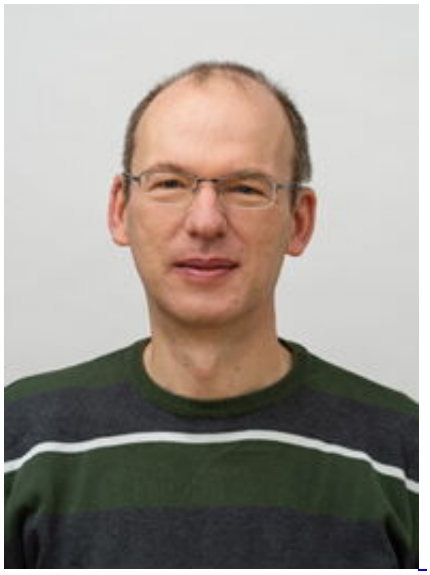

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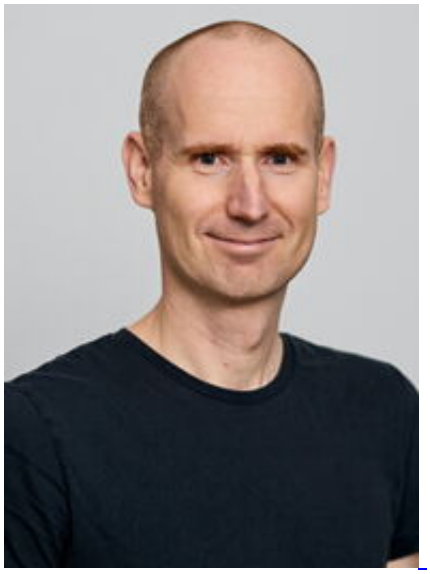

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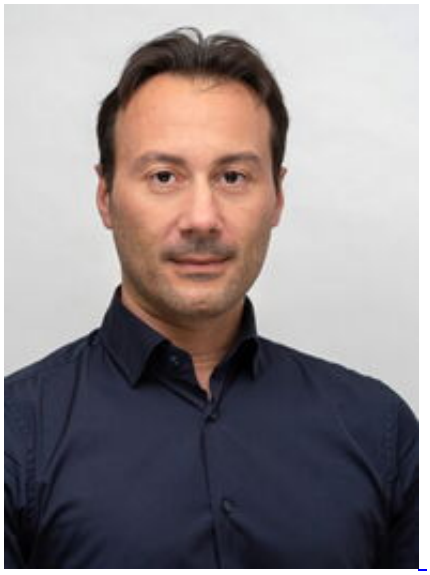

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