

The Zn²Cys₆-type transcription factor LeuB cross-links regulation of leucine biosynthesis and iron acquisition in *Aspergillus fumigatus*.

Long N, Orasch T, Zhang S, Gao L, Xu X, Hortschansky P, Ye J, Zhang F, Xu K, Gsaller F, Straßburger M, Binder U, Heinekamp T, Brakhage AA, Haas H, Lu L (2018) The Zn²Cys₆-type transcription factor LeuB cross-links regulation of leucine biosynthesis and iron acquisition in *Aspergillus fumigatus*. *PLOS Genet* 14(10), e1007762.

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Abstract

Both branched-chain amino acids (BCAA) and iron are essential nutrients for eukaryotic cells. Previously, the Zn²Cys₆-type transcription factor Leu3/LeuB was shown to play a crucial role in regulation of BCAA biosynthesis and nitrogen metabolism in *Saccharomyces cerevisiae* and *Aspergillus nidulans*. In this study, we found that the *A. fumigatus* homolog LeuB is involved in regulation of not only BCAA biosynthesis and nitrogen metabolism but also iron acquisition including siderophore metabolism. Lack of LeuB caused a growth defect, which was cured by supplementation with leucine or iron. Moreover, simultaneous inactivation of LeuB and HapX, a bZIP transcription factor required for adaptation to iron starvation, significantly aggravated the growth defect caused by inactivation of one of these regulators during iron starvation. In

agreement with a direct role in regulation of both BCAA and iron metabolism, LeuB was found to bind to phylogenetically conserved motifs in promoters of genes involved in BCAA biosynthesis, nitrogen metabolism, and iron acquisition in vitro and in vivo, and was required for full activation of their expression. Lack of LeuB also caused activation of protease activity and autophagy via leucine depletion. Moreover, LeuB inactivation resulted in virulence attenuation of *A. fumigatus* in *Galleria mellonella*. Taken together, this study identified a previously uncharacterized direct cross-regulation of BCCA biosynthesis, nitrogen metabolism and iron homeostasis as well as proteolysis.

Involved units

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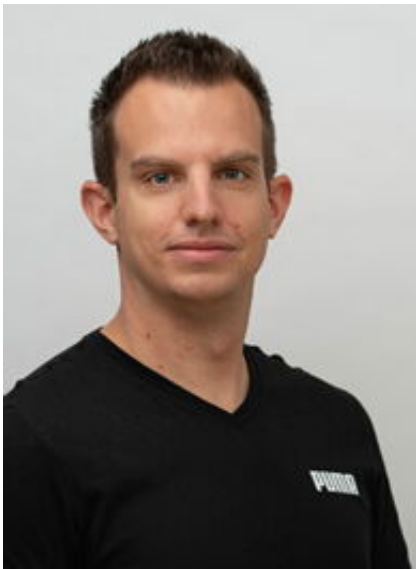
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