HapX Mediates Iron Homeostasis in the Pathogenic Dermatophyte *Arthroderma benhamiae* but Is Dispensable for Virulence.


Abstract

For many pathogenic fungi, siderophore-mediated iron acquisition is essential for virulence. The process of siderophore production and further mechanisms to adapt to iron limitation are strictly controlled in fungi to maintain iron homeostasis. Here we demonstrate that the human pathogenic dermatophyte *Arthroderma benhamiae* produces the hydroxamate siderophores ferricrocin and ferrichrome C. Additionally, we show that the iron regulator HapX is crucial for the adaptation to iron starvation and iron excess, but is dispensable for virulence of *A. benhamiae*. Deletion of hapX caused downregulation of siderophore biosynthesis genes leading to a decreased production of siderophores during iron starvation. Furthermore, HapX was required for transcriptional repression of genes involved in iron-dependent pathways during iron-depleted conditions. Additionally, the ΔhapX mutant of *A. benhamiae* was sensitive to high-iron concentrations indicating that HapX also contributes to iron detoxification. In contrast to other pathogenic fungi, HapX of *A. benhamiae* was redundant for virulence and a ΔhapX mutant was still able to infect keratinized host tissues in vitro. Our findings underline the highly conserved role of the transcription factor HapX for maintaining iron homeostasis in ascomycetous fungi but, unlike in many other human and plant pathogenic fungi, HapX of *A. benhamiae* is not a virulence determinant.

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