SreA-mediated iron regulation in *Aspergillus fumigatus*.

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Abstract

Aspergillus fumigatus, the most common airborne fungal pathogen of humans, employs two high-affinity iron uptake systems: iron uptake mediated by the extracellular siderophore triacetylfusarinine C and reductive iron assimilation. Furthermore, A. fumigatus utilizes two intracellular siderophores, ferricrocin and hydroxyferricrocin, to store iron. Siderophore biosynthesis, which is essential for virulence, is repressed by iron. Here we show that this control is mediated by the GATA factor SreA. During iron-replete conditions, SreA deficiency partially derepressed synthesis of triacetylfusarinine C and uptake of iron resulting in increased cellular accumulation of both iron and ferricrocin. Genome-wide DNA microarray analysis identified 49 genes that are repressed by iron in an SreA-dependent manner. This gene set, termed SreA regulon, includes all known genes involved in iron acquisition, putative novel siderophore biosynthetic genes, and also genes not directly linked to iron metabolism. SreA deficiency also caused upregulation of iron-dependent and antioxidative pathways, probably due to the increased iron content and iron-mediated oxidative stress. Consistently, the sreA disruption mutant displayed increased sensitivity to iron, menadion and phleomycin but retained wild-type virulence in a mouse model. As all detrimental effects of sreA disruption are restricted to iron-replete conditions these

data underscore that A. fumigatus faces iron-depleted conditions during infection.

Beteiligte Forschungseinheiten

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