

The *Aspergillus fumigatus* conidial melanin production is regulated by the bifunctional bHLH DevR and MADS-box RlmA transcription factors.

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Abstract

Melanins play a crucial role in defending organisms against external stressors. In several pathogenic fungi, including the human pathogen *Aspergillus fumigatus*, melanin production was shown to contribute to virulence. *A. fumigatus* produces two different types of melanins, i.e., pyomelanin and dihydroxynaphthalene (DHN)-melanin. DHN-melanin forms the grey-green pigment characteristic for conidia, playing an important role in immune evasion of conidia and thus for fungal virulence. The DHN-melanin biosynthesis pathway is encoded by six genes organized in a cluster with the polyketide synthase gene *pkcP* as a core element. Here, cross species promoter analysis identified specific DNA binding sites in the DHN-melanin biosynthesis genes *pkcP*-*arp1* intergenic region that can be recognised by bHLH and MADS-box transcriptional regulators. Independent deletion of two genes coding for the transcription factors DevR (bHLH) and RlmA (MADS-box) interfered with sporulation and reduced the expression of the DHN-melanin gene

cluster. In vitro and in vivo experiments proved that these transcription factors cooperatively regulate pksP expression acting both as repressors and activators in a mutually exclusive manner. The dual role executed by each regulator depends on specific DNA motifs recognised in the pksP promoter region. This article is protected by copyright. All rights reserved.

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