

Characterisation of the laccase-encoding gene *abr2* of the dihydroxynaphthalene-like melanin gene cluster of *Aspergillus fumigatus*.

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Abstract

Aspergillus fumigatus is an important pathogen of the immunocompromised host. Previously, it was shown that the polyketide synthase encoded by the *pksP* (*alb1*) gene represents a virulence determinant. *pksP* is part of a gene cluster involved in dihydroxynaphthalene (DHN)-like melanin biosynthesis. Because a putative laccase-encoding gene (*abr2*) is also part of the cluster and a laccase was found to represent a virulence factor in *Cryptococcus neoformans*, here, the *Abr2* laccase was characterised. Deletion of the *abr2* gene changed the gray-green conidial pigment to a brown color and the ornamentation of conidia was reduced compared with wild-type conidia. In contrast to the white *pksP* mutant, the susceptibility of the *Deltaabr2* mutant against reactive oxygen species (ROS) was not increased, suggesting that the intermediate of DHN-like melanin produced up to the step catalysed by *Abr2* already possesses ROS scavenging activity. In an intranasal mouse infection model, the *Deltaabr2* mutant strain showed no reduction in virulence compared with the wild type. In the *Deltaabr2* mutant, overall laccase activity was reduced only

during sporulation, but not during vegetative growth. An *abr2p-lacZ* gene fusion was expressed during sporulation, but not during vegetative growth confirming the pattern of laccase activity due to Abr2.

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