

# Production of pyomelanin, a second type of melanin, via the tyrosine degradation pathway in *Aspergillus fumigatus*.

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## Abstract

*Aspergillus fumigatus* is the most important airborne fungal pathogen of immunosuppressed humans. *A. fumigatus* is able to produce dihydroxynaphthalene melanin, which is predominantly present in the conidia. Its biosynthesis is an important virulence determinant. Here, we show that *A. fumigatus* is able to produce an alternative melanin, i.e., pyomelanin, by a different pathway, starting from L-tyrosine. Proteome analysis indicated that the L-tyrosine degradation enzymes are synthesized when the fungus is grown with L-tyrosine in the medium. To investigate the pathway in detail, we deleted the genes encoding essential enzymes for pigment production, homogentisate dioxygenase (*hmgA*) and 4-hydroxyphenylpyruvate dioxygenase (*hppD*). Comparative Fourier transform infrared spectroscopy of synthetic pyomelanin and pigment extracted from *A. fumigatus* cultures confirmed the identity of the observed pigment as pyomelanin. In the *hmgA* deletion strain, HmgA activity was abolished and the accumulation of homogentisic acid provoked an increased pigment formation. In contrast, homogentisic acid and pyomelanin were not observed with an *hppD* deletion mutant. Germlings of the *hppD* deletion mutant showed an increased sensitivity to

reactive oxygen intermediates. The transcription of both studied genes was induced by L-tyrosine. These results confirmed the function of the deleted genes and the predicted pathway in *A. fumigatus*. Homogentisic acid is the major intermediate, and the L-tyrosine degradation pathway leading to pyomelanin is similar to that in humans leading to alkaptonmelanin.

## Beteiligte Forschungseinheiten

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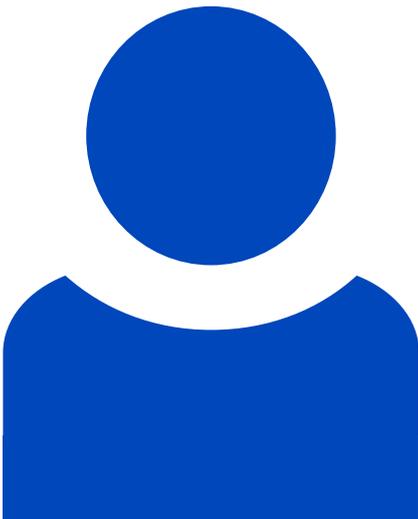
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