

Functional genomic profiling of *Aspergillus fumigatus* biofilm reveals enhanced production of the mycotoxin gliotoxin.

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Abstract

The opportunistic pathogenic mold *Aspergillus fumigatus* is an increasing cause of morbidity and mortality in immunocompromised and in part immunocompetent patients. *A. fumigatus* can grow in multicellular communities by the formation of a hyphal network encased in an extracellular matrix. Here, we describe the proteome and transcriptome of planktonic- and biofilm-grown *A. fumigatus* mycelium after 24 and 48 h. A biofilm- and time-dependent regulation of many proteins and genes of the primary metabolism indicates a developmental stage of the young biofilm at 24 h, which demands energy. At a matured biofilm phase, metabolic activity seems to be reduced. However, genes, which code for hydrophobins, and proteins involved in the biosynthesis of secondary metabolites were significantly upregulated. In particular, proteins of the gliotoxin secondary metabolite gene cluster were induced in biofilm cultures. This was confirmed by real-time PCR and by detection of this immunologically active mycotoxin in culture supernatants using HPLC analysis. The enhanced production of gliotoxin by in vitro formed biofilms reported here may also play a

significant role under in vivo conditions. It may confer *A. fumigatus* protection from the host immune system and also enable its survival and persistence in chronic lung infections such as aspergilloma.

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