

Deletion of the gliP gene of *Aspergillus fumigatus* results in loss of gliotoxin production but has no effect on virulence of the fungus in a low-dose mouse infection model.

Kupfahl C, Heinekamp T, Geginat G, Ruppert T, Härtl A, Hof H, Brakhage AA (2006) Deletion of the gliP gene of *Aspergillus fumigatus* results in loss of gliotoxin production but has no effect on virulence of the fungus in a low-dose mouse infection model. *Mol Microbiol* 62(1), 292-302.

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Abstract

Gliotoxin is a secondary metabolite produced by several fungi including the opportunistic human pathogen *Aspergillus fumigatus*. As gliotoxin exerts immunosuppressive effects in vitro and in vivo, a role as a virulence determinant in invasive aspergillosis has been discussed for a long time but evidence has not been provided until now. Here, by the use of different selection marker genes *A. fumigatus* knock-out strains were generated that are deficient for the non-ribosomal peptide synthetase GliP, the putative key enzyme of the gliotoxin biosynthesis. Deletion of the gliP gene resulted in loss of gliotoxin production, as analysed by high performance liquid chromatography and tandem mass spectrometry. No differences in morphology or growth kinetics between wild-type and gliP-deletion strains were observed. In vitro, the culture supernatant of the gliP-deficient strains showed a reduced cytotoxic effect on both macrophage-like cells and T cell lines. In a low-

dose murine infection model of invasive aspergillosis, gliotoxin was detected in the lung and absent when mice were infected with the gliP deletion strain. However, gliP deletion strains showed no difference in virulence compared with the corresponding wild-type strains. Taken together, the non-ribosomal peptide synthetase GliP is essential for gliotoxin production in *A. fumigatus*. Gliotoxin is not required for pathogenicity of the fungus in immunocompromised mice, despite the fact that a reduced cytotoxicity of the culture supernatant of gliP deletion strains was demonstrated.

Involved units

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