

Identification of the antiphagocytic trypacidin gene cluster in the human-pathogenic fungus *Aspergillus fumigatus*.

Mattern DJ, Schoeler H, Weber J, Novohradská S, Kraibooj K, Dahse HM, Hillmann F, Valiante V, Figge MT, Brakhage AA (2015) Identification of the antiphagocytic trypacidin gene cluster in the human-pathogenic fungus *Aspergillus fumigatus*. *Applied Microbiology and Biotechnology* 99(23), 10151-10161.

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Abstract

The opportunistic human pathogen *Aspergillus fumigatus* produces numerous different natural products. The genetic basis for the biosynthesis of a number of known metabolites has remained unknown. The gene cluster encoding for the biosynthesis of the conidia-bound metabolite trypacidin is of particular interest because of its antiprotozoal activity and possible role in the infection process. Here, we show that the genes encoding the biosynthesis enzymes of trypacidin reside within an orphan gene cluster in *A. fumigatus*. Genome mining identified *tynC* as an uncharacterized polyketide synthase with high similarity to known enzymes, whose products are structurally related to trypacidin including endocrocin and fumicycline. Gene deletion of *tynC* resulted in the complete absence of trypacidin production, which was fully restored when the mutant strain was complemented with the wild-type gene. When confronted with macrophages, the *tynC* deletion mutant conidia were more frequently phagocytosed than those of the parental wild-type strain. This was also found for phagocytic amoebae of the species *Dictyostelium discoideum*,

which showed increased phagocytosis of DtnC conidia. Both macrophages and amoebae were also sensitive to trypanidin. Therefore, our results suggest that the conidium-bound trypanidin could have a protective function against phagocytes both in the environment and during the infection process.

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