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The role of virulence determinants of the human pathogenic fungus *Aspergillus fumigatus* in the defense against fungivorous amoeba

Infections with opportunistic pathogens are among the leading causes of morbidity and mortality in humans. The filamentous fungus *Aspergillus fumigatus* represents a classical example for this group, as it normally thrives as saprophyte in the soil, but disperses asexual conidia as infectious agents. Upon inhalation by immunocompromised host, these conidia can germinate and invade the surrounding tissue. Lethality of such an invasive aspergillosis is high due to limited diagnostic and therapeutic options. A multitude of general virulence factors can lead to invasive growth and rapid disease progression with often enormously high death rates, exceeding even 90% in certain patient cohorts (Brakhage and Langfelder, 2002). Little is known on the evolutionary origin of this armory. In a recent study we could show that two major virulence determinants, formation of the protective DHN-melanin and the second metabolite gliotoxin are also effective against the soil amoeba *Dictyostelium discoideum* (Hillmann et al., 2015). An amoeba defensive function was also detectable for tryptacidin, a spore born toxin of *A. fumigatus* with antiphagocytic properties (Mattern et al., 2015). These results supported the idea some basic mechanisms of fungal virulence could have emerged long before the appearance of innate immune systems and foster the hypothesis that they could be driven from the selection pressure imposed by amoeba predation. A central question of my thesis is therefore if interactions with fungivorous amoeba could have stimulated the development of such virulence mechanisms. To address this point I will exploit an extended model

system based on the amoeba *Protostelium mycophaga*, an obligate fungivore which was isolated from a forest site near Jena. Preliminary results in the group of Falk Hillmann indicate that *P. mycophaga* has wide food spectrum of ascomycetous or basidiomycetous yeasts, but can also attack fungal hyphae. My work program will analyze the molecular interactions with fungal conidia during phagocytosis, but will include first approaches to analyze the chemical communication between these two antagonistic organisms.

Publications

Ferling I, Dunn JD, Ferling A, Soldati T, Hillmann F (2020) Conidial Melanin of the Human-Pathogenic Fungus *Aspergillus fumigatus* Disrupts Cell Autonomous Defenses in Amoebae. *mBio* 11(3), [Details PubMed](#)

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Novohradská S, Ferling I, Hillmann F (2017) Exploring Virulence Determinants of Filamentous Fungal Pathogens through Interactions with Soil Amoebae. *Front Cell Infect Microbiol* 7, 497. [Details PubMed](#)

Geib E, Gressler M, Viedernikova I, Hillmann F, Jacobsen ID, Nietzsche S, Hertweck C, Brock M (2016) A Non-canonical Melanin Biosynthesis Pathway Protects *Aspergillus terreus* Conidia from Environmental Stress. *Cell Chem Biol* 23(5), 587-597. [Details PubMed](#)

Supervisor

[Falk Hillmann](#)

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Start of PhD

August 1, 2015

Doctoral Disputation

December 4, 2019

