The impact of spore surface attributes of *Lichtheimia corymbifera* during infection of human cells

Dolly Montano^{1,2}, Volker U. Schwartz^{1,2}, Mohamed Hassan^{1,2}, Hans-Martin Dahse², Kerstin Voigt^{1,2}.

[1] Friedrich-Schiller University, Faculty of Biological Sciences, Institute of Microbiology. Jena, Germany.

[2] Leibniz Institute for Natural Product Research and Infection Biology – Hans Knöll Institute. Jena, Germany.

Introduction

Lichtheimia corymbifera is a causative agent of mucormycosis, a life-threatening infection caused by members of the fungal order Mucorales. This pathogen can invade blood vessels of immunocompromised patients, leading to infarction, thrombosis and tissue necrosis [1]. Currently, therapeutic options against mucormycosis are limited due to difficult early-diagnosis, antifungal drug resistance and lower number of studies related to host-pathogen interactions.

Scientific background

- Spore cell-wall proteins and pigments are known to play an important role in other fungal pathogens when interacting with host cells [2].
- The full genome sequences of *L. corymbifera* provides a new molecular basis to study pathogenicity-associated features [3].
- Current studies in our group predict genes encoding proteins involved in host-pathogen interactions.

Research Question

How do spore surface proteins and pigments of *L. corymbifera* contribute to the infection of human host cells?

Work packages

- Establish *in vitro* infection models with non-professional phagocytes, and alveolar macrophages, the first barrier to pulmonary infections.

Determine host-pathogen interactions during initial stages of infection

Methods: fluorescence staining, laser scanning microscopy, and flow cytometric analysis.

- Generate specific antibodies against candidate spore surface proteins in order to block ligand-receptor interactions.

Screening-system for detection of relevant proteins involved in recognition by host cells

Methods: generation of antibodies, yeast-surface-display system, protein purification, and phagocytosis assays.

- Evaluate the long-term survival of spores with different pigment phenotypes.

Determine the contribution of spore pigments in the long-term survival

Methods: laser scanning microscopy, flow cytometric analysis, and apoptosis assay.

- Silence genes involved in the initial host-pathogen interactions and employ yeast surface display as a gain-of-function system.

Confirm the role of relevant spore surface proteins

Methods: genome engineering with CRISPR, and yeast-surface-display.

Outlook

With all these strategies we expect to determine a set of spore surface proteins that play an important role during recognition by human cells. Furthermore, we hope to disclose whether pigments of the fungus contribute to its long-term survival inside macrophages, which could provide us insights to develop novel diagnostics and therapeutic strategies to counteract infections caused by *L. corymbifera*.

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Dolly.montano@hki-jena.de