Proteome analysis reveals the conidial surface protein CcpA essential for virulence of the pathogenic fungus *Aspergillus fumigatus*.

Voltersen V, Blango MG, Herrmann S, Schmidt F, Heinekamp T, Strassburger M, Krüger T, Bacher P, Lother J, Weiss E, Hünniger K, Liu H, Hortschansky P, Scheffold A, Loeffler J, Krappmann S, Nietzsche S, Kurzai O, Einsele H, Kniemeyer O, Filler S, Reichard U, Brakhage AA (2018) Proteome analysis reveals the conidial surface protein CcpA essential for virulence of the pathogenic fungus *Aspergillus fumigatus*. *mBio* 9(5), e01557-18.

Details



Abstract

Aspergillus fumigatus is a common airborne fungal pathogen of humans and a significant source of mortality in immunocompromised individuals. Here, we provide the most extensive cell wall proteome profiling to date of *A. fumigatus* resting conidia, the fungal morphotype pertinent to first contact with the host. Using liquid chromatography-tandem mass spectrometry (LC-MS/MS), we identified proteins within the conidial cell wall by hydrogen-fluoride (HF)-pyridine extraction and proteins exposed on the surface using a trypsin-shaving approach. One protein, designated conidial cell wall protein A (CcpA), was identified by both methods and was found to be nearly as

abundant as hydrophobic rodlet layer-forming protein RodA. CcpA, an amphiphilic protein, like RodA, peaks in expression during sporulation on resting conidia. Despite high cell wall abundance, the cell surface structure of ΔccpA resting conidia appeared normal. However, trypsin shaving of ΔccpA conidia revealed novel surface-exposed proteins not detected on conidia of the wild-type strain. Interestingly, the presence of swollen ΔccpA conidia led to higher activation of neutrophils and dendritic cells than was seen with wild-type conidia and caused significantly less damage to epithelial cells in vitro In addition, virulence was highly attenuated when cortisone-treated, immunosuppressed mice were infected with ΔccpA conidia. CcpA-specific memory T cell responses were detectable in healthy human donors naturally exposed to *A. fumigatus* conidia, suggesting a role for CcpA as a structural protein impacting conidial immunogenicity rather than possessing a protein-intrinsic immunosuppressive effect. Together, these data suggest that CcpA serves as a conidial stealth protein by altering the conidial surface structure to minimize innate immune recognition. IMPORTANCE The mammalian immune system relies on recognition of pathogen surface antigens for targeting and clearance. In the absence of immune evasion strategies, pathogen clearance is rapid. In the case of *Aspergillus fumigatus*, the successful fungus must avoid phagocytosis in the lung to establish invasive infection. In healthy individuals, fungal spores are cleared by immune cells; however, in immunocompromised patients, clearance mechanisms are impaired. Here, using proteome analyses, we identified CcpA as an important fungal spore protein involved in pathogenesis. *A. fumigatus* lacking CcpA was more susceptible to immune recognition and prompt eradication and, consequently, exhibited drastically attenuated virulence. In infection studies, CcpA was required for virulence in infected immunocompromised mice, suggesting that it could be used as a possible immunotherapeutic or diagnostic target in the future. In summary, our report adds a protein to the list of those known to be critical to the complex fungal spore surface environment and, more importantly, identifies a protein important for conidial immunogenicity during infection.

Beteiligte Forschungseinheiten

Molekulare und Angewandte Mikrobiologie Axel Brakhage Mehr erfahren

Fungal Septomics Oliver Kurzai Mehr erfahren

Transfergruppe Antiinfektiva Axel Brakhage Mehr erfahren

Leibniz-HKI-Autor*innen



Matthew Blango

Details



Axel A. Brakhage

Details



Thorsten Heinekamp

Details



Peter Hortschansky

Details



Kerstin Hünniger

Details



Olaf Kniemeyer

Details



Thomas Krüger

Details



Oliver Kurzai

Details



Franziska Schmidt

Details



Maria Straßburger

Details



Vera Voltersen

Details

Identifier

doi: 10.1128/mBio.01557-18

PMID: 30279286