

Challenges and Strategies for Proteome Analysis of the Interaction of Human Pathogenic Fungi with Host Immune Cells.

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Abstract

Opportunistic human pathogenic fungi including the saprotrophic mold *Aspergillus fumigatus* and the human commensal *Candida albicans* can cause severe fungal infections in immunocompromised or critically ill patients. The first line of defense against opportunistic fungal pathogens is the innate immune system. Phagocytes such as macrophages, neutrophils and dendritic cells are an important pillar of the innate immune response and have evolved versatile defense strategies against microbial pathogens. On the other hand, human-pathogenic fungi have sophisticated virulence strategies to counteract the innate immune defense. In this context, proteomic approaches can provide deeper insights into the molecular mechanisms of the interaction of host immune cells with fungal pathogens. This is crucial for the identification of both diagnostic biomarkers for fungal infections and therapeutic targets. Studying host-fungal interactions at the protein level is a challenging endeavor, yet there are few studies that have been undertaken. This review draws attention to proteomic techniques and their application to fungal

pathogens and to challenges, difficulties, and limitations that may arise in the course of simultaneous dual proteome analysis of host immune cells interacting with diverse morphotypes of fungal pathogens. On this basis, we discuss strategies to overcome these multifaceted experimental and analytical challenges including the viability of immune cells during co-cultivation, the increased and heterogeneous protein complexity of the host proteome dynamically interacting with the fungal proteome, and the demands on normalization strategies in terms of relative quantitative proteome analysis.

Beteiligte Forschungseinheiten

[Molekulare und Angewandte Mikrobiologie Axel Brakhage](#) [Mehr erfahren](#)

Leibniz-HKI-Autor*innen



Olaf Kniemeyer

[Details](#)



Thomas Krüger

[Details](#)



Ting Luo

[Details](#)



Hella Schmidt

[Details](#)



Iordana Shopova

[Details](#)

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