Phenotypic and Proteomic Analysis of the *Aspergillus fumigatus* ΔPrtT, ΔXprG and ΔXprG/ΔPrtT Protease-Deficient Mutants.

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Abstract

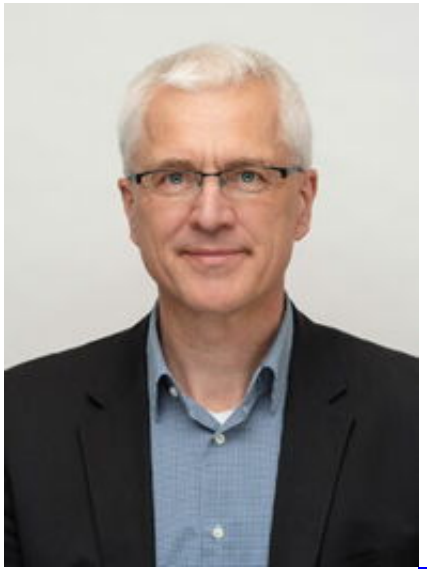
Aspergillus fumigatus is the most common mold species to cause disease in immunocompromised patients. Infection usually begins when its spores (conidia) are inhaled into the airways, where they germinate, forming hyphae that penetrate and destroy the lungs and disseminate to other organs, leading to high mortality. The ability of hyphae to penetrate the pulmonary epithelium is a key step in the infectious process. A. fumigatus produces extracellular proteases that are thought to enhance penetration by degrading host structural barriers. This study explores the role of the *A. fumigatus* transcription factor XprG in controlling secreted proteolytic activity and fungal virulence. We deleted xprG, alone and in combination with prtT, a transcription factor previously shown to regulate extracellular proteolysis. xprG deletion resulted in abnormal conidiogenesis and formation of lighter colored, more fragile conidia and a moderate reduction in the ability of culture filtrates (CFs) to degrade substrate proteins. Deletion of both xprG and prtT resulted in an additive reduction, generating a mutant strain producing CF with almost no ability to degrade substrate

proteins. Detailed proteomic analysis identified numerous secreted proteases regulated by XprG and PrtT, alone and in combination. Interestingly, proteomics also identified reduced levels of secreted cell wall modifying enzymes (glucanases, chitinases) and allergens following deletion of these genes, suggesting they target additional cellular processes. Surprisingly, despite the major alteration in the secretome of the xprG/prtT null mutant, including two to fivefold reductions in the level of 24 proteases, 18 glucanases, 6 chitinases, and 19 allergens, it retained wild-type virulence in murine systemic and pulmonary models of infection. This study highlights the extreme adaptability of A. fumigatus during infection based on extensive gene redundancy.

Beteiligte Forschungseinheiten

Molekulare und Angewandte Mikrobiologie Axel Brakhage Mehr erfahren

Leibniz-HKI-Autor*innen



Axel A. Brakhage

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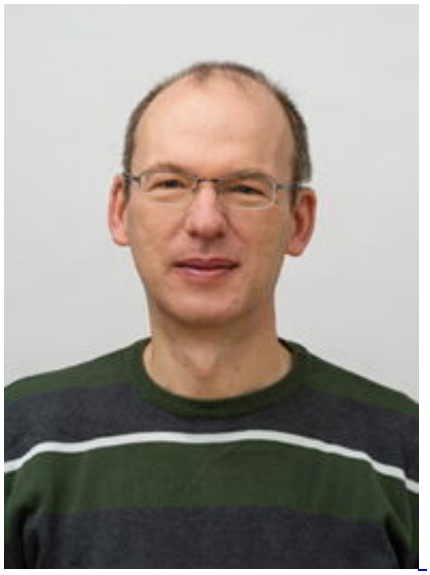

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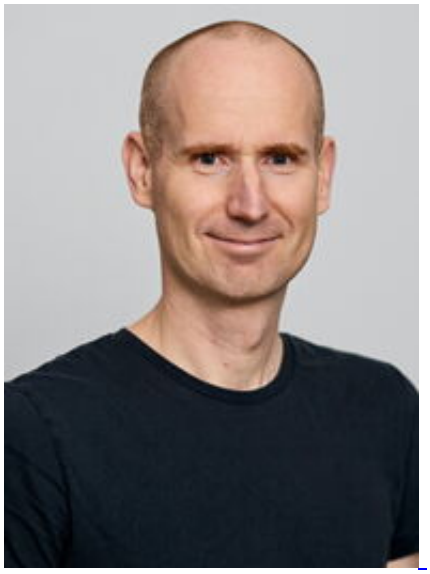

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