Cellular responses of *Candida albicans* to phagocytosis and the extracellular activities of neutrophils are critical to counteract carbohydrate starvation, oxidative and nitrosative stress.

Miramón P, Dunker C, Windecker H, Bohovych IM, Brown AJ, Kurzai O, Hube B (2012) Cellular responses of *Candida albicans* to phagocytosis and the extracellular activities of neutrophils are critical to counteract carbohydrate starvation, oxidative and nitrosative stress. *PLOS One* 7(12), e52850-e52850.

Abstract

Neutrophils are key players during Candida albicans infection. However, the relative contributions of neutrophil activities to fungal clearance and the relative importance of the fungal responses that counteract these activities remain unclear. We studied the contributions of the intra- and extracellular antifungal activities of human neutrophils using diagnostic Green Fluorescent Protein (GFP)-marked C. albicans strains. We found that a carbohydrate starvation response, as indicated by up-regulation of glyoxylate cycle genes, was only induced upon phagocytosis of the fungus. Similarly, the nitrosative stress response was only observed in internalised fungal cells. In contrast, the response to oxidative stress was observed in both phagocytosed and non-phagocytosed fungal cells, indicating that oxidative stress is imposed both intra- and extracellularly. We assessed

the contributions of carbohydrate starvation, oxidative and nitrosative stress as antifungal activities by analysing the resistance to neutrophil killing of C. albicans mutants lacking key glyoxylate cycle, oxidative and nitrosative stress genes. We found that the glyoxylate cycle plays a crucial role in fungal resistance against neutrophils. The inability to respond to oxidative stress (in cells lacking superoxide dismutase 5 or glutathione reductase 2) renders C. albicans susceptible to neutrophil killing, due to the accumulation of reactive oxygen species (ROS). We also show that neutrophil-derived nitric oxide is crucial for the killing of C. albicans: a yhb1Δ/Δ mutant, unable to detoxify NO•, was more susceptible to neutrophils, and this phenotype was rescued by the nitric oxide scavenger carboxy-PTIO. The stress responses of C. albicans to neutrophils are partially regulated via the stress regulator Hog1 since a hog1Δ/Δ mutant was clearly less resistant to neutrophils and unable to respond properly to neutrophil-derived attack. Our data indicate that an appropriate fungal response to all three antifungal activities, carbohydrate starvation, nitrosative stress and oxidative stress, is essential for full wild type resistance to neutrophils.

Beteiligte Forschungseinheiten

Mikrobielle Pathogenitätsmechanismen Bernhard Hube Mehr erfahren

Fungal Septomics Oliver Kurzai Mehr erfahren

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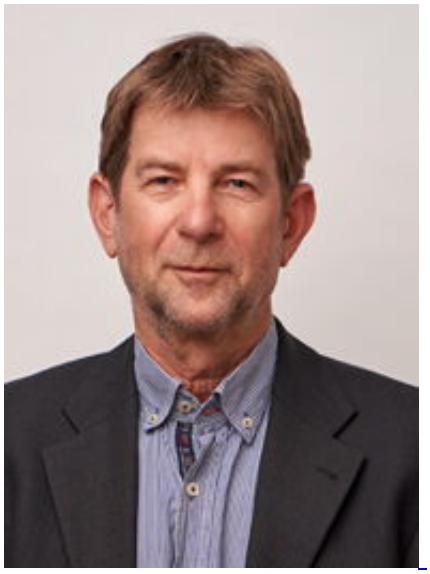
Details



Bernhard Hube

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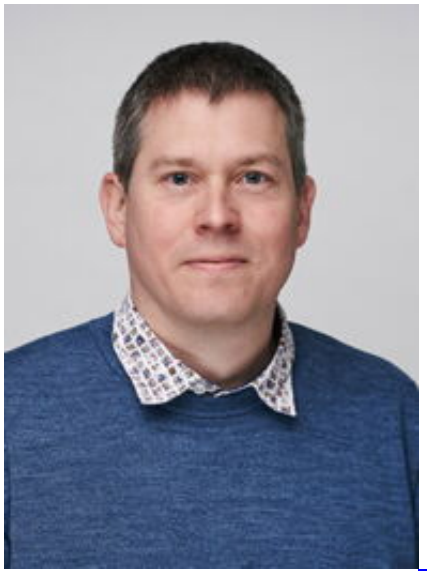

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