Small but crucial: the novel small heat shock protein Hsp21 mediates stress adaptation and virulence in *Candida albicans*.

Mayer FL, Wilson D, Jacobsen ID, Miramón P, Slesiona S, Bohovych IM, Brown AJ, Hube B (2012) Small but crucial: the novel small heat shock protein Hsp21 mediates stress adaptation and virulence in *Candida albicans*. *PLOS One* 7(6), e38584.

Details

PubMed

Abstract

Small heat shock proteins (sHsps) have multiple cellular functions. However, the biological function of sHsps in pathogenic microorganisms is largely unknown. In the present study we identified and characterized the novel sHsp Hsp21 of the human fungal pathogen Candida albicans. Using a reverse genetics approach we demonstrate the importance of Hsp21 for resistance of C. albicans to specific stresses, including thermal and oxidative stress. Furthermore, a hsp21Δ/Δ mutant was defective in invasive growth and formed significantly shorter filaments compared to the wild type under various filament-inducing conditions. Although adhesion to and invasion into human-derived endothelial and oral epithelial cells was unaltered, the hsp21Δ/Δ mutant exhibited a strongly reduced capacity to damage both cell lines. Furthermore, Hsp21 was required for resisting killing by human neutrophils. Measurements of intracellular levels of stress protective molecules demonstrated that Hsp21 is involved in both glycerol and glycogen regulation and plays a major role in trehalose homeostasis in response to elevated temperatures. Mutants

defective in trehalose and, to a lesser extent, glycerol synthesis phenocopied HSP21 deletion in terms of increased susceptibility to environmental stress, strongly impaired capacity to damage epithelial cells and increased sensitivity to the killing activities of human primary neutrophils. Via systematic analysis of the three main C. albicans stress-responsive kinases (Mkc1, Cek1, Hog1) under a range of stressors, we demonstrate Hsp21-dependent phosphorylation of Cek1 in response to elevated temperatures. Finally, the hsp21Δ/Δ mutant displayed strongly attenuated virulence in two in vivo infection models. Taken together, Hsp21 mediates adaptation to specific stresses via fine-tuning homeostasis of compatible solutes and activation of the Cek1 pathway, and is crucial for multiple stages of C. albicans pathogenicity. Hsp21 therefore represents the first reported example of a small heat shock protein functioning as a virulence factor in a eukaryotic pathogen.

Involved units

Microbial Pathogenicity Mechanisms Bernhard Hube Read more

Microbial Immunology Ilse Jacobsen Read more

International Leibniz Research School Peter F. Zipfel Read more

Leibniz-HKI-Authors



Bernhard Hube

Details



Ilse Denise Jacobsen

Details



François Mayer

Details



Pedro Miramón

Details



Silvia Slesiona

Details



Duncan Wilson

Details

Identifier

doi: 10.1371/journal.pone.0038584

PMID: 22685587