Human albumin enhances the pathogenic potential of Candida glabrata on vaginal epithelial cells.

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Projects

How adaptation of *Candida albicans* to inflammatory mediators impacts immune recognition and pathogenesis
Details

Adaptation of *Candida albicans* to non-commensal host environments induced by host circulating proteins and immune mediators
Details

Abstract

The opportunistic pathogen Candida glabrata is the second most frequent causative agent of vulvovaginal candidiasis (VVC), a disease that affects 70-75% of women at least once during their life. However, C. glabrata is almost avirulent in mice and normally incapable of inflicting damage to vaginal epithelial cells in vitro. We thus proposed that host factors present in vivo may influence C. glabrata pathogenicity. We, therefore, analyzed the impact of albumin, one of the most abundant proteins of the vaginal fluid. The presence of human, but not murine, albumin dramatically increased the potential of C. glabrata to damage vaginal epithelial cells. This effect depended on macropinocytosis-mediated epithelial uptake of albumin and subsequent proteolytic processing. The enhanced pathogenicity of C. glabrata can be explained by a combination of beneficial effects for the fungus, which includes increased access to iron, accelerated growth, and increased adhesion. Screening of C. glabrata deletion mutants revealed that Hap5, a key regulator of iron homeostasis, is essential for the albumin-augmented damage potential. The albumin-augmented pathogenicity was reversed by the addition of iron chelators and a similar increase in pathogenicity was shown by increasing the iron availability, confirming a key role of iron. Accelerated growth not only led to higher cell numbers, but also to increased fungal metabolic activity and oxidative stress resistance. Finally, the albumin-driven enhanced damage potential was associated with the expression of distinct C. glabrata virulence genes. Transcriptional responses of the epithelial cells suggested an unfolded protein response (UPR) and ER-stress responses combined with glucose starvation induced by fast growing C. glabrata cells as potential mechanisms by which cytotoxicity is mediated.Collectively, we demonstrate that albumin augments the pathogenic potential of C. glabrata during interaction with vaginal epithelial cells. This suggests a role for albumin as a key player in the

pathogenesis of VVC.

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