The facultative intracellular pathogen *Candida glabrata* subverts macrophage cytokine production and phagolysosome maturation.

Seider K, Brunke S, Schild L, Jablonowski N, Wilson D, Majer O, Barz D, Haas A, Kuchler K, Schaller M, Hube B (2011) The facultative intracellular pathogen *Candida glabrata* subverts macrophage cytokine production and phagolysosome maturation. *J Immunol* 187(6), 3072-3086.

Abstract

Although Candida glabrata is an important human pathogenic yeast, its pathogenicity mechanisms are largely unknown. Immune evasion strategies seem to play key roles during infection, since very little inflammation is observed in mouse models. Furthermore, C. glabrata multiplies intracellularly after engulfment by macrophages. In this study, we sought to identify the strategies that enable C. glabrata to survive phagosome biogenesis and antimicrobial activities within human monocyte-derived macrophages. We show that, despite significant intracellular proliferation, macrophage damage or apoptosis was not apparent, and production of reactive oxygen species was inhibited. Additionally, with the exception of GM-CSF, levels of pro- and anti-inflammatory cytokines were only marginally increased. We demonstrate that adhesion to and internalization by macrophages occur within minutes, and recruitment of endosomal early endosomal Ag 1 and lysosomal-associated membrane protein 1 indicates phagosome maturation. However, phagosomes containing viable C. glabrata, but not heat-killed yeasts, failed to recruit cathepsin D and were only

weakly acidified. This inhibition of acidification did not require fungal viability, but it had a heat-sensitive surface attribute. Therefore, C. glabrata modifies the phagosome into a nonacidified environment and multiplies until the host cells finally lyse and release the fungi. Our results suggest persistence of C. glabrata within macrophages as a possible immune evasion strategy.

Involved units

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Topics

Interactions with immune cells (MPM)

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