

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

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[Details](#)



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.

Beteiligte Forschungseinheiten

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