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pH-regulated Antigen 1 of Candida albicans Mediates Fungal Recognition and Enhances the Antifungal Response of Human Neutrophils

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Candida albicans is an opportunistic human-pathogenic yeast and a leading cause of severe and invasive fungal infections in immunocompromised individuals. The virulence of the fungus is associated with its capability to filamentous growth. The pH-regulated antigen 1 (Pra1) of *C. albicans* is a cell wall associated and secreted protein that is highly expressed in the hyphal form. The aim of the present study was to analyze the role of Pra1 during interactions of *C. albicans* with human neutrophil granulocytes.

Recombinant Pra1p bound to neutrophils in a dose-dependent manner and complement receptor type 3 (CD11b/CD18) was identified as the major Pra1p receptor on human neutrophils by flow cytometry. In transwell assays, a *C. albicans* mutant strain lacking Pra1 (*pra1*Δ) supported neutrophil migration to a lower extent than did the parental wild-type strain. Neutrophils showed enhanced adhesion and migration to a Pra1 overexpression strain. Furthermore, adhesion of neutrophils to *C. albicans* could be increased by secreted Pra1 derived from culture supernatants. The *pra1*Δ strain induced lower amounts of reactive oxygen species in neutrophils, determined by a fluorescence assay. Similarly, lower amounts of the antimicrobial protein lactoferrin and myeloperoxidase were released by neutrophils when stimulated with the *pra1*Δ mutant strain. Furthermore, neutrophils coincubated with the *pra1*Δ cells secreted less interleukin 8. The reduced response of neutrophils in these functional assays could be reverted by preincubation of the *pra1*Δ strain with secreted Pra1.

In conclusion, Pra1 binds to neutrophils via CD11b/CD18, and *C. albicans* cells lacking Pra1 induce weaker neutrophil activation compared to the wild-type strain. These results suggest that Pra1 is one of the factors that mediate the stronger response of human neutrophils to *C. albicans* hyphae in contrast to yeast cells.

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