Secreted pH-regulated antigen 1 of *Candida albicans* blocks activation and conversion of complement C3.

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Abstract

The complement system forms the first defense line of innate immunity and is activated within seconds upon infection by human pathogenic yeast Candida albicans. In this study, we identified a new complement evasion strategy used by C. albicans. The fungus secretes a potent complement inhibitor, pH-regulated Ag 1 (Pra1), which in the direct surrounding of the pathogen binds to fluid-phase C3 and blocks cleavage of C3 to C3a and C3b, as shown by ELISA, native gel electrophoresis, and Western blotting. Consequently, complement activation via the alternative and classical pathways is inhibited. In addition, the release of the anaphylatoxins C3a and C5a, as well as C3b/iC3b surface deposition, is reduced, as demonstrated by Western blotting, ELISA, confocal microscopy, and flow cytometry. By reducing C3b/iC3b levels at the yeast surface, Pra1 decreases complement-mediated adhesion, as well as uptake of C. albicans by human macrophages, as shown by flow cytometry. Thus, Pra1 is, to our knowledge, the first potent fungal complement inhibitor that favors C. albicans immune escape by inactivating and controlling host complement attack at the level of C3.

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