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Anaphylatoxin Escape by *Candida albicans* Complement Regulator Acquiring Surface Protein 2

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Candida albicans evades multiple attacks of the immune system to infect and remain alive within the host. Immediately after passing epithelial barriers *C. albicans* is confronted by complement that counteracts fungal infection by releasing high amounts of opsonizing, inflammatory and antimicrobial activation compounds. The anaphylatoxin C3a is such an activation compound and displays both inflammatory and antimicrobial activity. In addition C3a enables human granulocytes to release IL-8 and start chemotactic movement. Although a few microbial proteases degrade C3a, no virulence factors are known to operate as directly interacting C3a inhibitors. Here we show that *C. albicans* complement regulator acquiring surface protein 2 (CRASP2) binds C3a and inhibits C3a-mediated effector functions. CRASP2 binds C3a as shown in ELISA and seems to prefer regions of C3a that represent the active parts of this molecule. CRASP2 inhibits antifungal activity of both C3a and C3a-peptides resulting in an increase of *C. albicans* survival up to 70 %. *ΔCRASP2* mutant shows elevated and *CRASP2* overexpression strain reduced susceptibility to antifungal effects of C3a. In addition clinical isolates of *C. albicans* display increased resistance upon C3a challenge and this strongly correlates with CRASP-levels at fungal surfaces. Furthermore CRASP2 reduces C3a-induced IL-8 release of human granulocytes and abolishes chemotaxis in response to C3a as shown in migration assays. Summarily, CRASP2 binds C3a, inhibits C3a-activated IL-8 release and chemotaxis of human granulocytes as well as antimicrobial activity. C3a binding and inhibition identifies a novel molecular mechanism utilized by microbial pathogens to evade complement attack.

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