Immune evasion of the human pathogenic yeast *Candida albicans*: Pra1 is a Factor H, FHL-1 and plasminogen binding surface protein.

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Abstract

The pathogenic yeast Candida albicans utilizes human complement regulators, like Factor H and Factor H like protein-1 (FHL-1) for immune evasion. By screening a C. albicans cDNA expression library, we identified the pH-regulated antigen 1 (Pra1) as a novel Factor H and FHL-1 binding protein. Consequently Pra1 was recombinantly expressed in Pichia pastoris and purified from culture supernatant. Recombinant Pra1 binds Factor H, FHL-1 and also plasminogen. Attached to Pra1, the three human proteins are functionally active. Factor H and FHL-1 inactivate complement and plasminogen can be activated to plasmin which then degrades the extra-cellular matrix component fibrinogen. Polyclonal Pra1 anti-serum was generated and used to localize Pra1 on the surface and also in the culture supernatant of both yeast cells and the hyphal form of C. albicans. Furthermore Pra1 expression was up-regulated upon induction of hyphal growth. Pra1, released by Candida cells binds back to the surface of Candida hyphae and in addition enhances the complement regulatory activity of Factor H in the fluid phase. A Pra1 overexpression strain, with about twofold higher levels of Pra1 on the surface binds more Factor H, and plasminogen. In summary, C. albicans Pra1 is a yeast immune evasion protein that binds host immune regulators and acts at different sites. As a surface protein, Pra1 acquires the two human complement regulators Factor H, FHL-1 and plasminogen, mediates complement evasion, as well as extra-cellular matrix interaction and/or degradation. As a released protein, Pra1 enhances complement control in direct vicinity of the yeast and thus generates an additional protective layer which controls host complement attack.

Identifier

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