Sequence variations and protein expression levels of the two immune evasion proteins Gpm1 and Pra1 influence virulence of clinical *Candida albicans* isolates.

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Projects

Candida albicans-host interaction, the many faces of candida Pra1
Details

Abstract

Candida albicans, the important human fungal pathogen uses multiple evasion strategies to control, modulate and inhibit host complement and innate immune attack. Clinical C. albicans strains vary in pathogenicity and in serum resistance, in this work we analyzed sequence polymorphisms and variations in the expression levels of two central fungal complement evasion proteins, Gpm1 (phosphoglycerate mutase 1) and Pra1 (pH-regulated antigen 1) in thirteen clinical C. albicans isolates. Four nucleotide (nt) exchanges, all representing synonymous exchanges, were identified within the 747-nt long GPM1 gene. For the 900-nt long PRA1 gene, sixteen nucleotide exchanges were identified, which represented synonymous, as well as non-synonymous exchanges. All thirteen clinical isolates had a homozygous exchange (A to G) at position 73 of the PRA1 gene. Surface levels of Gpm1 varied by 8.2, and Pra1 levels by 3.3 fold in thirteen tested isolates and these differences influenced fungal immune fitness. The high Gpm1/Pra1 expressing candida strains bound the three human immune regulators more efficiently, than the low expression strains. The difference was 44% for Factor H binding, 51% for C4BP binding and 23% for plasminogen binding. This higher Gpm1/Pra1 expressing strains result in enhanced survival upon challenge with complement active, Factor H depleted human serum (difference 40%). In addition adhesion to and infection of human endothelial cells was increased (difference 60%), and C3b surface deposition was less effective (difference 27%). Thus, variable expression levels of central immune evasion protein influences immune fitness of the human fungal pathogen C. albicans and thus contribute to fungal virulence.

Identifier

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