Candidalysin delivery to the invasion pocket is critical for host epithelial damage induced by Candida albicans.

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Projects

Dissection of the *Candida albicans* lipase gene family and its role in commensalism and pathogenicity
Details

Abstract

The human pathogenic fungus Candida albicans is a frequent cause of mucosal infections. Although the ability to transition from the yeast to the hypha morphology is essential for virulence, hypha formation and host cell invasion per se are not sufficient for the induction of epithelial damage. Rather, the hypha-associated peptide toxin, candidalysin, a product of the Ece1 polyprotein, is the critical damaging factor. While synthetic, exogenously added candidalysin is sufficient to damage epithelial cells, the level of damage does not reach the same level as invading C. albicans hyphae. Therefore, we hypothesized that a combination of fungal attributes is required to deliver candidalysin to the invasion pocket to enable the full damaging potential of C. albicans during infection. Utilising a panel of C. albicans mutants with known virulence defects, we demonstrate that the full damage potential of C. albicans requires the coordinated delivery of candidalysin to the invasion pocket. This process requires appropriate epithelial adhesion, hyphal extension and invasion, high levels of ECE1 transcription, proper Ece1 processing and secretion of candidalysin. To confirm candidalysin delivery, we generated camelid VH Hs (nanobodies) specific for candidalysin and demonstrate localization and accumulation of the toxin only in C. albicans-induced invasion pockets. In summary, a defined combination of virulence attributes and cellular processes is critical for delivering candidalysin to the invasion pocket to enable the full damage potential of C. albicans during mucosal infection. TAKE AWAYS: Candidalysin is a peptide toxin secreted by C. albicans causing epithelial damage. Candidalysin delivery to host cell membranes requires specific fungal attributes. Candidalysin accumulates in invasion pockets created by invasive hyphae. Camelid nanobodies enabled visualisation of candidalysin in the invasion pocket.

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