Candida albicans-induced epithelial damage mediates translocation through intestinal barriers.

Allert S[*], Förster TM[*], Svensson C-M, Richardson JP, Pawlik T, Hebecker B, Rudolphi S, Juraschitz M, Schaller M, Blagojevic M, Morschhäuser J, Figge MT, Jacobsen ID, Naglik JR, Kasper L, Mogavero S, Hube B; [*]authors contributed equally (2018) *Candida albicans*-induced epithelial damage mediates translocation through intestinal barriers. *mBio* 9(3), e00915.

Details

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Abstract

Life-threatening systemic infections often occur due to the translocation of pathogens across the gut barrier and into the bloodstream. While the microbial and host mechanisms permitting bacterial gut translocation are well characterized, these are still unclear for fungal pathogens such as *Candida albicans*, a leading cause of nosocomial fungal bloodstream infections. In this study, we dissected the cellular mechanisms of translocation of *C. albicans* across intestinal epithelia in vitro and identified fungal genes associated with this process. We show that fungal translocation is a dynamic process initiated by invasion, and followed by cellular damage and loss of epithelial integrity. A screen of > 2000 *C. albicans* deletion mutants identified genes required for cellular

damage of and translocation across- enterocytes. Correlation analysis suggests that hypha formation, barrier damage above a minimum threshold level, and a decreased epithelial integrity are required for efficient fungal translocation. This process occurs predominantly via a transcellular route, which is associated with fungal-induced necrotic epithelial damage, but not apoptotic cell death. The cytolytic peptide toxin of *C. albicans*, Candidalysin, was found to be essential for damage of enterocytes and was a key factor in subsequent fungal translocation, suggesting that transcellular translocation of *C. albicans* through intestinal layers is Candidalysin-mediated. However, fungal invasion and low-level translocation can also occur via non-transcellular routes in a Candidalysin-independent manner. This is the first study showing translocation of a human-pathogenic fungus across the intestinal barrier being mediated by a peptide toxin.

Involved units

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Topics

Damage to the host

Pathomechanisms at the mucosal interphase

Awards

DGHM: Paper of the month July 2018, Frontiers publication award February 2020; DMykG publication award 2018; Medac Research Award 2018; recommended by Faculty 1000 as very good

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