Damage to the host

The mechanism by which *Candida albicans* damages host cells has been considered to be multi-factorial, and presumed to rely on a combination of adhesion, invasion, hyphal extension, turgor pressure and the secretion of hydrolytic enzymes. Although toxin production by *C. albicans* has long been postulated and the culture supernatants of *C. albicans* hyphae have been shown to exhibit haemolytic activity, the mechanism underlying *C. albicans'* ability to lyse host cells has remained elusive. It is clear that hyphae are crucial for adhesion, invasion and damage. Thus, host cell damage is caused by hyphae and/or a hyphal associated factor. However, the exact molecular mechanisms by which *C. albicans* destroys these host cells has remained enigmatic.

We have identified a peptide toxin, secreted by *C. albicans,* which has remarkable similarities with melittin – the major component of bee venom. By deleting the encoding gene and *in vitro* synthesis of the fragment, we have shown that this peptide is, in itself, essential and sufficient for the lysis of host cells. In collaboration with Dr Julian Naglik, Kings College London/UK and other cooperation partners, we elucidated intracellular processing of the Ece1 polyprotein into different peptides including the secreted, damage-mediating candidalysin. Ongoing work and cooperations, e.g. with Dr Thomas Gutsmann, Forschungszentrum Borstel/Germany, now examine the exact mechanism by which this potent *C. albicans* cytolysin disrupts host cell integrity and investigate the role of non-candidalysin Ece1 peptides (NCEPs, PI-II, IV-VIII) for the biology of *C. albicans* and its interaction with the host.

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_ Structure of the Ece1 protein. Ece1 peptides (PI–VIII) are separated by lysine-arginine residues (KR) at their C-termini, which serve as recognition sites of the Kex2 protease. SP, signal peptide.
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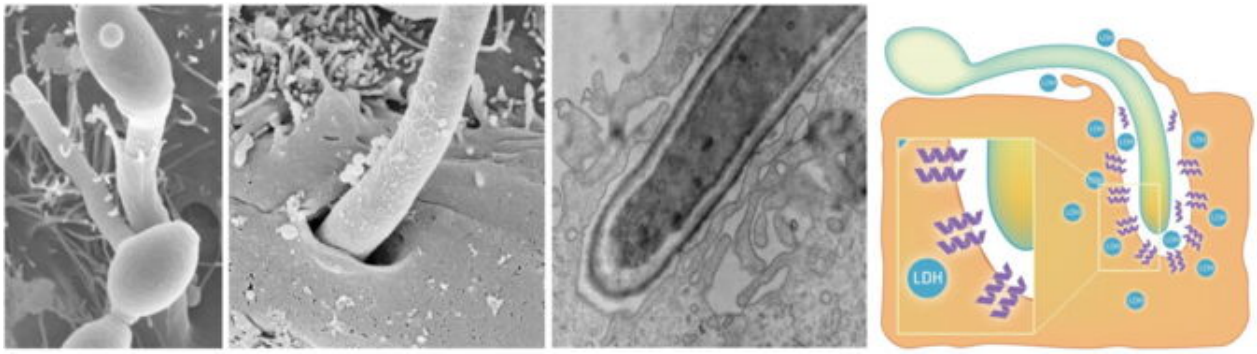

_ *C. albicans* hyphae invade epithelial cells forming invasion pockets. Secreted candidalysin forms pores in the surrounding host membrane causing host cell damage, detected by released cytoplasmic content including lactate dehydrogenase (LDH).