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How adaptation of *Candida albicans* to inflammatory mediators impacts immune recognition and pathogenesis

The yeast *Candida albicans* is a commensal that colonizes the human gastro-intestinal tract, mucosal surfaces of the oral cavity and female reproduction tract. A compromised immune response, and microbiota dysbiosis predisposes to infection. A severely compromised immune system or clinical intervention can facilitate a translocation through the intestinal epithelial barrier into the bloodstream and thereby causing life-threatening systemic candidiasis.

The co-existence of human and fungus is believed to have driven the co-evolution of *C. albicans* virulence properties in accordance with host-imposed stresses. Organisms, which have been trained in this so called "commensal virulent school" are able to sense and respond to hast stresses such as the immune system. Cytokines, essential communication signals of immune cells, have been reported to be sensed by certain bacteria and fungi. Even though, they da not impose cytokines a direct threat to pathogens they may serve as a direct marker for the upcoming threat of the immune response. Immune mediators consequently may also induce adaptation of *C. albicans* to an imminent
immune attack, a process so termed "predictive adaption".

The first part of the project will focus on the direct impact of immune mediators such as cytokines as well as serum proteins on *C. albicans*. A large-scale screening of a recombinant cytokine library can provide a

global insight into whether *C. albicans* can sense cytokines and induces adaptation mechanisms. Subsequent validation studies will investigate whether this contributes to *C. albicans* potentially increasing its pathogenicity or inducing strategies to evade immune recognitions.

The second part of the project investigates the capability of non-immune related factors to induce predictive adaption strategies in *C. albicans*. One major difference of the gut and blood stream is the flowrates of these two environments. Sensing the difference in the flowrate could trigger adaption processes required to survive and proliferate after translocation.

Publications

Pekmezovic M, Kaune AK, Austermeier S, Hitzler SUJ, Mogavero S, Hovhannisyan H, Gabaldón T, Gresnigt MS, Hube B (2021) Human albumin enhances the pathogenic potential of Candida glabrata on vaginal epithelial cells. *PLoS Pathog* 17(10), e1010037. Details PubMed

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