Implication of secreted fungal lipases during in vitro infection of human macrophages and dendritic cells with *Candida parapsilosis*.

T. Nemeth[1], *A. Toth*[1], *C. Vagvolgyi*[1], *Z. Hamari*[1], *K. Filkor*[2], *I. Nagy*[2], *A. Gacser*[1];
1University of Szeged, Szeged, HUNGARY,
2Bay Zoltán Foundation for Applied Research, Szeged, HUNGARY.

Candida parapsilosis typically is a commensal of human skin. However, when host immune defense is compromised or the normal microflora balance is disrupted, *C. parapsilosis* transforms itself into an opportunistic pathogen. *Candida*-derived lipase has been identified as potential virulence factor. Putative roles for lipases include the digestion of lipids for nutrient acquisition, adhesion to host cells, synergistic interactions with other enzymes, unspecific hydrolysis and a potential alteration of inflammatory processes by affecting immune cells. We previously showed that *C. parapsilosis* secreted lipase impacted the capacity of the fungus to grow in lipid rich medium, to produce biofilm, and to survive in murine macrophage-like cells. The production of lipase was essential for *C. parapsilosis* to attach, invade and damage reconstituted oral epithelium, and to invade host tissues in a murine infection mode. Concomitantly, we have evaluated the role of Lip8, a key lipase in C. albicans, and recapitulated our findings that lipases can be important virulence factors in *Candida*. Thus, the aim of our study was to assess the function of dendritic cells and PBMC derived macrophages in fighting *C. parapsilosis* and to determine the role that *C. parapsilosis*-derived lipase plays in the interaction with these phagocytes.

Monocyte-derived immature and mature dendritic cells (iDCs, mDCs) as well as macrophages (MΦ) co-cultured with live wild type or lipase deficient *C. parapsilosis* strains were studied to determine the phagocytic capacity and killing efficiency of host cells. We determined that all cell types efficiently phagocytosed and killed *C. parapsilosis*, furthermore our results show that the phagocytic and fungicidal activities of both iDCs and mDCs are more potent for lipase deficient compared to wild type yeast cells. Notably, MΦ showed elevated fungal killing activity to lipase knock out cells but no increased phagocitic capacity was detectable. In addition, the lipase deficient *C. parapsilosis* cells induce higher gene expression and protein secretion of pro-inflammatory cytokines and chemokines in all cell types relative to the effect of co-culture with wild type yeast cells. Our results show that both DCs and MΦ are activated by exposure to *C. parapsilosis*, as shown by increased phagocytosis, killing and pro-inflammatory protein secretion. Moreover, these data strongly suggest that *C. parapsilosis* derived lipase has a protective role during yeast:phagocyte interactions, since lipase production in wt yeast cells decreased the phagocytic capacity (in case of DCs) and killing efficiency of host cells and down-regulated the expression of host effector molecules.

The publication/presentation is supported by the European Union and co-funded by the European Social Fund. Project title: “Broadening the knowledge base and supporting the long term professional sustainability of the Research University Centre of Excellence at the University of Szeged by ensuring the rising generation of excellent scientists.” Project number: TÁMOP-4.2.2/B-10/1-2010-0012