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Candidalysin is a key player in activating vaginal cell ROS in an *in vitro* infection model

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Abstract

C. albicans can behave as a commensal yeast colonizing the vaginal mucosa and in this condition is tolerated by the epithelium. When the epithelial tolerance breaks down, due to *C. albicans* overgrowth and hyphae formation, the generated inflammatory response and cell damage lead to vulvovaginal candidiasis symptoms. Here, we studied the induction of reactive oxygen species (ROS) in vaginal epithelial cells caused by *C. albicans* infection and the involvement of fungal burden, morphogenesis and candidalysin (CL) production in such induction.

Wild-type *C. albicans*, *C. albicans* PCA-2 and *C. albicans* 529L strains were employed to infect in vitro a reconstituted vaginal epithelium (RVE), starting from A-431 cell line. ROS production was kinetically monitored by using MitoSOXTM probe. *C. albicans*-induced cell damage and proinflammatory cytokines production by infected cells are also being tested.

Wild-type *C. albicans* induced fast and high ROS production by vaginal epithelial cells, in parallel to the increase of the fungal load and to the number of hyphae. Under the same experimental conditions, the 529L *C. albicans* strain, known to be defective in CL production, induced a slow and scant ROS production, thus highlighting a key role of CL in causing epithelial oxidative distress. PCA-2 induced comparable but slower ROS production with wild-type *C. albicans* yeasts.

We conclude that CL production, more than fungal load and hyphae formation, seems to play a key role in the rapid activation of ROS by epithelial cells. The consequences of such quick ROS activation on cell-damage and inflammatory response are presently under investigation.