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PRO-METASTATIC EFFECT OF CANDIDA ALBICANS MANNOPROTEINS ON HEPATIC ENDOTHELIAL CELLS

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Candida albicans is an opportunistic fungus, which causes infections mainly among immunosupressed population, such as HIV, transplanted or oncology patients. The worst presentation of these diseases is the systemic infection, in which the yeast reaches the bloodstream and disseminates to other body parts. Once in the blood, the liver is the main organ responsible for the clearance of the infection. When the yeasts reach liver blood vessels, they bind to the endothelial cells triggering an inflammatory response. During this process, cytokines and adhesion molecules are expressed and, in consequence, immune cells are recruited to the site of infection, where they attack C. albicans and clear the infection. However, our group hypothesized that in oncology patients, who are usually immunosupressed, tumor cells released from primary tumors can attach to the liver vessels instead of leukocytes, which are in very low number, through the expressed adhesion molecules. This could lead to a new focus of cancer in the liver. In the last years, our group has identified the cell wall mannoproteins that induce this inflammatory process, being the most important ones Adh1 and Kre9. We have tested their effect on hepatic endothelial cells, and found that they induce an increase in tumor cells adhesion. Moreover, we have produced monoclonal antibodies against these proteins, and studied their effect on decreasing the tumor cell adhesion and on inhibiting the yeast growth. Furthermore, anti-Kre9 antibody was able to specifically recognize C. albicans hyphae, not yeast, and did not bind to C. dubliniensis hyphae, the only other Candida able to form true hyphae; being a possible marker that helps differentiation between this two species. This study of C. albicans mannoproteins could open the door to find new therapeutic strategies based on monoclonal antibodies, which were efficient at the same time against metastatic process and fungal infection.