

TITLE: CAN LIPIDS OF THE *CANDIDA ALBICANS* BIOFILM'S SECRETOME INDUCE A RESPONSE IN CANCER CELLS?

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ABSTRACT:

Biofilms are microbial communities that produce their own extracellular matrix with their function and structure. Biofilms are found in the majority sites of human body, i.e., *Candida albicans* in the oral cavity. *Candida albicans* biofilms are composed by proteins, carbohydrates, nucleic acids and lipids. Regarding oral diseases, *Candida albicans* is present in some cases of dysplasia and cancer, however this relationship is not a consensus and it is under discussion. In this study, *Candida albicans* lipids i.e., Phosphatidylinositol (PI), Phosphatidylcholine (PC) and Phosphatidylglycerol (PG) were isolated from 36 hours biofilm's secretome and identified by ¹H-NMR analysis. These lipids were tested in DOK (dysplasic oral cells) and SCC-25 (Primary Oral Squamous Cells Carcinoma). *Candida albicans* lipids increased the cell proliferation profile of DOK and SCC-25, demonstrated by alamar blue and flow cytometry assays in cell phenotype-dependent manner. The metabolic routes of lipids are usually altered in malignant cells, allowing the internalization of lipids present in the extracellular media. In this work, DOK and SCC-25 internalized PI, PC and PG from *Candida albicans* biofilm's secretome. This internalization was demonstrated by intracellular lipid droplets formation, by Confocal Laser Scanning Microscope (CLSM). The presence of lipid droplets is one of the recently studied hallmarks of cancer development, progression and resistance to therapy. For this propose, DOK and SCC-25 cells, 72 h after *C. albicans* lipids interaction, were challenged in the presence of the antitumor drug, camptothecin (CPT) a topoisomerase inhibitor. It was observed a mitigation of the CPT antitumoral effect on DOK and SCC-25 cells under this condition. The CLSM assay demonstrated that the CPT internalization was not affected; however, the intracellular distribution was disturbed. The intracellular CPT was co-localized inside the lipid droplets vesicles, promoted by *C. albicans* lipids stimuli. In conclusion, lipids from the 36 h *Candida albicans* biofilm's secretome induced malignant cells proliferation and a mitigation of the antitumoral effect of CPT, which highlights the importance of investigating the role of the molecules secreted by microorganisms within the tumoral microenvironment.

Keywords: *Candida albicans*, Lipids, Cancer, Biofilms, Lipids Droplets

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