Crosstalk Between Epithelial to Mesenchymal Transition as a Model for Cancer Metastasis and Redox/Energy Metabolism

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INTRODUCTION Cancer progression and metastasis involve a series of interconnected events. The deregulated control of cell proliferation and migration during cancer progression determines the capacity of tumor cells to escape from the primary tumors and metastasize to adjacent tissues or distant organs. In this scenario, not only the epithelial to mesenchymal transition (EMT) process, that results in loss of epithelial phenotype and cytoskeleton reorganization to acquire morphological and functional features of mesenchymal-like phenotype, has been fundamental, but also corresponding adjustments of redox/energy metabolism in order to fuel cell growth and division, contributing to cancer cells invasiveness. **OBJECTIVES** In this study, we evaluated a possible interplay between EMT process induced by epidermal growth factor (EGF) and metabolic alterations in Caov-3 human ovarian adenocarcinoma cells. **MATERIAL AND METHODS** Caov-3 cells were induced to EMT with EGF (10 ng/ml) during 96 hours. Morphological, functional and molecular evaluations of EMT were assessed by contrast-phase microscopy, multiple reaction monitoring (MRM) analysis, immunofluorescence microscopy and qRT-PCR. Quantitative proteomic analysis was based on SILAC method fallowed by bioinformatics enrichment tools using STRING and PANTHER databases. **RESULTS AND DISCUSSION** EMT-induced Caov-3 cells showed high levels of Vimentin, N-cadherin, Snail and Annexin A2 proteins, and decrease of E-cadherin protein, in association with upregulation of FN1 and CTNNB1. Quantitative proteomic analysis was able to identify 3060 proteins. Of these, 206 proteins were differentially expressed and data functional interpretation showed regulation of

proteins relevant for energy metabolism (PGM2, PYGL, PFKM, LDHB, PDHB, CTH, ALDH3A2, CAD, ASNS) and redox homeostasis (TXNDC5, PRDX4, PRDX2, GSTO1, GSTZ1) in Caov-3 cells after EMT induced by EGF. **CONCLUSIONS** After a well-characterized induction of EMT our data reveal a clear regulation of relevant proteins for energy metabolism by EGF-induced EMT in Caov-3 cells, contributing to support the implication of the metabolic alterations in EMT process development.

Keywords: Epithelial to Mesenchymal Transition, Redox**/**Energy metabolism, Ovarian cancer.

Supported by: FAPESP and CTC-CEPID.