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involved in this process. HCT116 cells were treated with oxaliplatin (10 µM), doxorubicin (5 µM) or 5-fluorouracil (10 µM) in the presence or absence of PTHrP. Trypan blue dye exclusion test showed that oxaliplatin and doxorubicin significantly decrease the number of viable cells. However, PTHrP treatment attenuates the cytotoxicity induced by both drugs. Besides, the antitumor effect of 5-fluorouracil was effective in HCT116 cells but PTHrP did not interfere with its cytotoxicity. We previously observed that, in HCT116 cells, PTHrP activates the signaling pathways of β-catenin and Met (a receptor with tyrosine kinase activity), which are key in the progression of CRC. The inhibition of Met and β-catenin pathways using specific inhibitors restored the cytotoxicity of CPT-11, oxaliplatin, and doxorubicin even in the presence of PTHrP, suggesting that this cytokine decreases the sensitivity of CRC cells to these three drugs through both pathways. To evaluate the impact of the tumor microenvironment on this chemoresistance, we performed the same experiments using a conditioned medium (CM) from the stromal endothelial HMEC-1 cells. Preliminary studies suggested that the CM of these cells, previously treated with PTHrP, attenuates the cytotoxic effect of the drug CPT-11. This work expands the knowledge of the molecular mechanisms associated with PTHrP-induced chemoresistance in CRC cells.

A29
EARLY EFFECTS OF FACTORS RELEASED BY TUMOR CELLS DERIVED FROM CERVICAL CANCER ON THE MORPHOLOGY AND PROTEIN PROFILE OF VASCULAR ENDOTHELIAL CELLS

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Tumor angiogenesis plays a crucial role in cervical cancer (CC) from early stages. Research for potential biomarkers and therapeutic targets has been hampered by heterogeneity, plasticity, and molecular differences of the endothelial cells that form the tumor vasculature. This is due, in part, to the effect of factors released by tumor cells. The aim of this work was to investigate the early effects of factors released by CC-derived tumor cells on the morphology and protein profile of endothelial cells. Treatment with CC-derived HeLa cells conditioned medium (TCM) for 3 h increased the number of HMEC-1 endothelial cells with cytoplasmic processes and a more elongated shape. Furthermore, qRT-PCR analysis revealed that HMEC-1 cells exposed to TCM decreased VE-cadherin endothelial marker mRNA and increased α-smooth muscle actin mRNA, a cancer-associated fibroblast marker. These findings could be associated with early stages of tumor angiogenesis characterized by increased cell migration and a partial transition from endothelial to mesenchymal phenotype (EndoMT). Next, the proteome response of HMEC-1 cells was studied under these experimental conditions, performing a Label-Free quantitative (LFQ) mass spectrometry (MS) (CEQUIBIEM Proteomics Center). Proteins were identified and quantified with the Proteome Discoverer software and the Uniprot database. Using the Perseus software, 9 negatively regulated proteins and 24 positively regulated proteins were obtained in HMEC-1 cells treated with TCM ($P \leq 0.05$ and fold change > 1.5), where clusterin (CLU) presented the highest fold change. CLU is a glycoprotein with a key role in cellular stress response and cancer, regulating processes such as cell migration. In addition, the classification of positively regulated proteins, according to their class, with the PANTHER bioinformatics tool, showed 2 cytoskeletal proteins, actin alpha cardiac muscle 1 (ACTC1) and tubulin beta-8 chain (TUBB8). ACTC1 can promote cell migration and modulate the length of actin tension fibers. qRT-PCR additional analysis also revealed an increased mRNA expression of CLU and ACTC1 in HMEC-1 cells treated with TCM. These results suggest that the recently identified proteins are involved in the early stages of biological processes leading to angiogenesis or EndoMT in CC and could be considered as potential biomarkers.

A30
THE DOPAMINERGIC AGONIST CABERGOLINE INDUCES AUTOPHAGY IN PANCREATIC BETA CELLS *IN VITRO*

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The dopamine D2 receptor (D2R) plays an important role in glucose homeostasis. Acting at the central nervous system and pituitary level, D2R agonists have shown an inhibitory effect on hyperglycemia in patients with type 2 diabetes, while the administration of neuroleptics, which antagonize dopamine receptors, causes hyperinsulinemia in normal subjects, or is associated with diabetes in psychiatric patients. Concordantly, D2RKO mice show hyperglycemia and decreased glucose-stimulated insulin secretion, highlighting a role of pancreatic D2Rs. *In vitro* studies point to the participation of pancreatic D2R not only in insulin secretion, but also in β-cell proliferation and apoptosis. On the other hand, autophagy constitutes a mechanism for maintaining cellular homeostasis through the constant elimination of potentially toxic ubiquitinated proteins and damaged organelles. Since its dysregulation, in the pancreatic β-cell, contributes to the development of diabetes, modulators of autophagy could be novel therapeutic agents for the treatment of human diabetes. Previous data indicate that D2R activation can alter autophagy in various cell types, though no data have been presented in pancreatic β-cells. Therefore, we studied the effect of the D2R agonist cabergoline (CAB) on the autophagy process in the MIN6B1 murine pancreatic β-cell line. Cell cultures were stimulated with CAB 10^{-5} M for 1, 6, and 24 h in order to evaluate the kinetics of autophagic vesicle formation, and on the other hand, with CAB 10^{-5} M for 24 h in the presence or absence of chloroquine (CQ), a late-stage autophagy inhibitor, in order to analyze autophagic flux. The autophagy markers LC3 (autophagic vesicle marker) and p62/SQSTM1 (receptor of cargo to be degraded by autophagy, and substrate degraded by autophagy) were analyzed by immunofluorescence and confocal microscopy. The results showed an increase in LC3 nucleation as a function of the stimulation time