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Ethoxzolamide reduces the expression of aggressiveness and invasiveness biomarkers in pancreatic cancer cells

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Pancreatic cancer is one of the most lethal of human malignancies ranking 4th among cancer-related deaths in the western world. Moreover, the drugs presented on the market fail on treatment of pancreatic cancer. In this regard, novel compounds that diminish the aggressiveness behavior of pancreatic cancer cells are urgently called for. Currently the carbonic anhydrase (CA) inhibitors, aromatic and heterocyclic sulfonamides (e.g. ethoxzolamide - ETZ), have been investigated as chemotherapics, since the acidification of the tumor microenvironment contributes to the metastatic behavior of cancer cells. The main goal of this study was to examine the molecular action by which ETZ diminished the proliferation rate of pancreatic cells (PANC-1) by checking the expression/function of some aggressiveness biomarkers by western blot and zymography. ETZ decreases PANC-1 cells viability with an IC_{50} value at 200 μM after 48h of treatment, as assessed through MTT reduction. In agreement, pro-survival kinases, AKT and Pim-1, were down regulated. It was also observed that the level of protein serine/threonine phosphatase PP2A (non-methylated C subunit) was also decreased by ETZ, which indicates an activation of this enzyme, and consequently inhibition of AKT and Pim-1. Accordingly, it was observed that ETZ caused cell cycle arrest at G1 phase by decreasing CDK4 and cyclin D expression. Importantly, both MMP-2 and MMP-9 expressions and activities were diminished after PANC-1 treatment with ETZ. The present study shows for the first time the potential of ETZ as anti-pancreatic cancer, mainly due to negative modulation of the aggressiveness and invasiveness biomarkers.

Biography

Cintia completed the Bachelor in Biotechnology in 2011 in Faculty of Biochemistry and Biological Sciences at the National University of the Litoral, Argentina. She worked at Department of Genetic and Evolution, University of Campinas (UNICAMP), SP, Brazil. Currently, she is enrolled as master degree student in Post graduation Program in Functional and Molecular Biology. Since 2011 she has been working under supervision of Prof. Carmen Veríssima Ferreira at Laboratory of Bioassays and Signal Transduction, Department of Biochemistry, UNICAMP. The main topic of the project is to define the molecular mechanism by which ethoxzolamide diminishes pancreatic cancer cells aggressiveness.

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