World Academy of Science, Engineering and Technology
International Journal of Mathematical and Computational Sciences
Vol:14, No:12, 2020

In Vitro Effect of Cobalt(II) Chloride ($CoCl_2$)-Induced Hypoxia on Cytokine Production by Human Breast Cancer Cells

Authors : Radoslav Stojchevski, Leonid Poretsky, Dimiter Avtanski

Abstract : Proinflammatory cytokines play an important role in cancer initiation and progression by mediating the intracellular communication between the cancer cells and tumor microenvironment. Increased tumor growth causing reduced oxygen concentration and oxygen pressure commonly result in hypoxia. Mechanistically, hypoxia is characterized by stabilization and nuclear translocation of hypoxia-inducible factor 1 alpha (HIF-1α) followed by propagation of molecular pathway cascade involving multiple downstream targets. Cobalt(II) chloride ($CoCl_2$) is commonly used to mimic hypoxia in experimental conditions since it directly induces the expression of HIF-1α. The aim of the present study was to investigate the in vitro effects and the molecular mechanisms by which hypoxia regulates the cytokine secretory profile of breast cancer cells. As a model for this study, we used several breast cancer cell lines bearing various molecular characteristics and metastatic potential (MDA-MB-231 (clauding low, ER-/PR-/HER^{2-}), MCF-7 (luminal A, $ER^+/PR^+/HER^{2-}$), and BT-474 (liminal B, $ER^+/PR^+/HER^{2+}$)). We demonstrated that breast cancer cells secrete numerous cytokines and cytokine ligands, including interleukins, chemokines, and growth factors. Treatment with $CoCl_2$significantly modulated the breast cancer cells' cytokine expression in a concentration- and time-dependent manner. These effects were mediated via activation of several signaling pathways (JNK/SAPK1, NF-κB, STAT5A/B, and Erk/MAPK1/2). Taken together, the present data define some of the molecular mechanisms by which hypoxia affects the breast cancer cells' cytokine secretory profile, thus contributing to the development of novel therapies for metastatic breast cancer.

Keywords : breast cancer, cytokines, cobalt(II) chloride ($CoCl_2$), hypoxia
Conference Title : ICSRD 2020 : International Conference on Scientific Research and Development
Conference Location : Chicago, United States
Conference Dates : December 12-13, 2020