Potential Candidate Genes Driving Cancer Stemness and their Regulation by CDDO-Im in Triple Negative Breast Cancer

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Cancer stem cells have been shown to be enriched in triple negative breast cancer and are associated with resistance to chemotherapy and radiation. Treatment of cancer cells with novel pharmacologic agents, such as CDDO-Im, have the potential to mitigate the aggressive phenotype that cancer stem cells confer. CDDO-Im is a synthetic triterpenoid previously shown to reduce tumor sphere forming efficiency as well as size of spheres in mammosphere culture of human triple negative breast cancer cells. The purpose of this study was to determine genes that are important in cancer stemness, and whether CDDO-Im treatment would regulate the expression of these genes. RNA sequencing analysis was performed on human SUM159 triple negative breast cancer cells to determine genes that were highly regulated when cells were enriched for cancer stem cells. Genes were then selected from RNA seq data through analyzing expression level change and physiological relevance to triple negative breast cancer and cancer stem cell phenotype. Human SUM159 cells were cultured in mammosphere as well as treated with CDDO-Im. Messenger RNA was then collected and expression was analyzed by quantitative PCR. Key pathways involved in the transition from monolayer to mammosphere identified by Ingenuity Pathway Analysis, IPA, included TNFα, TGFβ, HIF1α, VEGF, and EGF, all of which are integral to the cellular processes of growth and proliferation. In addition, treatment of mammospheres with CDDO-Im downregulated the TNF pathway, and this was shown by IPA to be regulated by HMOX1. Further qPCR validation will be performed to identify novel genes critical to cancer stem cell phenotype. Supported by the Grover Scholar Fund.