Investigating Estrogen as a Mediator for Epithelial-mesenchymal Transition in Estrogen Receptor-Positive Breast Carcinoma

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Estrogen receptor-positive (ER+) breast cancer differs from the triple negative subtype in that tumor cells respond to estrogen signaling through estrogen receptors. Binding of this hormone promotes tumor progression by increasing cell proliferation and the self-renewing stem cell population. In addition to cancer cell growth, tumor progression can also be measured through epithelial-mesenchymal transition (EMT) activity-- a process in which epithelial cells undergo a mesenchymal phenotypic change to promote metastasis. In advanced stages of tumor progression, transforming growth factor-beta (TGFB) acts as a mediator for EMT to introduce a more aggressive and invasive nature in epithelial cells. Based on these observations, we hypothesize that estrogen-mediated expansion of cancer stem cells increases EMT activity through the TGFB type II receptor (TGFBR2) mechanism. The purpose of the study was to investigate the effects of estrogen signaling on the induction of cancer stem cell markers and EMT-related gene expression, particularly TGFBR2, in ER+ breast cancer. MCF-7, a human ER+ mammary epithelial breast cancer cell line, were cultured into tumorspheres with 1nM of estrogen for 4 days. mRNA was then extracted to perform RT-qPCR analysis for the cancer stem cell marker CD44 along with EMT target genes including TGFBR2; snail2 (SNAI2), a transcription factor that represses E-cadherin synthesis necessary to maintain organized cell contact; and vimentin (VIM), a type III intermediate filament that provides structural integrity to mesenchymal cells. Our results showed a decreased in VIM expression and an increase in CD44 and progesterone receptor--a downstream target of estrogen receptor activation--expression. In conclusion, estrogen increases cancer stem cell markers but does not contribute to increased EMT activity in ER+ breast cancer. Supported by NIH R25ES020721.