Effects of Stroma on ER+ Breast Cancer Cell Metastasis

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ABSTRACT
Breast cancer is one of the most wide-spread diseases among women in America. If the cancer is local, it is easily controlled by surgical resection. However, if the cancer cells metastasize, patient survival is significantly reduced. 70% of breast cancers can be targeted through estrogen receptors (ER) on the membrane, with compounds such as tamoxifen. However, tamoxifen shows unreliable outcomes on different patients and it is believed that the ineffectiveness of tamoxifen is related to the epithelial-mesenchymal transition (EMT) of cancer cells. To address this problem, we are designing a system that stimulates metastasis activation with the aim of incorporating the results in target identification for drugs. To mimic the cellular microenvironment in both 3D and 2D, scaffold and plate seeding of T47D cell line, an ER+ breast cancer cell line, and human mammary fibroblast (HMF) has been utilized. To understand the activation state of secondary metastasis and identify the presence of drug-targeted receptors, IHC staining has been used. Only co-cultured samples of T47D and HMF in 3D showed EMT. The morphology of both cells, when kept isolated from each other, did not change, but epithelial markers appeared at the cytoplasm instead of the membrane after 7-days of co-culture. Our results suggest that communication of breast cancer cells with fibroblasts in 3D initiates secondary metastasis. We hypothesize that the EMT leads to loss of estrogen receptors and reduce medicines efficacy.

KEYWORDS
Breast Cancer, ER+, T47D, Stroma, Fibroblast, ECM, Metastasis