077

Analyzing Estrogen Receptor response to Breasts Cancer Cells at Stiffness Relative to the Bone Marrow

Bone metastases are a prevalent problem for breast cancer patients. About 70% of patients who have metastatic disease have bone metastases and currently there is no therapy to cure this disease. The bone marrow microenvironment is highly dynamic and can involve many physical factors such as hydrostatic pressure and increased stiffness that can affect the behavior of cells in the site. However, it is unclear on how the physical environment affects breast cancer cells that metastasize to the bone. Estrogen receptor (ER) status plays a pivotal role in patient survival with metastatic disease. Clinical studies have indicated that both ER+ and ER- patients develop bone metastases, however, there is minimal work to establish how the physical factors of the bone marrow can affect ER sensitivity. We hypothesize that higher stiffness ranges of the bone marrow can increase BC invasiveness and decrease estrogen receptor sensitivity of metastasized tumor cells. Estrogen receptor signaling canonically activates by locating to the nucleus and transcribing genes related to cell function. Previous literature suggests that cells that experience higher stiffnesses cause an increase in estrogen receptor localization to the nucleus at the primary site, however, this has not been studied at the varying stiffnesses of the bone marrow. Here, we analyze the localization estrogen receptor at different stiffnesses relative to the bone marrow. Using CytoSoft Rigidity Plates ®, we seeded ER+ (MCF7) and ER- (MDA) cell types on stiffness plates with stiffnesses at 0.5 kPa and 32 kPa to mimic the sinusoidal and endosteal regions of the bone marrow, respectively. Using immunofluorescence staining, we identified estrogen receptor in the outside and inside the nucleus of the cells. Additionally with ImageJ, we quantified the localization in the ER receptor to the nucleus.