

Mechanosensitivity Analysis of Breast Cancer Tumor Cells from Needle Biopsy

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Abstract

Tumor stiffness has been associated with malignancy and increased risk for metastasis. Extensive research has been done investigating breast cancer cell lines' responsiveness to surfaces of varying rigidities as well as examining the biophysical properties of breast cancer tumor samples. However, there is a critical gap regarding the relationship between cells' mechanosensitivity in conjunction to biophysical properties of their extracellular matrix environment. To explore this relationship, we will analyze single-cell mechanosensitivity in comparison to tumor rigidity via shearwave ultrasound elastography (SWE). Given the putative affiliation, we hypothesize that cells expressing invasive mechanosensitivity profiles will correlate with stiffer tumor regions. Using collagen gels containing different cell types, we derived biopsy-sized samples allowing us to optimize single-cell mechanosensitivity analysis. Cells were stained using different dyes corresponding to invasiveness. Subsequently, we analyzed their morphology. Morphological identification within organoid environments would allow for single-cell analysis without the aggression of tissue digestion, though preliminary results suggest high heterogeneity may not allow for confident cell identification solely on morphology. Thus, inquisition into cell viability and integrity was explored by analyzing the effects of tissue digestion with HyQtase on single-cells. Cell count and live-dead stain via flow cytometry allowed for analysis of single-cell viability. Lastly, cell integrity was evaluated by a 2D adhesion assay of isolated cells. The live/dead stain revealed that digestion resulted in isolation of approximately 10% of the original 500,000 cell population with 90–97% of the isolated population being live-cells (invasive and non-invasive respectively). Furthermore, the adhesion assay showed that these isolated single cells retained the ability to adhere to new surfaces, with no difference between the invasive and non-invasive cell types. These results show that cells are able to retain mechanosensitive properties following enzymatic digestion. However, they also suggest our digestion procedure is not aggressive enough to isolate invasive subpopulations that are more strongly embedded in the original tissues. Development of these novel techniques will allow for accurate and confident analysis of precious human biopsy samples. Insight into the relationship between single-cell mechanosensitivity and tumor biophysical properties could elucidate pathways for metastasis inhibition and prevention.

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