Engineered 3D Cellular Co-Culture to Study How Fibroblasts Alter Extracellular Matrix Composition Estrogen Receptor Positive Breast Cancer

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A novel approach to mimicking in vivo tissue microenvironments is to grow cells as 3D spheroids to provide a model system to analyze cell growth. Droplet microfluidic devices provide a platform to overcome limitations found in other approaches, like the hanging drop method, by generating uniform spheroids with minimal mass transfer limitations. A previously developed microfluidic device can encapsulate ER+ MCF7 breast cancer cells in a biocompatible and degradable thiol acrylate hydrogel, which serves as a scaffold to grow 3D spheroids from a small number of cells. After the development of a gravity driven nutrient delivery device was proved to support cellular growth in the microfluidic device, it was tested for efficacy as a model to study 3D spheroid cellular responses to changes in the microenvironment. To further study the extracellular matrix and microenvironment of spheroids, a method of co-culturing MCF-7 cells and fibroblasts was developed to investigate the role of collagen in the cancer tumor spheroid development process, as compared to a monoculture of MCF-7 cells. We found that a ratio of 1:4 (MCF-7: Fibroblast) produced a high collagen response in the co-cultured cells, specifically the spheroid core. This ratio allowed for defined layers and better tracking of spheroid formation. The monoculture had a less defined response, showing less collagen in staining. Imaging showed that the presence of fibroblasts furthered spheroid growth and development over the culture period. The results of this study will help to further the knowledge of how cancer cells interact and function with collagen production and how collagen can be used as a biomarker to identify the presence of cancer.

Awards Won: