Generation of 3D Co-Cultured Breast Cancer Spheroids to Study the Spatial Distribution of Fibroblast-Produced Collagen

Moe, Margaret (School: Saint Joseph's Academy)

Recent studies have found that estrogen receptor positive (ER+) breast cancer cells exhibit enhanced proliferation and drug resistance when grown in a 3D environment when compared to 2D cell growth. It has been suspected that the interactions between breast cancer cells and other members of the tumor microenvironment (TME) including fibroblasts and extracellular matrix (ECM) proteins like collagen I further drive cancer progression and drug resistance. A novel approach to mimicking the in vivo TME is to grow cells as 3D spheroids to better recreate the complex cell-to-cell interactions that drive cancer progression and drug resistance. Droplet microfluidic devices provide a platform to overcome limitations associated with other 3D cell culture approaches by generating uniform spheroids with minimal mass transfer limitations. This work utilized a droplet microfluidic trapping array can encapsulate MCF7 breast cancer cells in a biocompatible and degradable thiol acrylate hydrogel, which serves as a temporary scaffold to grow 3D spheroids from a small number (<10) of cells. Incorporation of a gravity driven nutrient delivery device was proved to support cell growth in the microfluidic device for >10 days. To study how co-culturing components alter breast cancer progression, a method of combining MCF-7 cells and fibroblasts was developed to investigate the role of collagen I expression in the 3D tumor spheroids as a growth agent and biomarker for cancer progression. We found that larger spheroids developed multiple “hotspots” to produce enough collagen for larger masses of cancerous cells. The results of this study will provide new insight into the role of cancer progression and drug resistance and help to identify new biological targets for therapeutics.

Awards Won:

National Anti-Vivisection Society: Second Award of $5,000