Fabricating Breast-Cancer-Cell-Laden Microspheres With Microfluidics to Simulate the Tumor Microenvironment

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Metastatic (migratory) cancer accounts for 90% of cancer deaths, yet not much is known about the specific factors driving tumor migration, including interstitial flow. In order to characterize the effects of interstitial flow on metastasis, an in vitro model of the tumor microenvironment must be developed with the capabilities of adjusting matrix permeability and interstitial flow. Such a model may utilize two layers of hydrogel with differing mechanical properties, with cancer cells encapsulated inside an inner layer of polymerized gelatin methacryloyl (GelMa). This study investigates the feasibility and necessary parameters to encapsulate MDA-MB-231 breast cancer cells within polymerized microscale droplets (microspheres) using a microfluidic device with flow-focusing geometry. Microfluidic devices were fabricated using soft photolithography. The microfluidic device allowed for tunability of microsphere diameter via adjusting oil and GelMa flow rates. Microspheres were consistent in shape and diameter after on-chip production and after permanent UV photopolymerization. These microspheres provided a suitable environment for the cells, but a low viability was observed, likely due to the lack of cell culture medium during the microsphere formation and polymerization. Therefore, the experimental protocol needs to be further optimized by reducing production time, potentially by automation. To work towards an automated system, microsphere volumes were accurately predicted with a mathematical model prior to exiting the microfluidic device. Furthermore, microspheres were mechanically suitable for applications in a dual-gel model of metastasis. This study provides necessary insight in developing an in vitro model to study the effects of interstitial flow on metastasis.

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