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Tumor-microenvironment-on-chip to mimic tumor heterogeneity

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ABSTRACT

Ductal Carcinoma *In Situ* (DCIS) is a non-invasive cancer that forms around breast milk ducts that can potentially progress into invasive breast cancer if untreated. Lack of models to study its diverse pathophysiology and differential response to treatments poses a challenge to develop standard treatment modalities with improved therapeutic outcomes. The traditional *in vitro* models such as cell monolayer are convenient but insufficient to represent the physiological characteristics of DCIS tumor microenvironment and often fail to predict clinical outcomes. The animal models effectively simulate the *in vivo* environment but also lack the ability to control the environmental parameters to match specific conditions making it difficult to address the heterogeneities in disease state and patient-to-patient variations. It is critical to develop a new DCIS model system that offers physiologically relevant features with high degree of control. In order to address this need, a novel microfluidic *in vitro* model was developed. A lumen structure to represent the milk duct in breast was generated along the microfluidic channel using a fluid dynamic phenomenon called viscous finger patterning in which as the less viscous fluid passes through, it leaves a continuous trail that makes a hollow tubular structure in the collagen hydrogel. Consequently, MCF-7 breast cancer cell lines were cultured along the lumen surface with BR5 stromal fibroblast in collagen hydrogel. A relatively straight, smooth lumen was achieved at a higher concentration of collagen gel by viscous finger patterning with an optimal flow rate. The interaction between a non-invasive breast cancer cell line, MCF-7 and stromal fibroblast most likely remain unchanged, thus mimicking the DCIS. This new model system is a potential tool to study DCIS progression and treatment response by offering physiologically relevant features that can be tailored to match disease state and patient specific conditions.

KEYWORDS

DCIS, breast cancer, microfluidics, viscous finger pattering

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