Modeling Pancreatic Cancer Tumor Microenvironment using a Microfluidics Culture System.

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Pancreatic ductal adenocarcinoma (PDAC) is the fourth leading cause of cancer-related deaths in the United States, with an overall five year survival rate of 7%. This is partly due to the lack of effective models that simulate the complex PDAC tumor microenvironment and allow for high throughput drug screening. Some of the key features of the PDAC tumor microenvironment are the presence of a dense stroma which impedes effective drug delivery to the pancreatic cancer cells (PCCs), as well as the presence of cancer associated fibroblasts (CAFs) that have been shown to modulate disease progression. The objective of this project is to develop an in vitro microfluidic cell culture system that allows researchers to recapitulate the PDAC tumor environment. The system, Tumor-Microenvironment-on-Chip (T-MOC) is manufactured using a replica molding technique. The chip consist of two polydimethylsiloxane (PDMS) layers separated by a porous membrane for gas exchange. This device forms an enclosed transparent device with input channel for cell entry and inner channels which mimic fluidic transport found in vivo. To analyze the potential of the device to simulate in vivo conditions, PCCs (GFP+) and CAFs (RFP+) were co-cultured with collagen and inserted into the device. Initial data analysis indicates that the device supports the growth of PCCs and allows formation of 3D tumor spheroids. In addition, analysis of GFP and RFP intensity demonstrated the effect of CAFs on PCCs growth, which diminished PCCs growth. This provides evidence that the microfluidic device can be used to replicate tumor environment allowing for future studies to screen potential drug candidates before in vivo studies.

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