Formation of Microtumors in Hydrogel environment

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Introduction

Tumors are large clusters of cancer cells in which their propagation is unregulated by normal means of cell function.

Many times when a patient is diagnosed with cancer, the main battle is to ensure the cancer does not spread to other tissues by means of the circulatory system. Tumor cells are released from the main proliferation site and travel through the blood stream to other parts of the body. This spread of this disease is incredibly dangerous as cancer is highly unpredictable and quickly becomes harder to get under control if not identified early.

This study was preformed to develop the means of creating an In-vitro microtumor through microfluidic enabled engineering techniques. This should provide means of continued research of the tumor microenvironment

Methods

Soft lithography was utilized for the formation of the PDMS "lab on a chip" microfluidic device. A 3D rendering is shown in Figure 1. An oil emulsion, consisting of 8 mL of mineral oil, 133uL of SPAN 80, and 1.5mL of 1g/ml CaCl2 was emulsified using a sonicator.
The core shell solution consisted of 900uL of 1% alginate and .5% Hyaluronic acid in saline and 100uL of the desired cell concentration in DMEM complete Mędia.
Three high precision syringe pumps where used to create microcapsules. Oil was flowed in at a rate of 5ml/hr. Alginate solution 250uL/hr. Core solution 100uL/hr. The pumps were ran for 2 hours while allowing the microtumors to flow into a solution of mannitol. The remaining oil was then removed from the mannitol solution and the microtumors were put into a 6 well plate with DMEM complete media and placed into an incubator.

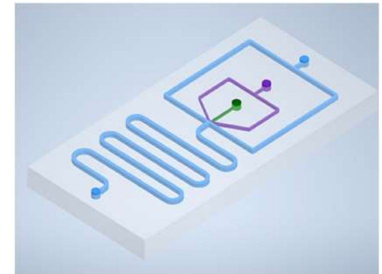


Figure 1. CAD rendering of "lab on chip" device. blue=oil emulsion, purple=purified alginate, green=core shell solution.

Results

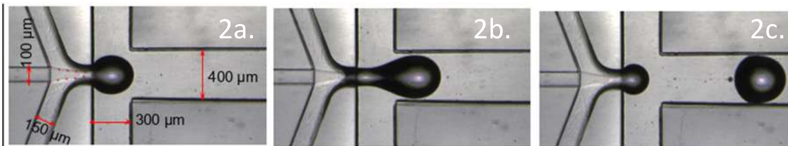


Figure 2. Dynamic creation of microtumor in 3D 'lab on a chip" device
Each channel is different sizes as indicated by the first panel of the figure (2a). Flow rates are described in the Methods section. Collection of these microtumors was conducted by allowing the capsules to flow into a solution of mannitol after letting the system run for a couple hours.

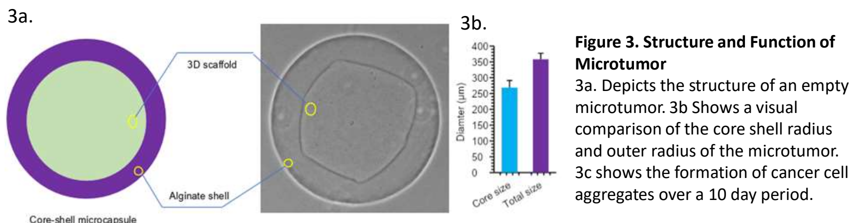
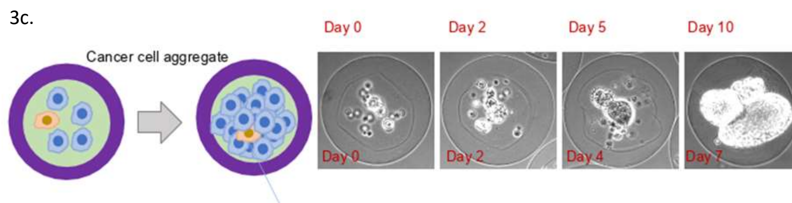


Figure 3. Structure and Function of Microtumor
3a. Depicts the structure of an empty microtumor. 3b Shows a visual comparison of the core shell radius and outer radius of the microtumor. 3c shows the formation of cancer cell aggregates over a 10 day period.



Discussion and Future Work

Results of the first part of this study shows promising basis for the continued study of the microtumor environment. As shown in Figure 3c, the team was successful in creating an in-vitro tumor model utilizing methods of microfluidics and hydrogel synthesis.

The continuation of this project is focused on the conditions of detached cells from the original tumor propagation site, and those cells' viability to create another tumor downstream of the original proliferation site.

Conditions that are currently being analyzed are single cell encapsulations , cluster-of-cells encapsulations, and more than one individual cell in the same encapsulation.

By the end of the study, the goal is to better understand the microtumor environment and what factors contribute to cancer cell viability and probability of new tumor formation.

Acknowledgments

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