Analyzing Morphological Shifts of Breast Cancer Under Varying Stromal Conditions Using Microfluidic Technology

Cristian Zamora, Biomedical Engineering
Mentor: Dr. Mehdi Nikkhah, Associate Professor
School of Biological and Health Systems Engineering
Ira A. Fulton Schools of Engineering
Arizona State University

Introduction

Current treatments and diagnosis of triple negative breast cancer are not effective because of triple negative protein expression, meaning it lacks the main receptors targeted in cancer treatments. By analyzing the shape descriptors of breast cancer cells, a deeper understanding can be obtained of the influence of the tumor microenvironment on breast cancer. Through the study of the morphological changes of the cells, and by focusing on the area, aspect ratio, circularity and protrusiveness. We aim to understand how the tumor microenvironment will influence the progression of breast cancer.

Methods

Figure 1: **Tumor-on-chip model.** Schematic representation of COC microfluidic model with interconnected tumor and stromal region (Left). Actual microfluidic device next to a coin to depict the size of the device (Right).

The tumor region (red) is encapsulated with SUM159 triple negative breast cancer cells. The stromal region (green) introduces immune cells and cancer associated fibroblasts. While the media region (white) houses the cell culture medium.

Experimental Setup

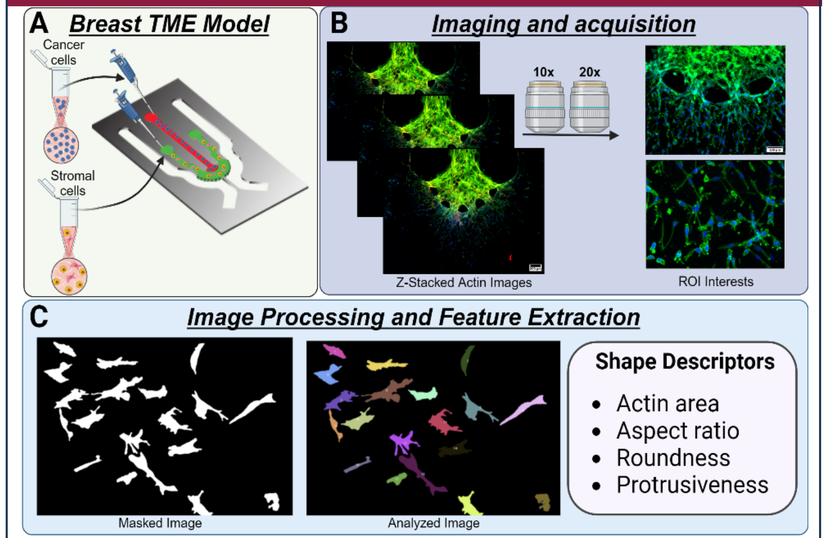

Figure 2: **Experimental workflow of the proposed study.** A) Depicts the two-layer cancer on a chip model housing the cancer and stromal cells. B) Shows a visual of the imaging and acquisition of immunofluorescent (IF) stained cells in the stromal region. C) Illustrates the mask being generated and analyzed in ImageJ based on the previous IF image to acquire the desired Shape Descriptors.

To obtain a higher resolution of the cells from the microscopic images, max stack analysis was performed utilizing the Z-project tool within ImageJ. The image was divided into three channels and assigned different colors for the cell body and nucleus. The morphological features were hand traced using the freehand tool and uploaded to create a mask. Upon creating the mask, using the particle analyzer plugin, shape descriptors were quantified across each condition.

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Results

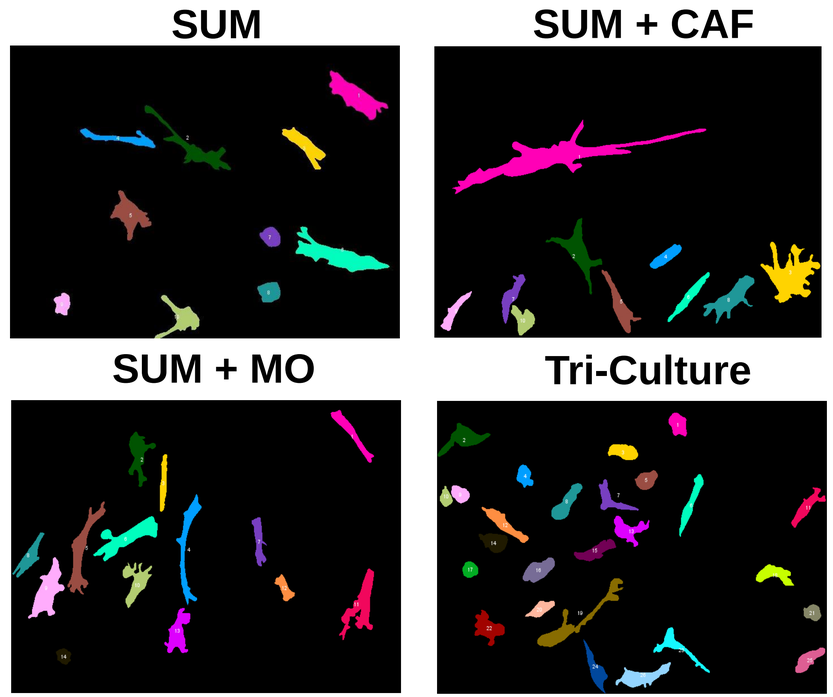

Figure 3- **Binary images of cancer cells in 3D**

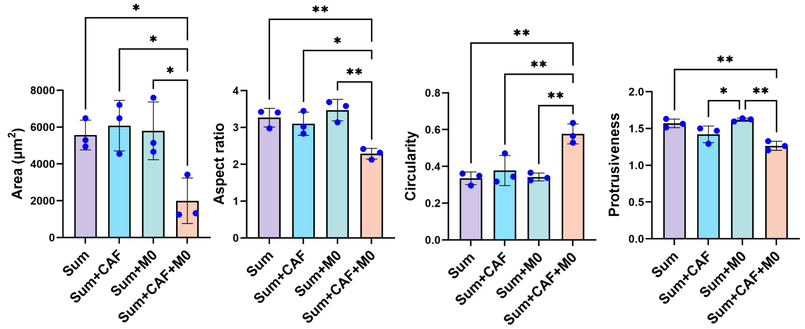

Figure 4- **Graphical representation of different morphological features**

Tri-Culture has varying significance in circularity because the data was analyzed with both cancer cells and macrophages. Analysis was done with three replicates for each stromal condition.