The effect of different matrix interfacial adhesive strength in promoting the metastatic pattern of tumor spheroids using an encoder-decoder model

Keywords: machine learning, multicellular tumor spheroids, tissue interface, adhesion strength.

Introduction

The pre-existing structure formed in the tissue serves as a critical variable in influencing cancer spread[1]. While such extracellular matrix (ECM) arraignment is known to govern cell adhesion, morphology, and migration, the adhesive strength characteristics between the interfacial contact have remained elusive. 3D avascular tumor models have been widely employed to explore invasion and metastasis processes and the influence of medications on metastatic potential. However, there are currently only limited tools to automatically analyze the 3D metastatic cancer differential interference contrast (DIC) images' morphology. This study presents a novel and practical end-to-end pipeline to automatically quantify cell migration behavior when cultured under conditions with different interfacial adhesive strengths.

Method

MDA-MB-231 breast multicellular tumor spheroids (MCTS) were grown for four days and embedded in the collagen type I gel. Different matrix-substrate interfacial adhesion strength was achieved by layering the MCTS-contained collagen onto the surface of glass modified by either Poly-D-Lysine (PDL), Glutaraldehyde (GA), or Pluronic (Figure 1a). DIC images were analyzed using a series of workflows consisting of pre-processing images, followed by the DIC segmentation model and post-processing that describes the cell behaviors (Figure 1b). The model is an encoder-decoder model used to segment core and invasive cell areas. Intersection over Union (IoU) was computed to evaluate the model performances. After the model was trained, invasive area, invasive radius, core area, and core radius were computed.

Results

The IoU for the Invasive and Core model were 0.8959±0.0398 and 0.8734±0.0407, respectively. By applying the models, we verified that different interfacial adhesive strengths would significantly affect the extent of the spread, invasion, and migration modes of the MCTS. In both cases of surface modification, pluronic (most minor adhesive strength) and PDL (intermediate strength) permitted the most augmented cancer invasion in comparison with control (low strength) and GA (maximum strength). Interestingly, despite the fact that the invasive area is similar in both pluronic and PDL coated conditions, the core area retained much higher in pluronic than in PDL, suggesting different modes of invasion that favored partial or complete dissociation (Figure 1c).

Discussion

Our results also indicated that interfacial adhesion strength substantially impacts the 3D metastatic cancer migration and invasion. We propose an automated end-to-end strategy for describing spheroid invasion dynamics, with feature segmentation, extraction, modeling, and statistical analysis capabilities. We believe that by establishing this experimental and machine learning model, our study will identify essential patterns for this breast cancer cell-matrix interface migration.

Reference:

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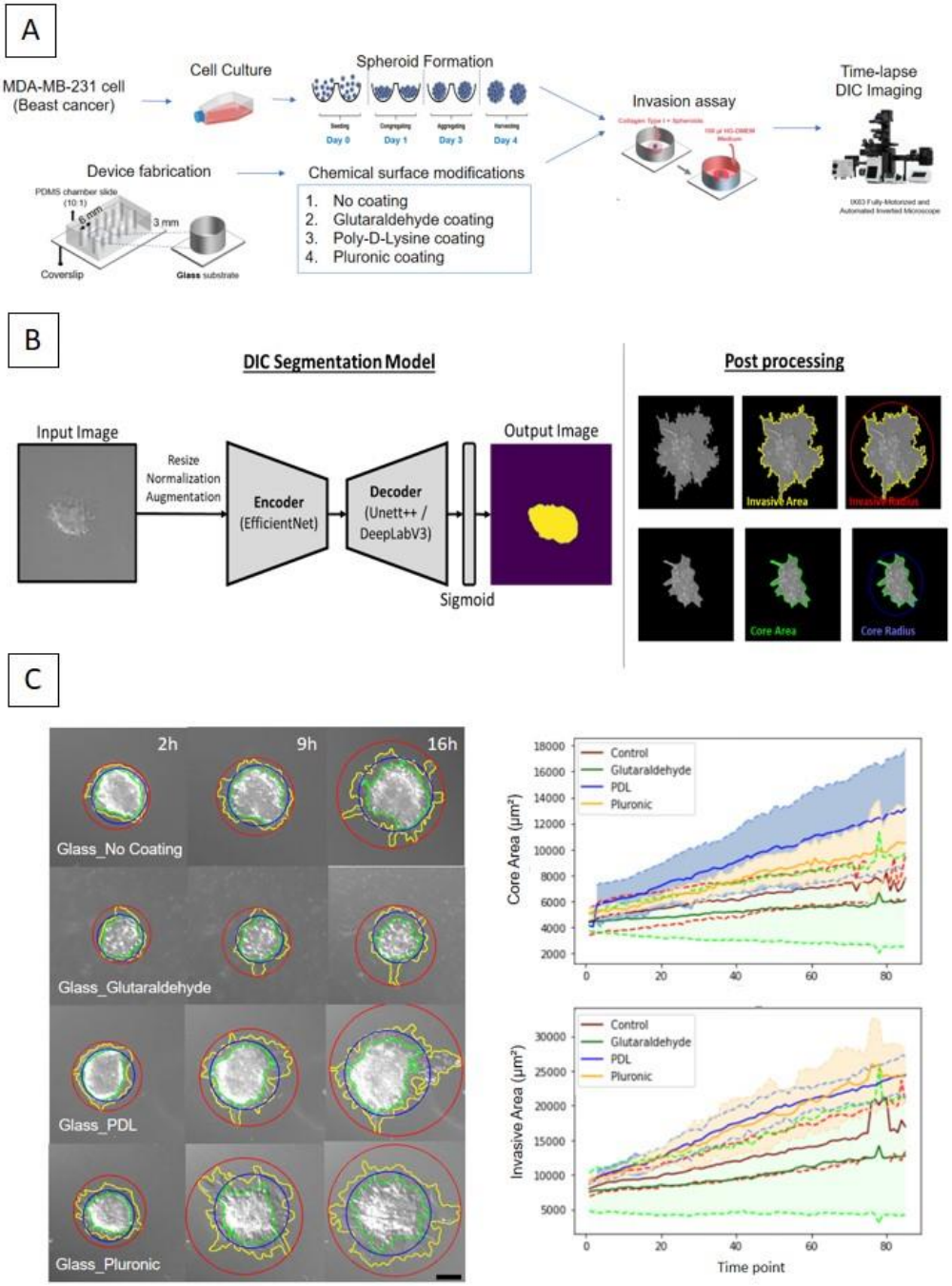

Figure 1: (A) Workflow for spheroid DIC (Differential interference contrast) imaging. (B) Workflow for DIC segmentation model. (C) Feature extraction results. The red circles are invasive radius; blue circles are core radius; yellow line are invasive area and green line are core area of spheroids for Control, Glutaraldehyde, PDL and Pluronic at each time points (Time point: 10 Minutes). Scale bar is 50 μm.