Abstract:

We develop techniques involving microgeometries and photonics to study mechanical properties of metastatic cancer cells. Using confined microchannel environments with patterned geometric constraints, we quantify cell behavior during invasion into tight spaces. With nearfield photonic structures, we actively manipulate particles and cells via optical forces. Our techniques provide ways of probing single cells on-chip.

Summary of Research:

It has been demonstrated that in confined microchannel environments with cross-sectional areas comparable to the size of cells, cells can spontaneously migrate unidirectionally with high velocities and persistence [1]. To further investigate the effect of mechanical confinement on cell invasion and behavior, which may provide insights towards cancer metastasis, we introduce mechanically perturbative elements to elicit cell responsivity. Specifically, as shown in Figure 1, our device consists of confined PDMS microchannels with cross-sectional areas comparable to cell size, and a spatially tapered region in the channel reduces the cross-sectional area from $15 \, \mu m \times 10 \, \mu m$ to $4 \, \mu m \times 10 \, \mu m$. We analyzed the behavior of three different cell types: bovine aortic endothelial cells (BAECs), MCF-10A (human mammary epithelial cells), and MDA-MB-231 (highly metastatic breast carcinoma cells)-in the tapered junction (Figure 1 (a and c)) and characterized the relative probabilities of cell invasion vs. repolarization.

We found that MDA-MB-231 cells were the most invasive of the three. Furthermore, we analyzed the migration dynamics of cells as they exhibited physical spatial gradients. As shown in Figure 1 (b and d), we fitted the velocity profile of cells in the tapered junction to a dual-sigmoid function and characterized the cell transition dynamics with two time constants and a delay constant. There appears to be two acceleration phases separated by a transition lag [2].

Additionally, to actively probe cells, we have developed and fabricated optical waveguides with accessible evanescent fields, which can be used to induce localized optical forces [3]. Live and adherent cells can proliferate on these waveguides, and we can subsequently induce guided particle-cell collisions, as demonstrated in Figure 2.

References:


[3] “Optofluidic trapping and transport on solid core waveguides within a microfluidic device”; Schmidt, BS, Yang, AHJ, Erickson, D, Lipson, M; Optics Express, 15, 14322-14334 (2007).
Figure 1: Migration dynamics of repolarizing and permeating cells. A-B. Time-lapse image stack (A) juxtaposed on top of the data and sigmoid curve fit of the velocity profile on the same time interval (B) of a permeating MDA-MB-231 cell during transition in a spatially tapered junction, which connects a 15 µm × 10 µm channel to a 4 µm × 10 µm channel. C-D. Time-lapse image stack (C) juxtaposed on top of the data and sigmoid curve fit of the velocity profile on the same time interval (D) of a repolarizing MCF-10A cell during transition in the tapered junction.

Figure 2: Time-lapse image stack of a cell on an optical waveguide. An MDA-MB-231 cell adheres to a waveguide (2.8 µm wide) and 3 µm particles are optically propelled onto its surface. Each successive frame represents two seconds of time elapsed.