Real-time Cell Migration Force Monitored by Micropost Sensor Arrays on Top and Bottom Surfaces in Confined Channels

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Introduction. Mechanical force plays a key role in cell mechano-sensing and transduction, which involve the interactions between adhesion of cell-matrix and traction force generated from actomyosin contractility during cell migrations. Previous studies have shown cell-extracellular matrix (ECM) interactions on two dimensional (2D) surfaces. In reality, cells encounter three dimensional (3D) ECM in tissue. In order to understand the mechanisms of cell migration in a 3D environment, it is important to study the transformation of cell migration modes as well as migration speed and direction in 3D. In this study, cell traction force was measured in real time during cell migration in 3D with guiding topography and physical confinement.

Method and Results. Micropost sensing platform consisted of elastic posts were linearly deformed during cell migration, which could be used to measure the cell traction force. Arrays of micropost were integrated in channels with various channel widths and heights to monitor cell migration force dynamically as cells moved in confined channels. As shown in Fig. 1, polydimethylsiloxane platforms were replicated from a double-layer SU-8 master mold and bonded after an oxygen plasma treatment to generate a confined microfluidic channel with integrated micropost sensors. Cells were confined both vertically and laterally by adjusting the channel dimensions. To characterize the changes of the mechasymal migration inside the channels, MC3T3-E1 osteoblast cells were seeded into the microchannels. As shown in Fig. 2, the cells were elongated and showed a smaller size with increased physical confinement. Moreover, cells moved faster with traction force as they were further confined in smaller channels. The influence of cell contact with the top and bottom surfaces inside the channel was investigated by quantifying the traction force as cell migrated in the channels with micropost sensors on both the top and bottom surfaces. Cells could make contact with either the top or bottom microposts, and they could also partially adhere to one of the surfaces, as shown in Fig. 3. This cell force sensor system provides the integration of cell guiding topography with various degrees of cell confinement. The dynamic distribution of the cell traction force measured during cell migration could lead to a better understanding and control of cell interactions in a 3D ECM.

Conclusion. In this study, the cell shape, traction force, and speed of MC3T3-E1 cells were measured during cell migration in confined channels with different channel widths and heights. The physical confinement and topography could affect cell shape and migration speed. During cell migration in confined channel, cell traction force varied depending on the cell contact with the top and bottom surfaces. By understanding the dynamic changes of cell traction force during cell migration in confined channels, proper cell guiding topography could be designed to control cell movement and screen cells.

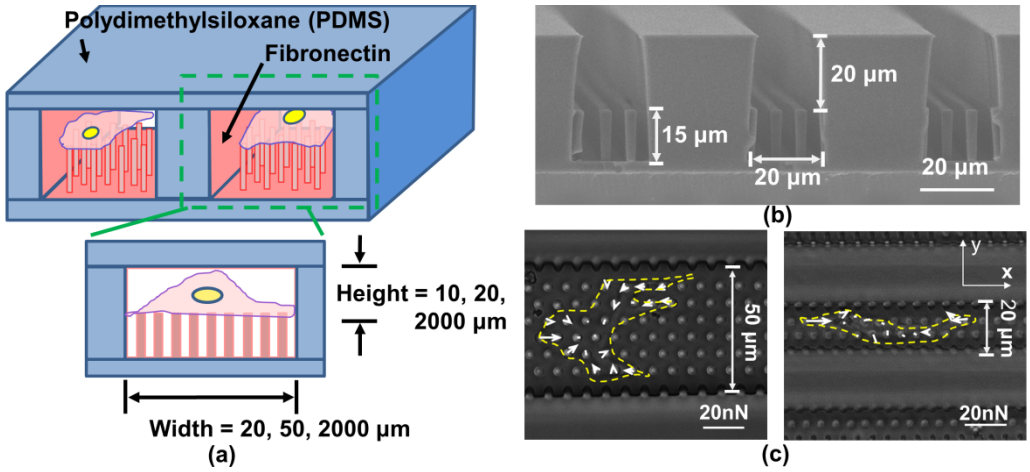

Figure 1: (a) Schematic of cell migration in confined channel with integrated micropost sensors. (b) Double-layer SU-8 master mold. (c) Force mapping of cell migration in 20 and 50 μm wide channels.

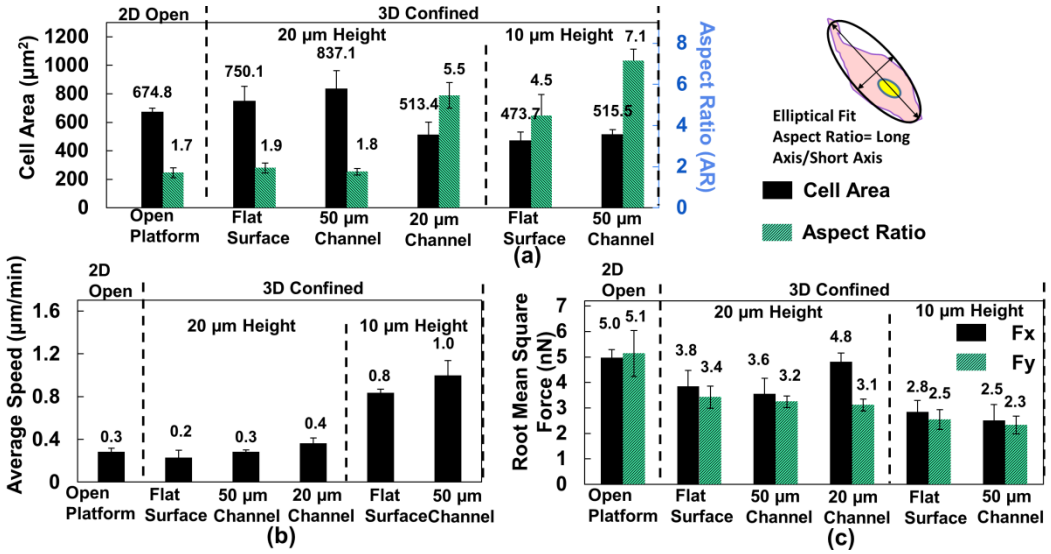

Figure 2: (a) Cell area and aspect ratio, (b) migration speed, and (c) traction force during cell migration on 2D surface and inside 3D confined channels.

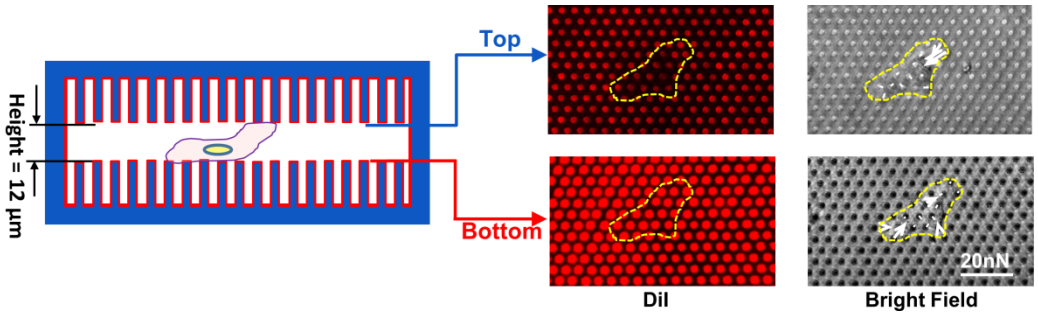

Figure 3: Measurement of traction force during cell migration in vertically confined channel with micropost sensors on both top and bottom surfaces.