Topographical Effect on Natural Killer Cell Locomotion in Confined Microenvironment

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Natural killer (NK) cells are lymphocytes which serve an important role in immune system by recognizing and killing potentially malign cells without antigen sensitization, and could be important in cancer therapy. NK cell locomotion is an important process for them to find and kill target cells, which is well known to be driven by chemotaxis effect. NK cells also experience topographical effect induced by extracellular matrix (ECM) during their locomotion. However, topographical effect on NK cell locomotion in 3D environment is not well understood.

In this study, microchannels with different shapes and decorated with varies topographies were fabricated in SU-8 molds followed by polydimethylsiloxane (PDMS) replication. NK-92MI cells and MCF7 breast cancer cells were seeded on the PDMS platforms and time-lapse microscopy was used to observe migration behavior of NK cells.

Figure 1a shows a series of microwells connected by 100 μm long, 10 μm wide microchannels. NK cells in smaller microwells were attracted to migrate towards larger microwells due to chemokine provided during NK-MCF7 interactions. Discontinuity structures such as bending can affect NK cell movements such as changing the migration direction of NK cells as shown in Fig. 1b. Different structures also showed different degrees of control on chemotaxis induced NK cell migration (Fig. 1c).

To highlight the topographical effect of microenvironment on NK cell locomotion, confined channels were used with no chemokine added. Figure 2 shows the migration of NK cells seeded in 10 μm high channels with 1 μm deep grating patterns decorated on the channel ceiling. With no chemokine added, NK cells still showed their preference to move across the gratings, resulting in migration trajectories aligned perpendicular to the grating direction. This result showed that NK cell migration can be controlled by contact guidance, which provides future possibility to manipulate NK cell migration in controlled *in-vitro* microsystems. All these preliminary results showed that the complex 3D microenvironment of ECM can have significant effect on NK cell locomotion, and could potentially provide insights for explaining dynamics of NK cell activities in tissues.

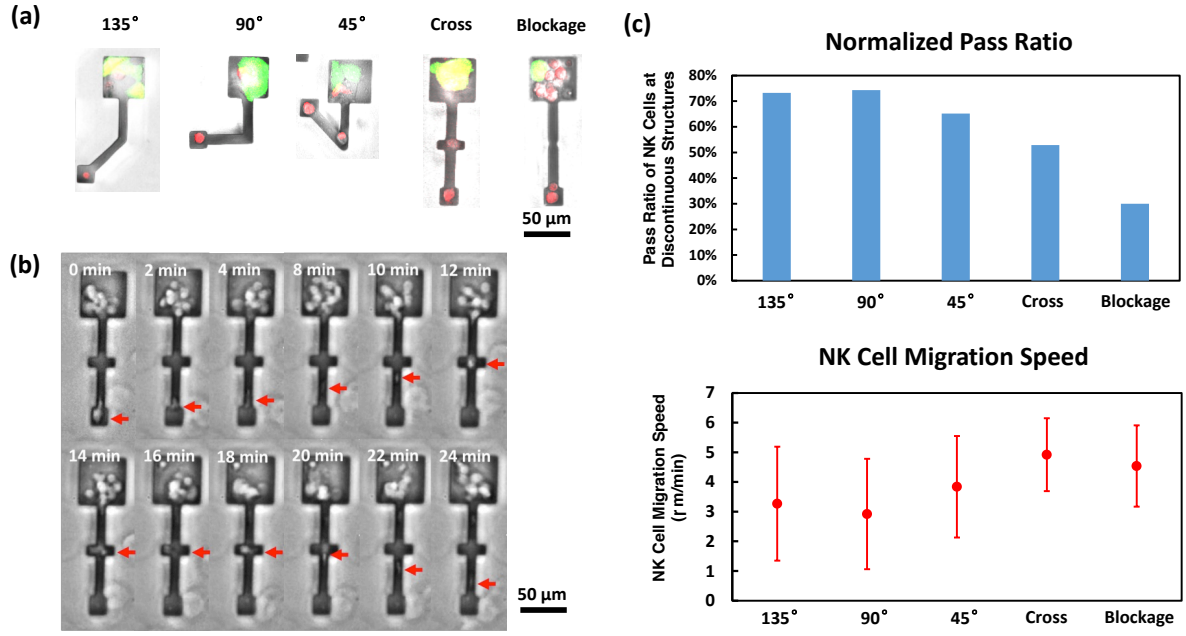

Figure 1: NK cell migration in microchannel induced by chemotaxis: (a) Different discontinuous structures located at center of channel. (b) Time-lapse images of NK cell reversing at cross structure. (c) Comparison of NK cell migration behavior in different channels.

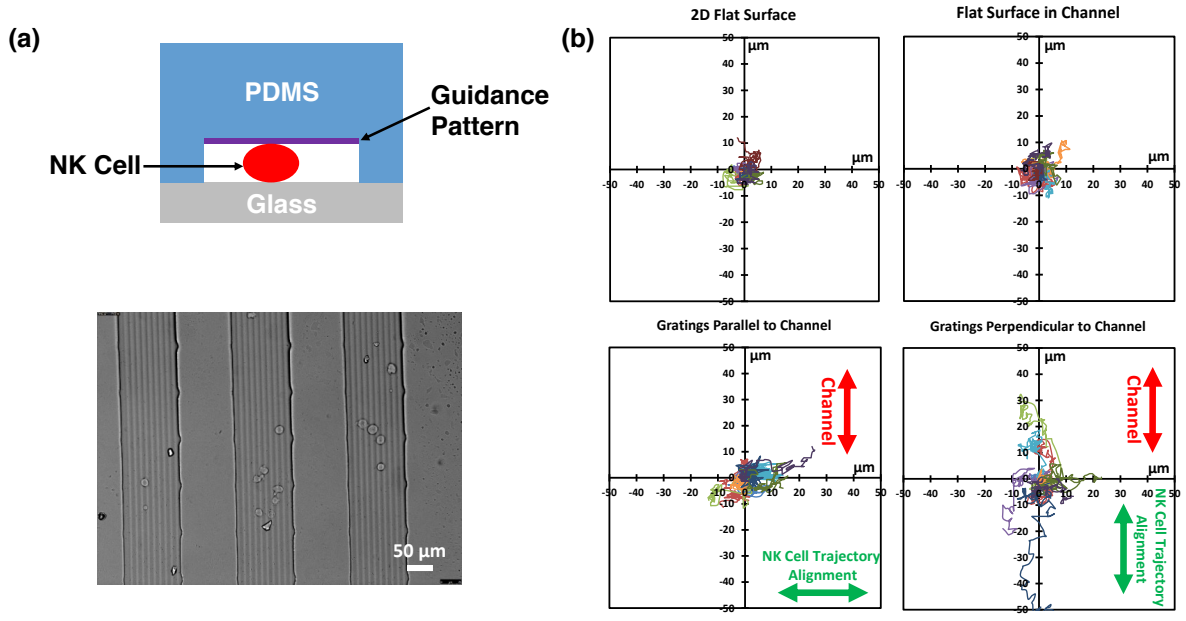

Figure 2: NK cell migration in 10 µm high microchannels: (a) Schematic of channel cross-section and top view micrograph. (b) Comparison of overlapped NK cell migration trajectories with different ceiling topographies inside channels.