Relating Unidirectional and Bidirectional Single Cell Migration with Oxygen Imaging

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Oxygen (O_2) plays a crucial role in various cellular processes, such as cellular respiration, energy production, and cell signaling pathways. Accurate measurement of O_2 consumption is essential for the understanding of cellular behavior and physiology. Detecting O_2 consumption is pivotal in optimizing conditions to maintain cellular activity and viability in various biological applications.

In this study, we developed a novel O_2 detection platform comprising a luminescent dye-based O_2 sensor and guiding structures. The objective was to explore the relationship between O_2 consumption of individual cells and their migration directions. We designed different surfaces featuring 6/4 μm wide ridge/trench and 4.5 μm deep gratings, and gratings patterned with 280 nm wide and 500 nm deep nanoholes and nanopillars on the grating ridges to direct and guide MC3T3-E1 cell movements. Figure 1(a-c) demonstrates that MC3T3-E1 cells exhibited the greatest elongation when bridging on the grating with nanopillars on the ridges, compared to cells on the gratings and gratings with nanoholes on the ridges. Nanopillars on the ridges promoted filopodia extension along the nanopillars sidewalls, facilitating cell exploration of larger areas. Figure 2 shows that during a 16 h period, 67% of cells altered their migration direction when traveling on the surfaces of gratings with nanopillars on the ridges, while only 29% of cells changed migration direction on surfaces of gratings with nanoholes on the ridges. The results showed that nanopillars on the grating ridges promoted MC3T3-E1 cells to migrate at a faster speed and change their migration directions during the movement.

To quantify the O_2 consumption of single MC3T3-E1 cells, we employed platinum octaethylporphyrin ketone (PtOEPK) which functions as a fluorescence dye. Figure 3 illustrates the changes in fluorescence intensity of the PtOEPK optical O_2 sensor for single MC3T3-E1 cells over 16 hours on different surfaces. The intensity of the PtOEPK dye exhibited greater variation when the cells changed their migration direction but remained relatively stable when the cells moved consistently in a single direction along the grating patterns. These results demonstrate that the PtOEPK O_2 sensor could detect intensity peaks corresponded to changes in cell shape and migration direction, accompanied by cytoskeleton reorganization, which is related to increased energy needed for changing direction and more O_2 consumption.

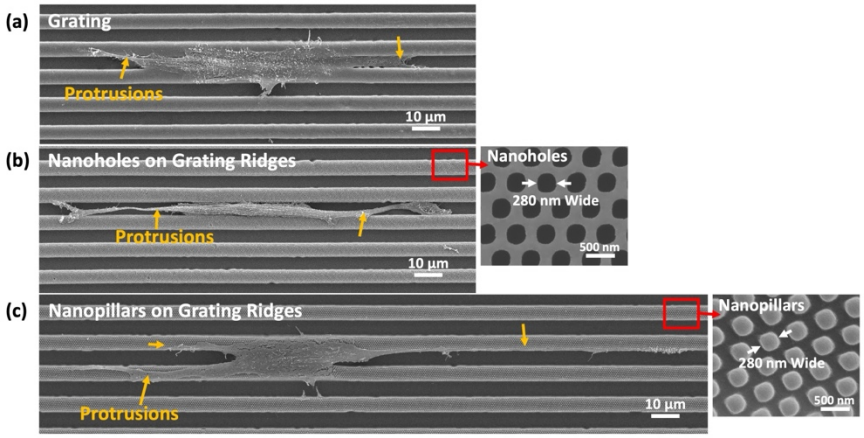

Figure 1: Scanning electron micrographs of MC3T3-E1 cells on different surfaces. (a) Grating with 6/4 µm wide ridge/trench and 4.5 µm deep*. (b) Nanoholes that were 280 nm wide and 500 nm deep on ridges of grating. (c) Nanopillars that were 280 nm wide and 500 nm deep on ridges of grating.*

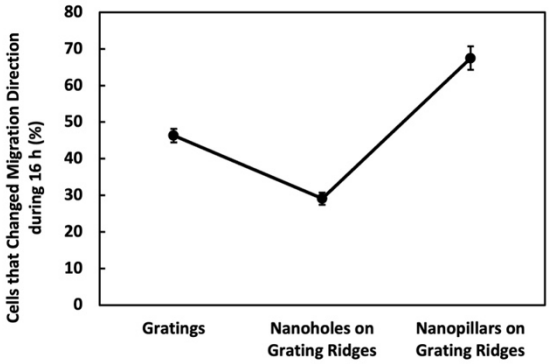

Figure 2: Percentage of MC3T3-E1 cells that changed migration direction on surfaces of gratings, gratings with nanoholes on ridges, and gratings with nanopillars on ridges.

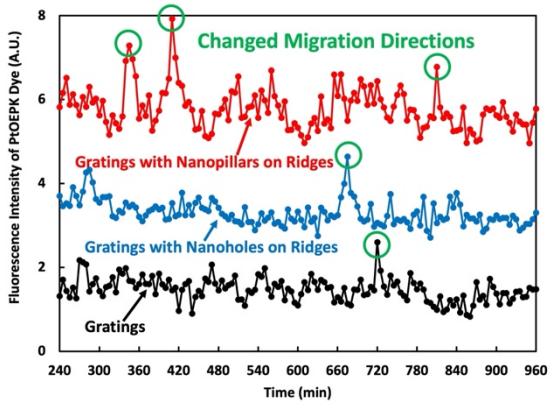

Figure 3: Changes of fluorescence intensity of platinum octaethylporphyrin ketone dye around MC3T3-E1 cell over time when they migrated on surfaces of gratings, gratings with nanoholes on ridges, and gratings with nanopillars on ridges.