Enhanced Unidirectional Cell Migration Persistence Induced by Asymmetrical Micropatterns with Nanostructures

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Unidirectional cell migration with enhanced persistence is critical for applications in tissue engineering and cancer research. Traditional micropattern platforms provide geometric cues for directional migration but often fail to sustain migration persistence over long distances. Recent efforts to combine micro- and nanoscale features have shown promise, as nanoscale topographies influence cytoskeletal alignment. However, achieving hierarchical guidance that effectively mimics natural environments remains challenging. In this study, we developed a novel platform integrating asymmetrical micropatterns with nanostructures, enabling enhanced persistent unidirectional cell migration.

Scanning electron micrographs revealed nanopillar arrays of 280 nm diameter (dia.), 535 nm period, 500 nm height incorporated into gratings with 5 μm width and spacing, and arrowhead micropatterns of 45º angle, 60 μm arm length, 50 μm width, 5 μm spacing between arms, and 50 μm spacing between rows as shown in Figs. 1a-e. Arrowheads without nanopillars served as controls to isolate the effect of nanoscale features as shown in Fig. 1f.

Arrowheads with nanopillars significantly enhanced migration persistence compared to other platforms. Cells on arrowheads with nanopillars exhibited increased displacement with lower total travel distance compared to other arrowhead patterns as shown in Figs. 2a-b. The straightness index of arrowheads with nanopillars indicated improved unidirectional guidance and directionality as shown in Fig. 2c. Furthermore, arrowheads with nanopillars guided more cells to migrate along the tips of arrowheads as shown in Fig. 2d. Immunofluorescence imaging of F-actin revealed that dot-like F-actin complexes less than 1 μm in dia. were found on both flat and nanopillar surfaces. These localized F-actin structures, essential for cell-substrate adhesion, cytoskeletal remodeling, and force transmission, displayed a more asymmetrical distribution on arrowheads with nanopillars compared to gratings with nanopillars as shown in Figs. 3a-b. Furthermore, the ratio of dot-like F-actin area to total cell area was higher on arrowheads with nanopillars as shown in Fig. 3c, indicating enhanced cytoskeletal reorganization that was related to directional guidance. These findings demonstrate the potential of combining asymmetrical patterns with nanoscale features for unidirectional cell migration control, which could be applied to accelerating wound healing and mimicking tissue interfaces for biomedical devices.

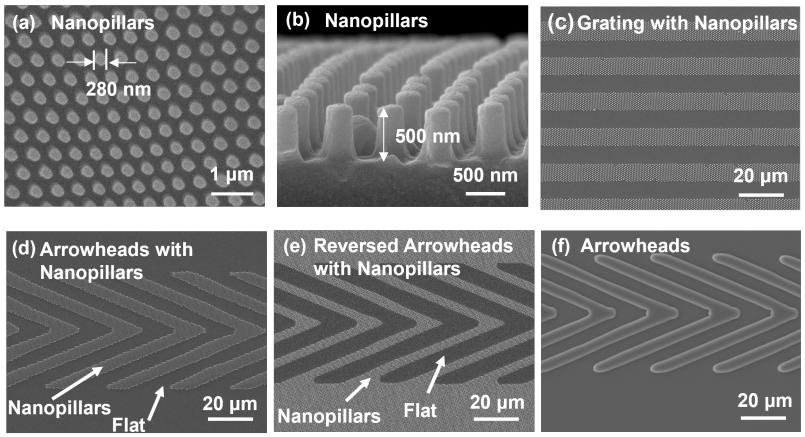

Figure 1: (a) Top view and (b) cross sectional view of nanopillars of 280 nm diameter, 535 nm period, and 500 nm height. (c) 5 μm width and 5 μm spacing grating with nanopillars. Arrowhead patterns with 45º angle, 60 μm arm length, 50 μm width, 5 μm spacing between arms, and 50 μm spacing between rows with (d) nanopillars in arrowheads, (e) nanopillars outside arrowheads, and (f) no nanopillars.

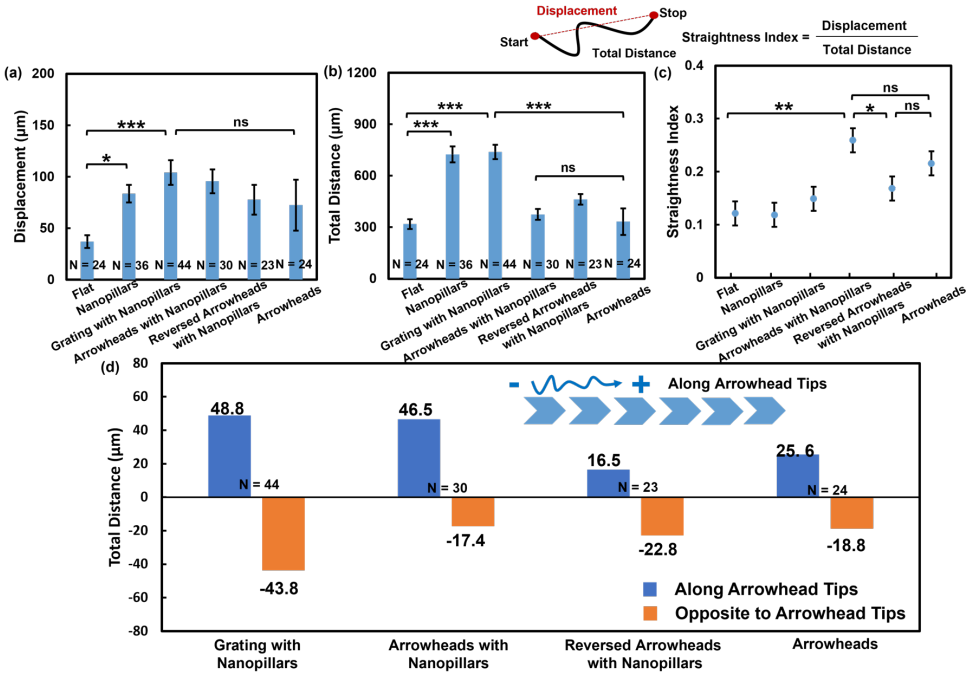

Figure 2: MC3T3 cell (a) displacement, (b) total distance traveled, and (c) straightness index on different platforms. (d) MC3T3 cell total distance traveled along and opposite to arrowhead tips.

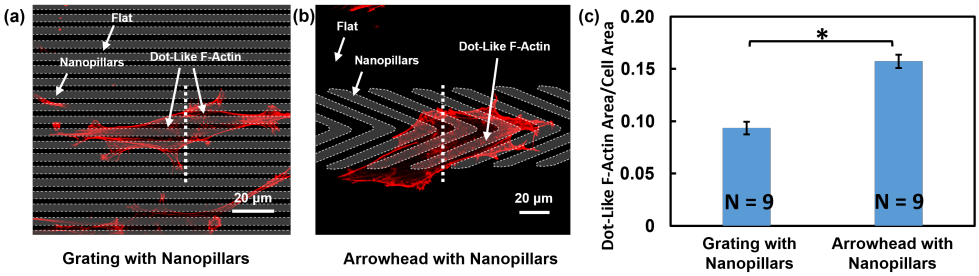

Figure 3: Immunofluorescence images of MC3T3 cells on (a) grating with nanopillars and (b) arrowheads with nanopillars. (c) Ratio between dot-like F-actin area and cell area of MC3T3 cells on grating with nanopillars and arrowheads with nanopillars.