Cell Motility and Persistence Controlled by Topography of Cell Culture Substrates

Wing Yin TONG[1], Qing Yuan TANG[2], Shi PENG[3], Stella W. PANG[2], and Yun Wah LAM[1]
Centre for Nanotechnology and Biomedical Microsystems, [1]Department of Biology and Chemistry, [2]Electronic Engineering, [3]Mechancial and Biomedical Engineering, City University of Hong Kong, Hong Kong

Statement of Purpose: Speed and directionality of cell movement are crucial to many physiological processes such as tissue development and wound healing[1, 2]. In order to develop strategies for modulating these processes, it is important to understand cell migration mechanisms[3]. Microfabricated patterns have widely been used to study cellular responses to physical cues. For example, the effects of patterned substrates on cell morphology, proliferation, and differentiation have been well documented. However, how substrate topography affects cell migration has not been systematically studied. In this study, we investigated the effect of topographical patterns on the motility and directionality of cells.

Methods: Topographical patterns that consisted of discontinuing parallel grooves of various dimensions were fabricated on a silicon wafer and transferred onto PDMS substrates. Flat surface and two grooved patterns, "5µm" and "2µm" were used (Fig. 1A). MC3TC-E1 cells, untreated or transfected with Actin-RFP, were seeded at 10^3 cells/cm^2 on the patterns, and were imaged on a confocal microscope. In some experiments, fixed cells were labeled with Phalloidin and Hoechst.

Results: Cells adopted a more elongated morphology on the 5µm, but not on 2µm or flat surfaces (Fig 1B). They moved randomly on flat surface, but are strongly guided by the 5µm pattern (Fig. 1C). Cells on the 5µm pattern also showed the significantly higher motility than on other surfaces (Fig. 1D).

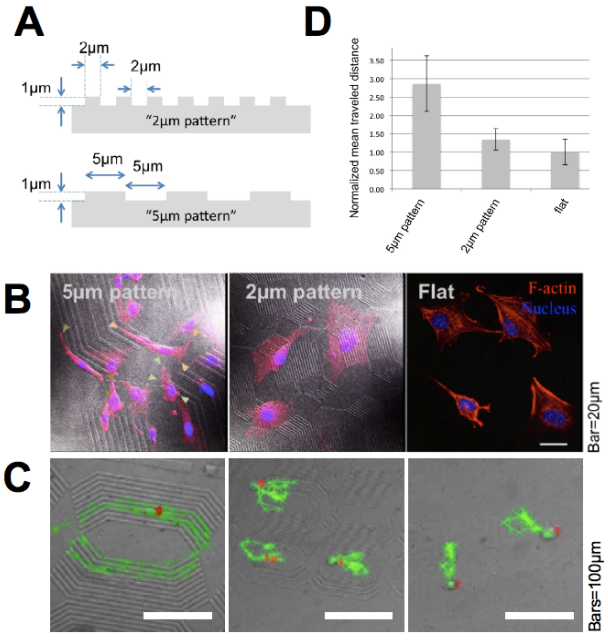

Figure 1. (A) Topographical pattern design. (B) Fixed cells labeled with Phalloidin and Hoechst. (C) Tracking of cell movements on various surfaces. (D) Mean distance covered by cells in 24 hours.

We then investigated the persistence of cell migration of these patterns (Fig. 2A). Fig 2B shows that on the 5µm pattern, but not the 2µm pattern, most cells changed migration directions at the end of the tracks ("bounced back") instead of continuing their existing path and leaving the groove ("Leave pattern"). This suggests that the transition of surface topography (from grooved to flat surface) can consistently induce changes in cell directions. To visualise this process in more detail, we imaged actin-RFP transfected MC3T3-E1 cells at these transition sites. We observed that at the end of the groove, cytoplasmic projections extended and retracted alternatively in both directions (Fig. 2C). This oscillation lasted for about 60 min, before the projection towards the end of the groove retracted and the cell migrated back into the track. This implies that actin polymerization at the transition was not stable, with the quick oscillation of leading edges at the opposite ends of the cell.

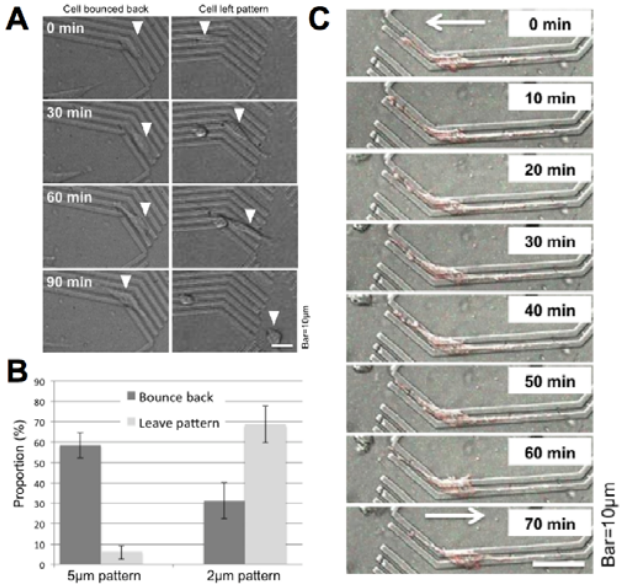

Figure 2. (A) Two decisions of cells reaching the end of the grooved"5µm" pattern. Arrows indicate the positions of the cell body (B) Preference of the two decisions. (C) Actin-RFP expressing cells bounced back at the end of "5µm" pattern. Arrow indicates the directions of migration.

Conclusions: We have demonstrated, for the first time, that topographical patterns of cell culture substrates can reproducibly control the speed and direction of MC3T3-E1 movement. The alteration of actin polymerization is likely involved. This pattern provides a valuable experimental model for the studies of cytoskeleton dynamics and cell migration in the future.

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