Effects of Dimensions, Topography, and Layers for Nasopharyngeal Carcinoma Cell Migration on Three-Dimensional Scaffold Platform

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Cross-linked collagen fibers with embedded micro and nanoscale features in extracellular matrix (ECM) could affect cell migration behaviour significantly. Previous studies have demonstrated the guidance effects of collagen fibers and micro or nanoscale topographies separately without showing the combined influence. Therefore, studying the cell migration behaviour on multiple layer scaffold platforms with embedded topography could lead to a better understanding of cell migration on ECM *in vivo*.

A three-layer scaffold platform in polydimethylsiloxane (PDMS) with grating topography on the middle layer ridges was fabricated by the reversal nanoimprint lithography. Similar three-layer scaffold platform without grating topography was also built for comparative study.

Figures 1 (a) and (b) show the micrographs of the three-layer scaffold platforms with and without the embedded gratings on the middle layer. The top and middle layers had 40/10 μm wide ridge/trench and the bottom layer had 18/18 μm wide ridge/trench. Grating on the middle layer had 2 μm wide width/spacing, 1 μm depth, and offset by 30^{o} relative to the trenches on the top layer as shown in Fig. 1(a). Nasopharyngeal carcinoma (NPC43) cells were seeded on the platforms for 7 hr and placed under a confocal microscope for time-lapse imaging.

About 70% of NPC43 cells could squeeze into the 10 μm wide top layer trenches with and without gratings on the middle layer as shown in Fig. 2 (a). Figure 2 (b) shows that NPC43 cells migrated slower with embedded gratings on the middle layer. It suggested that the gratings at offset angle to the top layer trenches could influence the cell migration direction and reduce the motility of cells. The migration trajectories of NPC43 cells with and without gratings on the middle layer were shown in Figs. 3 (a) and (b). NPC43 cells were guided by the top layer trench orientation with and without gratings on the middle layer, but the presence of the embedded gratings weakened the top layer trench guidance.

The results developed in this work show that NPC43 cell migration was affected by the combined guidance effect of the trench size, the embedded topography, and the migration through multiple layers. We will further investigate the effects of offset angles between different layers and the number of layers in the scaffold platform and how the scaffold could be designed to control the migration behavior of NPC43 cells. Potentially, the high precision 3D platform could be used to improve drug delivery efficiency and facilitate the treatment of NPC in the future.

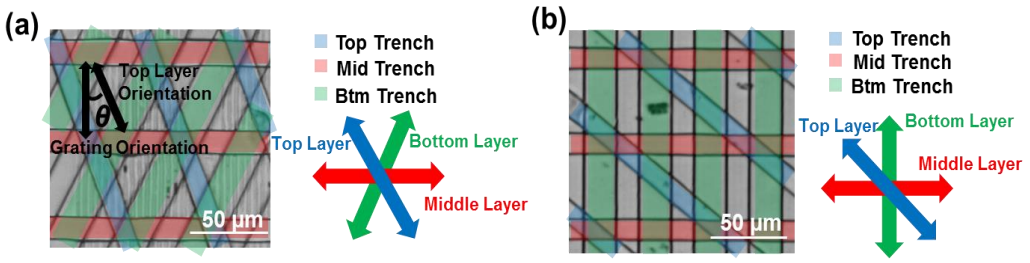

Figure 1: Micrographs of three-layer scaffold platforms (a) with and (b) without embedded gratings on middle layer. Top layer formed θ of 30^{o} with gratings on middle layer.

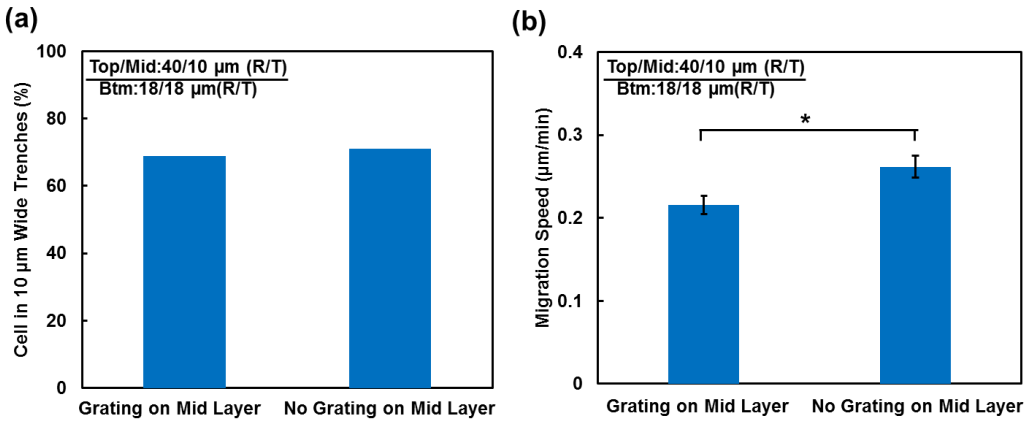

Figure 2: (a) Probability of NPC43 cells squeezing in 10 μm wide trenches on top layer and (b) migration speed of NPC43 cells in 10 μm wide top layer trenches on three-layer scaffold platform with and without gratings on middle layer (one-way ANOVA test, *p <0.05, N>15).

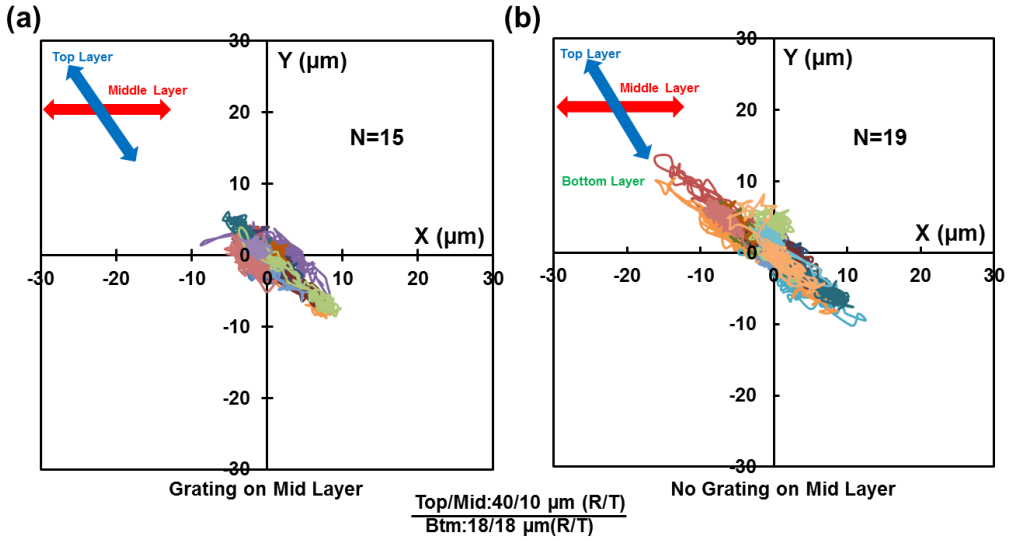

Figure 3: NPC43 cell migration trajectories on three-layer scaffold (a) with and (b) without grating on middle layer.