Nasopharyngeal Carcinoma Cell Migration in Three-Dimensional Platform

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Nasopharyngeal carcinoma (NPC) cells exist in obscure anatomical location, which make the discovery of NPC therapeutics difficult due to the lack of representative, physiological, and cost-effective model systems. Studying the NPC cell migration behavior in a three-dimensional (3D), multiple layer platform is the first step towards building a better understanding of the NPC.

In this work, reversal nanoimprint lithography was used to stack multiple layers of polydimethylsiloxane (PDMS) structures with designed ridges and trenches to mimic an extracellular matrix (ECM) for NPC cells to be seeded. This engineered platform can be formed with precise dimensions, layouts, and material properties, which will be useful to study the cell migration and interaction characteristics in an ECM.

Figure1 shows the process flow for the 3D scaffold platform with two layers. The bottom layer was obtained by replicating patterns in PDMS using a SU8 mold. The top layer was formed by imprinting PDMS using a Si mold, and stacked on top of the bottom layer after an oxygen plasma treatment. Additional layers can be added by repeating the steps shown in Fig. 1(b) and (c). The density and size of the interconnecting pores in the 3D scaffold platform can be designed and generated with high precision. All the layers were 15 µm thick.

Three types of platforms were used for comparative study of cell migration. Immortalized nasopharyngeal epithelial cells (NP460) were seeded on the platforms for 7 hr and time-lapse images were captured using a confocal microscope. Figure 2 shows cell morphologies on the three platforms during migration. On both the one-layer and two-layer platforms with 40/10 µm wide ridge/trench, cells elongated along the grating, while on the two-layer platform with 18/18 µm wide ridge/trench, cells tended to spread out more along the interface between the two layers.

Figure 3 shows the trajectories of the cell movements on different platforms. As shown in Fig. 3(a), the cells were guided along the grating. On the two-layer platform, most of the cells were found to migrate at the interface between the two layers. As some of the cells were in contact with gratings along the two orientations that were perpendicular to one another, 67% of the cells were guided within the 40 µm × 18 µm unit as shown in Fig. 3(b) and 77% of the cells would migrate within the 18 µm × 18 µm unit as shown in Fig. 3(c). This suggests that by decreasing the unit area from 40 µm × 18 µm to 18 µm × 18 µm for the two layer platforms, more cells would be confined within the unit area formed by the top and bottom layers. By studying NPC cell migration in a 3D microenvironment, the effects of the ECM characteristics on cell movement and interactions could be obtained, which could potentially lead to NPC treatment.

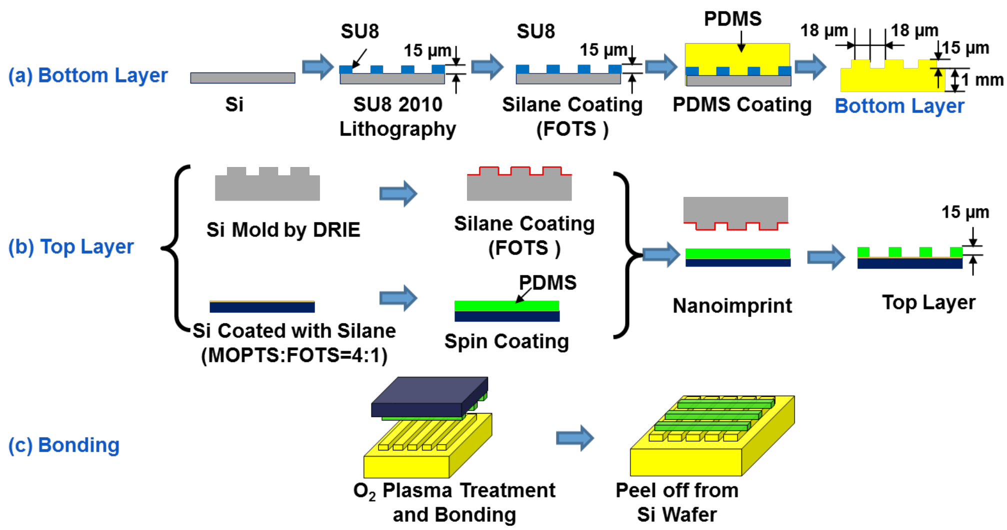

Figure 1: Two-layer platform process flow: (a) Bottom PDMS layer. (b) Top layer fabricated using nanoimprint. (c) Bonding two layers after O_2 plasma.

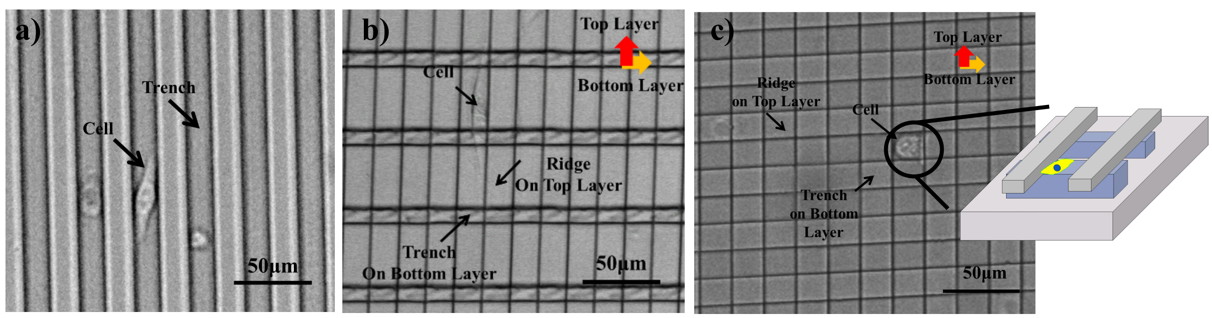

Figure 2: Cell Morphology: NPC cells on a) one layer grating (18/18 µm wide ridge/trench) platform, and two-layer scaffolds: b) 18/18 µm wide ridge/trench for top layer and 40/10 µm wide ridge/trench for bottom layer, and c) 18/18 µm wide ridge/trench for top and bottom layers. Insert demonstrates 3D view of cell on scaffold.

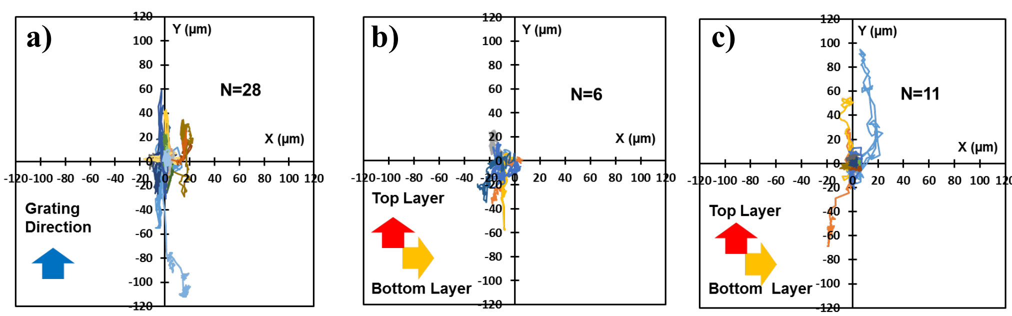

Figure 3: Cell Trajectory: Tracking of NPC cell movement on a) one layer grating (18/18 µm wide ridge/trench) platform, and two-layer scaffolds: b) 18/18 µm wide ridge/trench for top layer and 40/10 µm wide ridge/trench for bottom layer, and c) 18/18 µm wide ridge/trench for top and bottom layers.