Interactions of Nasopharyngeal Carcinoma and Epithelial Cells in Microwell Array

X. Hong, Y. H. Xu, and S. W. Pang
Department of Electrical Engineering
Center for Biosystems, Neuroscience, and Nanotechnology
City University of Hong Kong, Kowloon, Hong Kong, China
Email: pang@cityu.edu.hk

Cell migration is a crucial process for tumor formation and cancer metastasis. It is regulated by various factors, including the topography of extracellular matrix and the presence of neighbor cells. Though some previous work studied how physical topography affected cell behaviors, they mainly focused on individual cell, ignoring the influence of surrounding cells.

In this study, microwells with gratings on the bottom were designed to systematically study how the physical confinements, local topography changes, and cell-cell contacts affect cell migration and tumor formation. Various microwell structures were fabricated on silicon molds followed by the replication to form polydimethylsiloxane (PDMS) platforms. Nasopharyngeal carcinoma (NPC43) and immortalized nasopharyngeal epithelial (NP460) cells were then seeded on PDMS platforms. Time-lapse imaging was utilized to capture cell movements in microwells over 16 h.

Figure 1 shows the morphologies of NPC43 and NP460 cells seeded in microwells with different sizes and morphologies in bottom. NPC43 cells formed clusters after cell-cell contacts while NP460 cells tended to move individually. Both types of cells became more elongated on the bottom surfaces with gratings. The migration speed of NPC43 cells did not change with cell-cell contacts while NP460 cells had significantly increased speed with cell-cell contacts, as shown in Figs. 2 (a) and (b). Different levels of confinement and grating structure did not affect the migration speed of NPC43 and NP460 cells.

Figure 3 shows that when two kinds of cells were co-cultured, NPC43 cells formed clusters in the middle of the microwells and pushed NP460 cells towards the sidewalls. This result suggested that the NPC43 and NP460 cells exhibited heterotypic contact inhibition of locomotion as they occupied certain surfaces for their own migration, which mimicked the initial steps of tumor formation in a confined microenvironment. These findings revealed that cell-cell contacts in 3D platforms could have significant implications on NPC cell migration and initial tumor formation, which could provide insight for the NPC progression and dissemination.

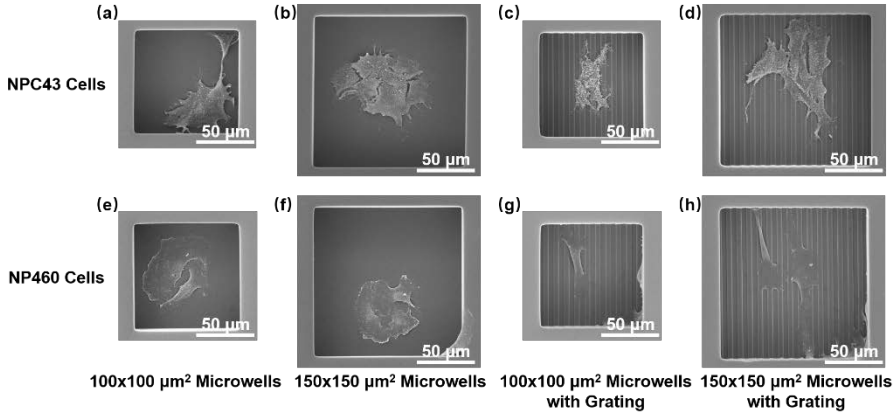

Figure 1. Micrographs of (a-d) NPC43 and (g-h) NP460 cells seeded separately in 100x100 μm^2 and 150x150 μm^2 microwell arrays without and with gratings in bottom.

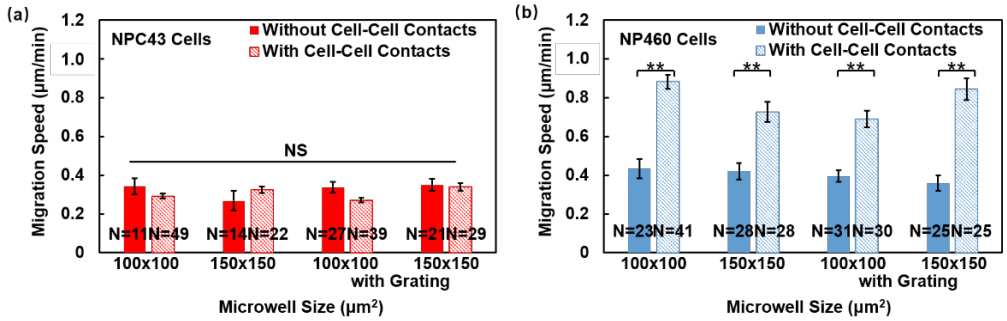

Figure 2. Effects of cell-cell contact, microwell size, and grating structure on migration speed of (a) NPC43 and (b) NP460 cells. One way ANOVA with Tukey's post hoc test, **p <0.01, NS – not significant.

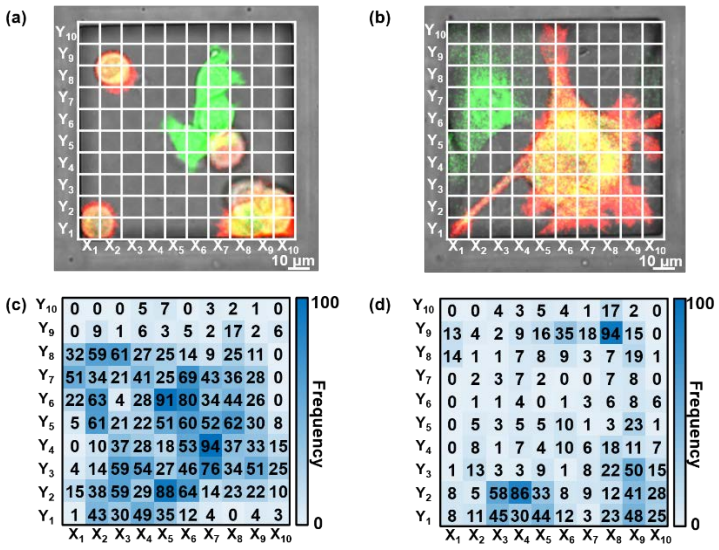

Figure 3. Distribution of NPC43 (red) and NP460 (green) cells in 100x100 μm^2 microwells. Cells distribution at (a) time = 0 h and (b) time = 16 h. 100x100 μm^2 microwell was separated into 100 regions. Distribution heatmap of (c) NPC43 and (d) NP460 cells. Numbers showed frequencies of cells positioned in each region during 16 h time-lapse imaging.