# Tumor Cell Traversing Behavior in Three-Dimensional Platform with Porous Topography

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Tumor cells could invade tissues by circulating through blood vessels and metastasize to other anatomical sites. In this work, a three-dimensional (3D) platform mimicking the extracellular matrix (ECM) topography, endothelia cells membrane, and blood vessels of the *in-vivo* microenvironment for nasopharyngeal carcinoma (NPC) cells were developed and fabricated. The three-layer platform consisted of the guiding grating, porous membrane, and trenches below. In order to reveal the effects of the blood vessel microenvironment on NPC cell migration, the topography of the porous membrane and the vessel-like trench depth were systematically varied and the cell traversing behavior through the porous membrane was investigated.

Figures 1 (a) and (b) show the 3D biomimetic platform with circular (left) and elliptical (right) pores. The guiding gratings on the top layer were 2/2 μm wide ridge/trench and 1 μm deep. The circular pores were 10 μm in diameter and the elliptical pores had the short and long axis lengths of 10 and 25 μm, respectively. The ridges and trenches on the bottom layer were 70/30 μm wide. The pores and bottom trenches were both 15 μm deep. Tumor cell line NPC43 was used in the cell seeding and time-lapse imaging was captured every 5 min for 15 hr. The probability of cell traversing through porous membrane was higher for the circular pores than the elliptical pores as shown in Fig. 1 (c).

Based on the time-lapse images, NPC43 cells tended to fully occupy the entire volume of the circular pores as shown in Fig. 1 (a) and they only attached to the part of the sidewalls of the elliptical pores as shown in Fig. 1 (b). Migration trajectories on the two platforms as shown in Fig. 2 also indicated that more cells could traverse through the circular pores compared to the elliptical pores. For cells that did not traverse through the pores, no cell guidance effect was found on the membrane with circular pores compared to having guidance effect along the long axis orientation on the membrane with elliptical pores.

Figure 3 shows the trenches with 15 μm depth provided the highest probability for cells to traverse through the porous membrane as well as the shortest time interval for cells starting to traverse. This could be related to the cell size, which is about 15 μm. Therefore, shallower trenches could squeeze the cells and deeper trenches could make it difficult for the cells to sense and contact the bottom surface of the trenches.

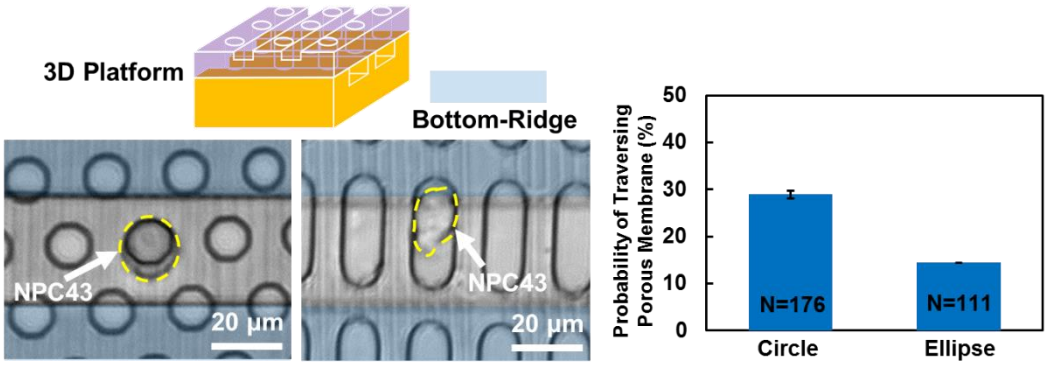


Figure 1: 3D platform with porous topography: a) circle (10 μm diameter) and b) ellipse (10 μm short axis and 15 μm long axis). Top layer: grating width and space - 2 μm, depth - 1 μm; middle layer: porous membrane depth - 15 μm; bottom layer: ridge - 70 μm, trench - 30 μm, and depth - 15 μm. c) Probability of NPC43 cells traversing through membrane.

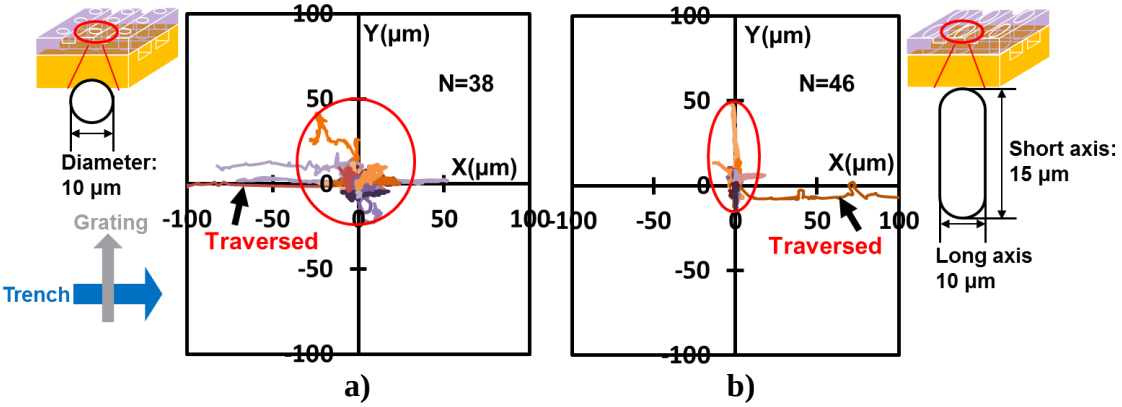


Figure 2: Cell migration trajectories of NPC43 cells on membrane with a) circular and b) elliptical pores. (Red circles indicate trajectory ranges of cells without traversing through pores)

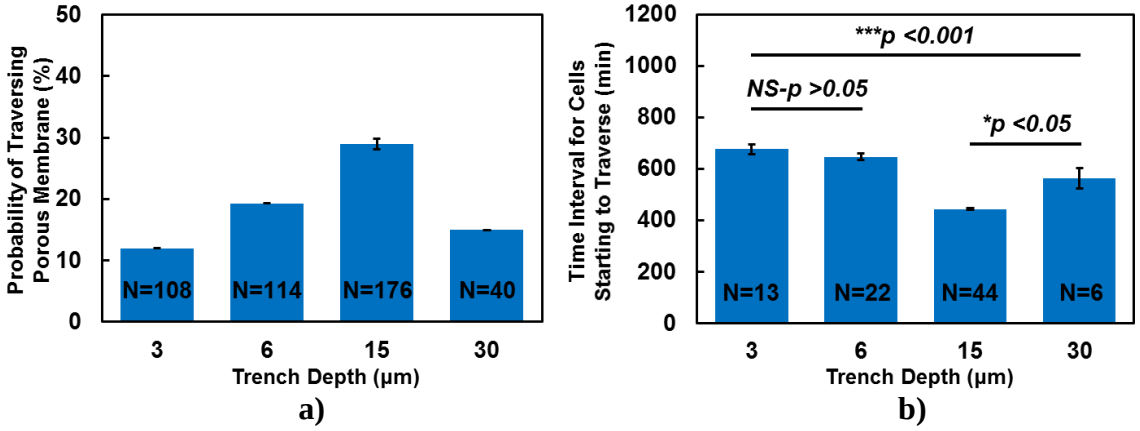


Figure 3: Effects of trench depth on (a) probability of traversing through porous membrane and (b) time interval for cells starting to traverse.