Rapid fabrication of thermoplastic nanoforest substrates for high efficient capture of cancer cells

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In recent years, the interaction between cells and the nanotopography of materials has been intensively studied, and incorporating nanostructures into microchips has been a useful strategy for cell detection. Circulating tumor cells (CTCs) are rare number cells (a few to hundreds per 10^9 hematologic cells) disseminating into blood from primary cancer site of cancer patients, and remain a great challenge for cell detection. Researchers have revealed that nanostructured surfaces modified with specific biomolecules could recognize and capture cancer cells with high efficiency and specificity. However, these nanostructured substrates required complicated fabrication processes associated with high equipment and material costs. In this study, we report a one-step simple and low-cost fabrication process to form nanoforest structures on thermoplastic substrates. The nanoforest structures are dense and high-aspect-ratio nanopillars, which exhibit superior capture properties for rare cells due to the 3D hierarchical nanostructures.

The fabrication processes of the silicon nanoforest mold and the thermoplastic nanoforest substrate were illustrated in Figure 1. The high-aspect-ratio nanopillars structures were formed by depositing nanoparticles on the silicon wafer and transferring the patterns by deep reactive ion etching (DRIE). Then a flexible polymer working stamp mold (Solvay MD700 with 2% Darocur 1173 photoinitiator) was replica cast from the silicon nanoforest mold by UV-curing the liquid prepolymer solution. Thermoplastics such as Cyclo Olefin Polymers (COP) were chosen as the device materials, because they were mechanically robust, chemically inert, optically transparent and suitable for industrial-level production. The polymer working stamp material was then repeatedly used to emboss the nanoforest profile directly into COP (Zeonor^{TM}) wafers using a nanoimprint machine. The prepared nanoforest substrates were modified by BSA and cell-capture DNA aptamer that was selected against EpCAM. MCF-7 cells (a breast cancer cell line) were taken as EpCAM-positive cancer cell model for cell capture. The cell capture effect of COP nanoforest substrate was further investigated. Figure 2 shows the SEM images of the thermoplastic nanoforest substrate and the cancer cell morphology captured on the nanostructures.

In summary, we have demonstrated a rapid fabrication method of thermoplastic substrates with nanoforest patterns. The synergistic effect of interface molecules and topographic interaction cooperatively contribute to excellent capture specificity and sensitivity of target cells. The reported device provides a simple

and low-cost platform for rare cancer cell capture, which is promising for cancer diagnosis and monitoring treatment response.

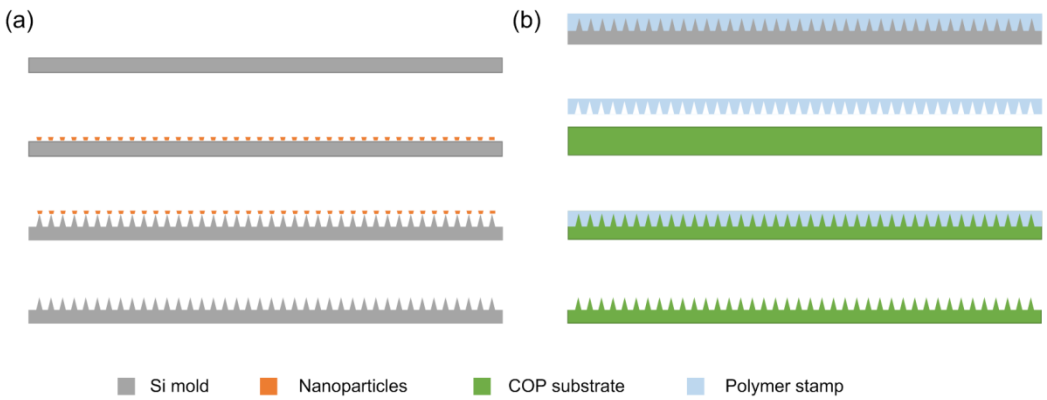

Figure 1: (a) Schematic fabrication process of the silicon nanoforest mold. The nanoparticles were deposited on the Si substrates, and DRIE was performed to etch the Si mold. (b) Schematic fabrication process of the thermoplastic nanoforest substrate. A flexible polymer stamp was used to replicate the nanoforest profile and emboss the patterns on the thermoplastic substrate.

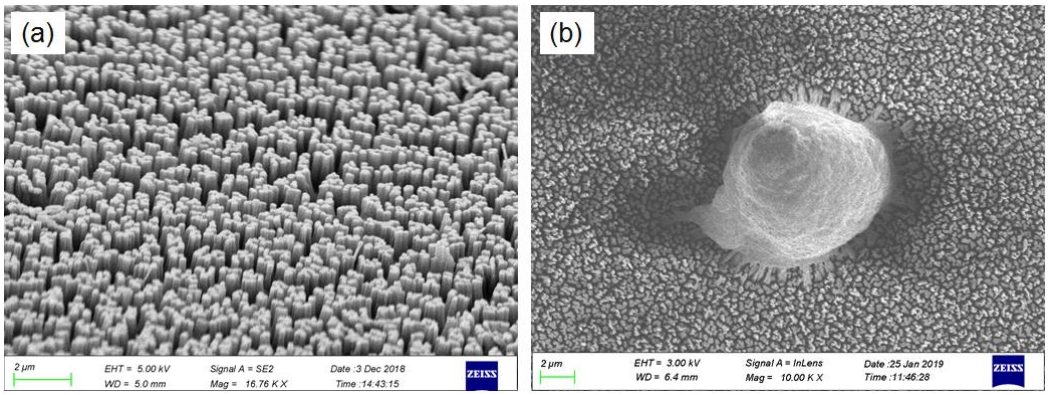

Figure 2: (a) SEM image of nanoforest structures on cyclo olefin polymer. The nanopillars were 50 nm in width and 1 µm in height. (b) SEM image of cancer cell morphology captured on the thermoplastic nanoforest substrates.