Injection-Compression Molding of Nanostructures for Three-Dimensional Cell-Culturing

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When cells are connected each other and form spheroids, the condition in organism is expected to mimic *in vivo* environment. However, the cells are separately stuck on general smooth-surface plates and any surface treatment cannot realize keeping both the formation of spheroids and their connection on the substrate. Therefore, so-called three-dimensional cell culturing using patterned surface has been increasingly expected in new drug researches and development.[1,2]

On the other hand, injection molding is a high-throughput thermal reproducing method for nonflat replica products such as various plastic cases, optical lens or cell culturing dishes. In particular, injection compression molding (ICM) is an expecting candidate of thermal nanoimprinting for bulk surface. Because ICM has a high-pressure compression immediately after injection of thermoplastic polymers, it is well-known that optical disks such as Digital Versatile Disks (DVDs) and Blu-ray disks (BDs) are fabricated by ICM. Furthermore, our group has investigated that higher-aspect ratio nanostructures can be replicated with higher temperature molds.[3] In this study, we fabricated cell-culturing dishes by ICM and investigated the homogeneity of the spheroid sizes.

Figure 1 shows the results of replication of cycloolefin.polymer (COP) measured by atomic force microscopy (AFM). The pattern width and depth of mold are 400 and 670 nm, respectively. With 60, 80-100, 110-120 ˚C, replicated depths were only 20 nm, 220-260 nm, 670 nm, respectively. Note that the demolding was carried out after the replicas were cooled to 85 ˚C in the ICM with mold heating more than 90 ˚C. The replication degrees were increased when the mold temperature was more than the glass transition temperature. Figure2(a) shows a photo of replica with 120 ˚C mold temperature.

Cell culturing were carried out with breast adenocarcinoma cells (MCF-7, RCB1904) on dishes replicated with 80, 120 ˚C. In both dishes with 80 and 120 ˚C, spheroids with an average size of approximately 80 μm were cultured. However, those in 120 ˚C dish had smaller dispersion than those on 80 ˚C. Figure 2(b) is a scanning electron microscope (SEM) image of typical spheroid cultured on 120 ˚C dish.

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[1] Y. Matsuda *et al.*, *Med. Mol. Morphol.*, 43 (2010) 211. [2] Y. Yoshii *et al.*, *Biomaterials*, 32 (2011) 6052.
[3] K. Nagato, T. Hamaguchi, M. Nakao, *J. Vac. Sci. Technol. B* 29 (2011) 06FG10-1-4.

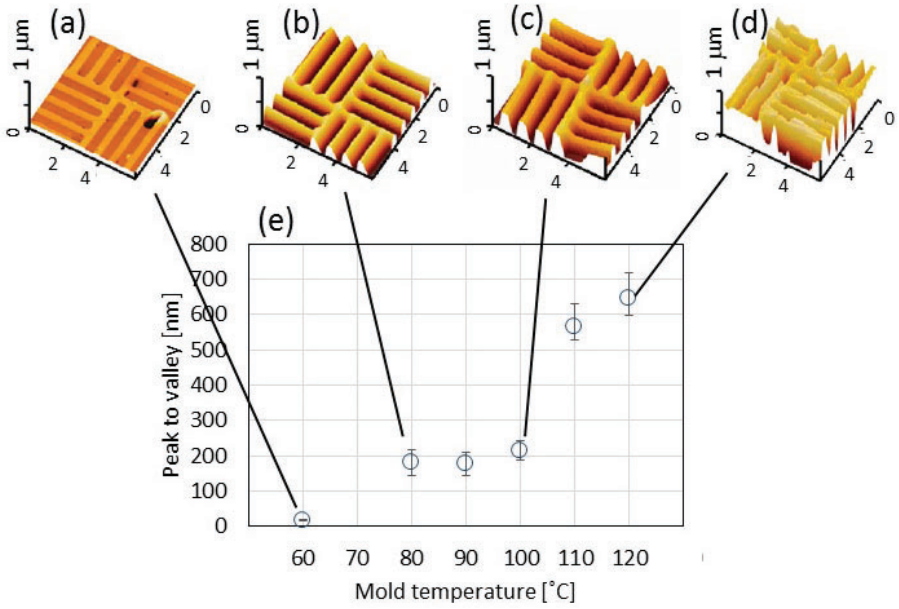

Figure1 AFM profiles of injection-compression-molded nanostructures with mold temperatures of (a)60, (b)80, (c)100, (d)120 ˚C, and peak-to-valleys of the nanostructures as a function of mold temperature.

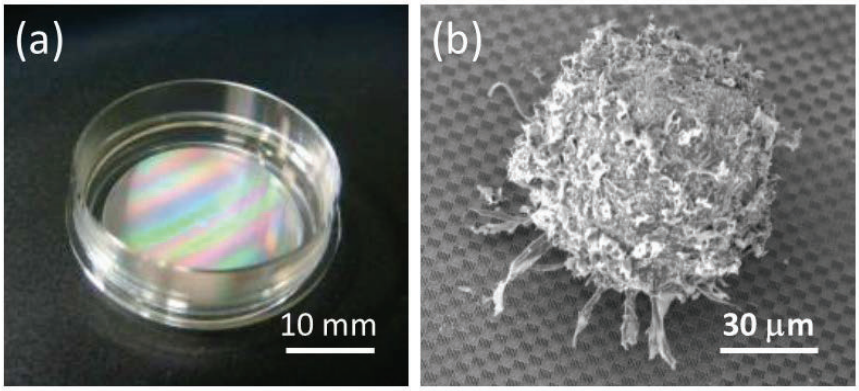

Figure 2 (a) Photo of a molded dish with nanostructures and (b) SEM image of a cultured spheroid (mold temperature for ICM: 120 ˚C).