Shape-memory Surfaces facilitate Time-dependent Observation of Cell Functions

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Statement of Purpose: In general, determination of cellular phenotypes such as growth, proliferation, differentiation or apoptosis is considered to be governed by a complex set of extrinsic cues in collaboration with intrinsic gene regulatory machinery. The extrinsic factors are mainly classified into the following three factors; i) biochemical, ii) physicochemical and iii) mechano-structural stimulus. Among them, an increasing number of studies have shown that the mechano-structural stimuli such as elasticity, topography and mechanical force alter growth and differentiation of a number of tissues and cells. From these perspectives, we propose a novel technique that explores dynamic cell behavior in response to surface changes in nanotopology using shape-memory crosslinked poly(ε-caprolactone) (PCL) materials that actuate on demand under biological conditions. Time-dependent cell behavior on shape-memory PCL was observed by inducing a surface nano geometry transition (Fig.1).

Methods: Shape-memory PCL films were prepared by cross-linking tetra-branched PCL with acrylate end-groups in the presence of linear PCL telechelic diacrylates. Permanent surface patterns were generated by crosslinking the PCL macromonomers in a mold. Temporary patterns were later embossed into the crosslinked PCLs above the Tm and memorized by cooling below the melting temperature (T_m). Shape-memory transition from temporary to original permanent pattern was triggered by heating again above the T_m. For cell alignment assay, NIH 3T3 fibroblasts were seeded on the temporal grooved surface and cultured at 32°C for 48 h. The cells were then subjected to a 37°C heat treatment for 2 h. The cell morphology was continuously monitored and imaged using a microscope.

Results: We first modulated the T_m of PCL materials by controlling branched arm numbers and molecular weight of crosslinked PCL. The sample with 50/50 wt% mixing ratio had a T_m around 33°C. The strain fixity rate and the strain recovery rate were approximately 99% and 90%, respectively. To investigate the role of dynamic and reversible surface nanopatterns on cell proliferation, specifically cell alignment on the PCL films before and after a topographic transition, NIH 3T3 fibroblasts were seeded on fibronectin-coated PCL films with a temporary grooved topography and cultured at 32 °C for 6 h. Cells aligned parallel to the grooves and migrated and grew horizontally to the temporary surface grooves with cultivation time (Fig.2). Although cell alignment was still observed just after the surface transition, the random cell migration ensued with time and reorientated horizontally to the original permanent grooves (parpendicular to the temporary grooves). Thus, the shape-memory PCL surfaces demonstrated the important role of surface nanotopology in time-dependent cytoskeleton remodeling under biological relevant conditions.

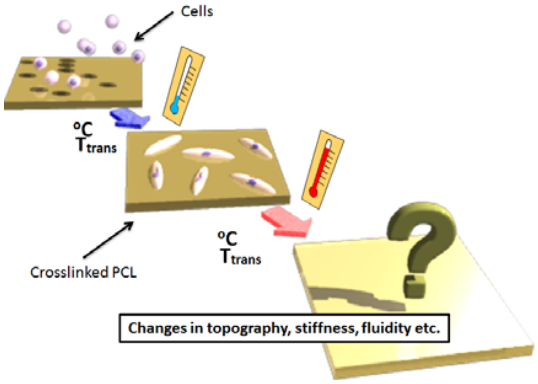

Figure 1. Schematic illustration of dynamic cell response on shape-memory crosslinked PCL surface.

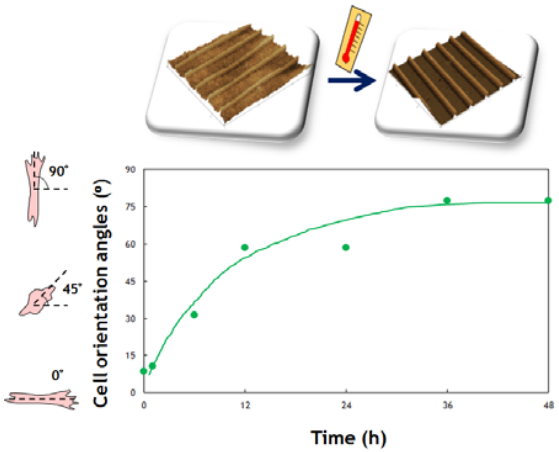

Figure 2. Time-dependent changes in cell orientation angles on the PCL film after shape-memory activation.

Conclusions: A novel approach has been developed to observe time-dependent changes in cell alignment using shape-memory surfaces. The temporary surface patterns could be easily programmed on the films and triggered to transition quickly to the permanent surface patterns. The versatility and biologically friendly nature of these PCL-based shape-memory surfaces could potentially enable the realization of novel and diverse applications, especially biomaterial development and basic cell biology.

References: Ebara M. et al., Adv Mater. 2012; 24: 273.