

Abstract



## Development of Gelatin-Based Flexible Three-Dimensional Capillary Pattern Microfabrication Technology for Analysis of Collective Cell Migration <sup>+</sup>

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Abstract: Collective cell migration is thought to be a dynamic and interactive behavior of cell cohorts that is essential for diverse physiological developments in living organisms. Recent studies revealed that the topographical properties of the environment regulate the migration modes of cell cohorts, such as diffusion versus contraction relaxation transport and the appearance of vortices in larger available space. However, conventional in vitro assays fail to observe changes in cell behavior in response to the structural changes. In this study, we developed a method to fabricate the flexible three-dimensional structures of capillary microtunnels to examine the behavior of vascular endothelial cells (ECs). Microtunnels with altering diameters were formed inside gelatin gel through spot heating a portion of gelatin by irradiating the um-sized absorption at the tip of the microneedle with a focused permeable 1064 nm infrared laser. The ECs moved and spread two-dimensionally on the inner surface of the capillary microtunnels as a monolayer instead of filling the capillary. In contrast to the 3D straight topographical constraint, which exhibited width-dependent migration velocity, the leading ECs altered its migration velocity according to the change in the supply of cells behind the leading ECs, caused by their progression through the diameter-altering structure. Our findings provide insights into the collective migration modes inside 3D confinement structures, including their fluid-like behavior and the conservation of cell numbers.

**Keywords:** three-dimensional culturing environment; collective cell migration; microfabrication technology; vascular endothelial cells; fluid-like behavior

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