Circumferential Alignment of Vascular Smooth Muscle Cells in a Cylindrical Microchannel

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We report the circumferential alignment of human aortic smooth muscle cells (HASMCs) in an orthogonally micropatterned circular microfluidic channel to form an in vivo-like smooth muscle cell layer. To realize a biomimetic smooth muscle cell layer which is aligned perpendicular to the axis of blood vessel, we first fabricated a half-circular polydimethylsiloxane (PDMS) microchannel by soft lithography using a convex PDMS mold. The orthogonally micro wrinkle patterns were generated inside the half-circular microchannel by stretching-releasing operation under UV irradiation. Upon UV treatment with uniaxial 40% stretch of a PDMS substrate and releasing process, the microwrinkle patterns perpendicular to the axial direction of the circular microchannel were generated, which could guide the circumferential alignment of HASMCs successfully during cultivation. The analysis of orientation angle, shape index, and contractile protein marker expression indicates that the cultured HASMCs revealed the in vivo-like cell phenotype. Finally, we produced circular microchannels by bonding two half-circular microchannels, and cultured the HASMCs circumferentially with high alignment and viability for 5 days. These results are the first demonstration for constructing an in vivo-like 3D smooth muscle cell layer in the circular microfluidic channel which can provide novel bioassay platforms for in-depth study of HASMC biology and vascular function.

Keywords: Circular microchannel, Circumferential alignment, Smooth muscle cell, Microwrinkle, Contractile protein marker

Constructing a Three-Dimensional Endothelial Cell Layer in a Circular PDMS Microchannel

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We described a simple and efficient fabrication method for generating microfluidic channels with a circular-cross sectional geometry by exploiting the reflow phenomenon of a thick positive photoresist. Initial rectangular shaped positive photoresist micropatterns on a silicon wafer, which were fabricated by a conventional photolithography process, were converted into a half-circular shape by tuning the temperature to around 105°C. Through optimization of the reflow conditions, we could obtain a perfect circular micro-pattern of the positive photore sist, and control the diameter in a range from 100 to 400 μm. The resultant convex half-circular photoresist was used as a template for fabricating a concave polydimethylsiloxane (PDMS) through a replica molding process, and a circular PDMS microchannel was produced by bonding two half-circular PDMS layers. A variety of channel dimensions and patterns can be easily prepared, including straight, S-curve, X-, Y-, and T-shapes to mimic an in vivo vascular network. To inform an endothelial cell layer, we cultured primary human umbilical vein endothelial cells (HUVECs) inside circular PDMS microchannels, and demonstrated successful cell adhesion, proliferation, and alignment along the channel.

Keywords: Polydimethylsiloxane, Circular microchannels, Cell culture, Reflow of photoresist, Human umbilical vein endothelial cells