Microfluidic enabled creation of vascularized 3D miniaturized tissue

Xiaochuan Yang*, Joung-hyun Lee**, Yinfeng Wang**, Woo Young Lee **, and Hongjun Wang*.
Chemistry, Chemical Biology and Biomedical Engineering Dept. *
Chemical Engineering and Material Science Dept. **
Stevens Institute of Technology, Hoboken, NJ, 07030

Statement of Purpose: Creation of miniaturized 3D tissue has many potential implications including as an in vitro model for drug screening, biomaterials evaluation and as a simplified model to study the tissue response to materials, just named a few. Micro-bioreactors draw particular attentions in this endeavor and introduce a well-controlled system for biomimetic design of physiologically relevant microenvironment to induce complex tissue formation. More specifically, the microfluidics present in micro-bioreactors is considered superior and believed to play a critical role in regulating neovascualrization. In this study, the effect of microfluidics on cell assembly and vascularization was studies in details.

Methods: Micro-chamber reactor was fabricated using PDMS (Fig. 1 A). Human dermal fibroblasts (HDF) and Human umbilical vein endothelial cells (HUVECs) were mixed at the density of $5x10^5$ cell/ml for each cell type in 4.8% type I collagen gel, co-cultured in the micro-chamber reactor for 2 hour allowing gel formation with the presence of 0.1 mg/ml riboflavin as a photo-crosslinker. Continuous medium flow was applied for the co-culture at the rate of 0.5 µl/min. Samples were imaged using light microscope during the culturing time, and sectioned for H&E staining after 7 days of culture.

Results: Human dermal fibroblasts and Human umbilical vein endothelial cells co-cultured in the collagen gel showed typical morphologies under static and dynamic culture condition (Fig 1 B, C). Severe gel contraction occurred in the dynamic culture after overnight culture, while no obvious contraction in static groups. Tubular like structure was observed after 7 days of dynamic culture. H&E staining of the co-cultured showed cells distributed across the 3-D collagen gel (Fig. 2).

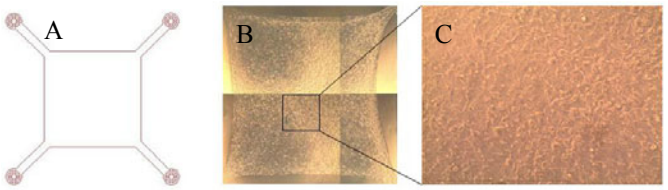

Fig. 1 Microfluidics reactor diagram (A), HDF and HUVECs co-cultured in the microfluidics reactor (B,C)

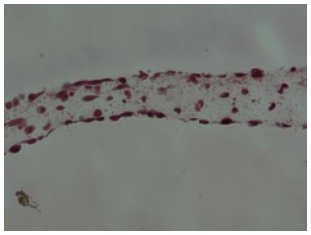

Fig. 2 H&E staining of the co-culture after 7 days.

Conclusions:

Clearly, microfluidics has a great impact on new tissue formation and is considered as a stimulatory factor in controlling new vasculature formation in the co-culture system using collagen gel.

References:

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