Adaptation of Vascular Network Formation Assay to Reconfigurable Culture Platform

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Summary: 2-D angiogenesis model using co-culture of human adipose-derived stem cells and endothelial progenitor cells has been adapted to micromechanical reconfigurable culture system; preliminary results are presented.

Recent studies have shown successful vascular cord formation in a two-dimensional culture format through the co-cultivation of cord-blood derived endothelial progenitor cells (EPC) with human adipose-derived stem cells (hADSC) [1]. In addition to the relative simplicity of two-dimensional culture, this model of vascularization is appealing due to the abundant supply of hDASC from clinical lipoaspirate waste. Notably, the authors reported that direct EPC-hADSC contact was required, but specific mechanisms remain uncertain. Here we report preliminary progress with adaptation of this model to a micromechanical reconfigurable culture (MRC) system to potentially uncover novel mechanisms of dynamic intercellular signaling.

The interlocking “comb” structure of the MRC (Fig. 1a) is fabricated from silicon using standard micromachining techniques; polystyrene surface treatment allows seeding of heterogeneous cell types. Simple rearrangement of the device places the two populations into direct contact, precise 80μm gap, or complete separation, and allows control of spatial and temporal dynamics of interaction [2].

With locally isolated EPC (CD31+) and hADSC (CD34+, CD31-, CD56-), we have achieved robust vascular cord formation using homogeneously mixed monolayer co-culture in standard tissue culture well-plates and on the MRC platform (Fig. 1b), with cell viability maintained over 6 days. In addition, contact-configured MRC initially seeded with spatially separated hADSC and EPC populations are competent in producing vascularization, though the extent to which cross-comb migration is responsible (Fig. 1c). In agreement with previous study, gap-configured populations did not produce vascular cord formation in the EPC population. However, EPC appear to exhibit an elongated morphology near comb fingertips, in proximity to the hADSC population, versus at the distal end of the combs, suggesting involvement of soluble factor signaling. We hope to elucidate these details of interaction through gene expression analysis of each isolated population, as well as testing dynamic modulation of contact and separation.