Incorporation of Growth Factors onto Hydrogels via Peptide Mediated Binding for Development of Vascular Networks

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Abstract: In vivo, the extracellular matrix (ECM) provides biochemical and mechanical properties that are instructional to resident cells to form complex tissues with characteristics to develop and support vascular networks. In vitro, the development of vascular networks can be guided by biochemical patterning of substrates via spatial distribution and display of peptides and growth factors to prompt cell adhesion, differentiation, and proliferation. We have developed a technique utilizing peptide ligands that specifically bind vascular endothelial growth factor (VEGF), erythropoietin (EPO), or angiopoietin-1 (ANG1) to spatiotemporally distribute growth factors to cells. This allows for the controlled release of each growth factor, ultimately enhancing the formation of a vascular network. Our engineered tissue constructs (ETCs) are fabricated out of gelatin methacryloyl (GelMA), which is an ideal substrate for tailored stiffness and bio-functionality, and covalently patterned with growth factor specific peptides. These peptides mimic growth factor receptors, facilitating the non-covalent binding of the growth factors to the ETC, allowing for facile uptake by the cells. We have demonstrated in the absence of cells the binding affinity of VEGF, EPO, and ANG1 to their respective peptides and the ability for each to be patterned onto a GelMA substrate. The ability to organize growth factors on an ETC provides different functionality to develop organized vascular networks. Our results demonstrated a method to incorporate biochemical cues into ETCs that enable spatial and temporal control of growth factors. Future efforts will investigate the cellular response by evaluating gene expression, quantifying angiogenic activity, and measuring the speed of growth factor consumption.

Keywords: growth factor, hydrogel, peptide, angiogenesis, vascular, patterning

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