

Vasculogenic Hydrogel: A Potential Substrate for Growth Factor Localization in Multi-Structural Tissue Engineering

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Introduction

While tissue engineering offers great potential, its successful application in clinics is currently hampered. The integration of engineered tissues after implantation is limited due to the lack of a vascular network. Therefore, vascularization has emerged as one of the major problems that prevent large-scale translation of the engineered tissues to the clinic.^{1,2} To this end, addition of pre-vascularized network into the engineered tissues during in vitro culture has been proved to enhance tissue survival after implantation.³⁻⁶ For pre-vascularized tissue engineering, the two basic strategies relies either on natural organization of endothelial cells or on the patterning of endothelial cells into desired vascular geometry using different micro-fabrication technologies. However, in the natural system there are various strong biochemical cues, e.g. growth factors, present to guide the endothelial cells organization towards a vascular tree.^{7,8} Due to the prolonged presence of these strong cues on the endothelial cells, the vascular structures tend to resist remodeling towards a random organization over time which provides long-term functionality to the network. Therefore, there is a need to strategically study the spatial and temporal effect of growth factors on the engineered tissues. This approach would result in a designable vascular network with long-term stability and anastomosis compatibility which could be further used in the formation of tissue building blocks for multi-structural tissue engineering.

Aim

To develop vasculogenic hydrogels and evaluate their cellular compatibility by using bone marrow derived human mesenchymal stem cells in 3D culture conditions.

Materials and Methods

The vasculogenic hydrogel was prepared by photopolymerization of gelatin methacrylate (GelMA) using Irgacure 2959 as photoinitiator. For cell viability (live/dead analysis) and cell adhesion (DAPI/Alexa fluor 546 Phalloidin) studies, bone marrow derived human mesenchymal stem cells (hMSCs) were used.

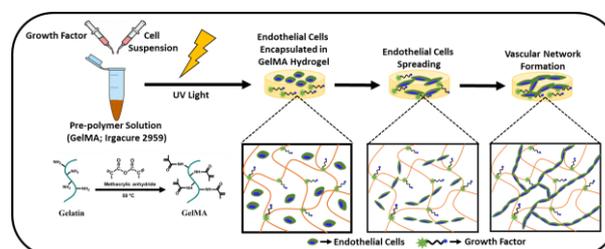
Results and Conclusions

The physicochemical properties analysis of the synthesized GelMA and vasculogenic hydrogel confirmed the successful crosslinking of gelatin backbone with methacrylate groups by FTIR and NMR spectroscopy. The scanning electron microscope results of the vasculogenic hydrogel revealed interconnected microporous structure with average pore size of 40-80 μm . The developed vasculogenic hydrogels supported the growth of hMSCs in terms of cell viability and adhesion over a span of 7 days within the hydrogels. The cells cultured in the hydrogel showed round morphology

and cellular behavior quite similar to native tissue-like growth.

Future Plans

In the present study we have optimized the vasculogenic hydrogel conditions in terms of its physicochemical properties and biocompatibility. In future, the optimized results from this study will be used to synthesize vasculogenic hydrogels for patterning growth factors (growth factor mimicking peptides) within the hydrogel and study their effect on the endothelial cells and with co-cultures of endothelial cells and mesenchymal stem cells (see Scheme 1).



Scheme 1. Schematic representation of the overall research plan.

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