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Synthesis and Characterization of Fibrin/Polyethylene Glycol-Based Interpenetrating Polymer Networks for Dermal Tissue Engineering

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Abstract : In skin regenerative medicine, one of the critical issues is to produce a three-dimensional scaffold with optimized porosity for dermal fibroblast infiltration and neovascularization, which exhibits high mechanical properties and displays sufficient wound healing characteristics. In this study, we report on the synthesis and characterization of macroporous sequential interpenetrating polymer networks (IPNs) combining skin wound healing properties of fibrin with the excellent physical properties of polyethylene glycol (PEG). Fibrin fibers serve as a provisional biologically active network to promote cell adhesion and proliferation while PEG provides the mechanical stability to maintain the entire 3D construct. After having modified both PEG and Serum Albumin (used for promoting enzymatic degradability) by adding methacrylate residues (PEGDM and SAM, respectively), Fibrin/PEGDM-SAM sequential IPNs were synthesized as follows: Macroporous sponges were first produced from PEGDM-SAM hydrogels by a freeze-drying technique and then rehydrated by adding the fibrin precursors. Environmental Scanning Electron Microscopy (ESEM) and Confocal Laser Scanning Microscopy (CLSM) were used to characterize their microstructure. Human dermal fibroblasts were cultivated during one week in the constructs and different cell culture parameters (viability, morphology, proliferation) were evaluated. Subcutaneous implantations of the scaffolds were conducted on five-week old male nude mice to investigate their biocompatibility in vivo. We successfully synthesized interconnected and macroporous Fibrin/PEGDM-SAM sequential IPNs. The viability of primary dermal fibroblasts was well maintained (above 90%) after 2 days of culture. Cells were able to adhere, spread and proliferate in the scaffolds suggesting the suitable porosity and intrinsic biologic properties of the constructs. The fibrin network adopted a spider web shape that covered partially the pores allowing easier cell infiltration into the macroporous structure. To further characterize the in vitro cell behavior, cell proliferation (EdU incorporation, MTS assay) is being studied. Preliminary histological analysis of animal studies indicated the persistence of hydrogels even after one-month post implantation and confirmed the absence of inflammation response, good biocompatibility and biointegration of our scaffolds within the surrounding tissues. These results suggest that our Fibrin/PEGDM-SAM IPNs could be considered as potential candidates for dermis regenerative medicine. Histological analysis will be completed to further assess scaffold remodeling including de novo extracellular matrix protein synthesis and early stage angiogenesis analysis. Compression measurements will be conducted to investigate the mechanical properties.

Keywords : fibrin, hydrogels for dermal reconstruction, polyethylene glycol, semi-interpenetrating polymer network
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