Hyaluronan-Based Multi-Phasic Scaffolds for Osteochondral Tissue Regeneration

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Osteoarthritis (OA) is the predominant form of arthritis in our aging population. With individuals living increasingly longer, we face new problems with the degradation of tissues throughout the body. Regenerative tissue engineering utilizing bio-polymer scaffolds allows treatment to begin at the first sign of OA, returning tissue to a pre-osteoarthritic condition. As the osteochondral tissues display a gradient of properties and structure, an integrated multi-phasic scaffold made of extracellular matrix (ECM) components was designed to mimic natural tissue. Our goal is to fabricate an integrated multi-phasic scaffold in the presence of drug-encapsulated microspheres to direct osteochondral tissue regeneration. Methacrylation of hyaluronan (HA) was performed through a novel method in dimethyl sulfoxide by ion exchange with an ammonium salt. The solution was reacted with methacrylic anhydride, hydrolyzed, lyophilized, and characterized by ^{1}H-NMR. Cytocompatibility of the HA-MA was verified with primary human mesenchymal stem cells (hMSCs). HA-MA (2-4% w/v) blends containing varying concentrations of ECM components were photocrosslinked in the presence of a photoinitiator. Integrated multi-phasic scaffolds were formed by successive layering and polymerization of varied polymer blends in a custom mold. Scaffolds were also formed with PEG-modified alginate (AA-PEG) microspheres for the purpose of controlled drug release as well as the formation of pores (after dissolution, 100-200μm). A layer-by-layer polymerization of HA-MA based blends was successful in fabricating an integrated multi-phasic scaffold. The individual layers of the scaffold were in-separable yet distinguishable. AA-PEG microspheres with nominal diameters of 500nm-1μm were homogenously dispersed through-out the polymerized scaffold. The HA-MA-based scaffolds demonstrate efficacy of incorporating ECM components and AA-PEG microspheres into the hydrogel network. Mechanical testing as well as differentiation and proliferation of hMSCs within our scaffold will be investigated to determine the optimal concentration of ECM components and drug release profiles within each layer of the scaffold.