

The Summer Undergraduate Research Fellowship (SURF) Symposium
6 August 2015
Purdue University, West Lafayette, Indiana, USA

Bio-inspired Composite Hydrogels for Osteochondral Regenerative Engineering

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ABSTRACT

Treatment of osteochondral defects encompassing injury or degeneration to both the articular cartilage as well as the underlying subchondral bone presents a significant medical challenge. Current treatment options including autografts and allografts suffer from limited availability and risk of immunogenicity, respectively. The long term goal of this work is to develop an integrated scaffold system for treatment of osteochondral defects via *in situ* regeneration of bone, cartilage and the bone-cartilage interface. Hydrogels composed of polymer networks swollen in water provide an attractive biomaterial platform for regeneration of cartilage. In the present study, we have developed a novel composite hydrogel consisting of thiolated hyaluronic acid (HA) and chondroitin sulfate (CS) crosslinked with polyethylene glycol (PEG). The combination of HA and CS offers a biomimetic microenvironment found in cartilage whereas the selection of PEG as a crosslinker is based on its established biocompatibility and chemical versatility. Variations in the crosslinking density enable the ability to fine-tune physical properties of hydrogels. For example, the rheology tests of different hydrogels with increased crosslinking densities showed an increase in equilibrium gel modulus. *In vitro* study with human mesenchymal stem cells (hMSCs) demonstrated the ability of the hydrogel to support three-dimensional cell encapsulation with high viability. Interestingly, increased crosslinking also promoted phosphorylation of focal adhesion kinase, a potential early mechanosensor that respond to changes in mechanical stiffness. Future *in vitro* and *in vivo* studies will be performed to optimize the hydrogels for chondrogenic cellular responses and osteochondral regeneration.

KEYWORDS

Hyaluronic acid, chondroitin sulfate, polyethylene glycol, hydrogels, scaffolds, osteochondral tissue engineering