

Hydrogel Development and Optimization for MSC-Based Cartilage Tissue Engineering

While there may exist an abundance of biomaterials created for the purpose of cartilage tissue engineering, many of them are limited by cell infiltration rates, the ability to maintain proper cellular phenotypes, and the development of functional properties. Hydrogels offer an approach where cells can be easily encapsulated within a carefully tailored environment. Using agarose hydrogels, we have created tissue engineered constructs seeded with isolated articular chondrocytes and mesenchymal stem cells (MSCs). As an alternative to agarose, we have also investigated the use of self-assembling peptide (Puramatrix) and hyaluronic acid (HA) hydrogels. HA is a large polysaccharide that is found ubiquitously in articular cartilage. In collaboration with the Polymeric Biomaterials Laboratory directed by Jason Burdick, we have successfully deployed a photo-crosslinkable HA hydrogel capable of supporting MSC chondrogenesis and functional cartilage tissue maturation¹⁻³. The formulation of this HA hydrogel has been optimized to generate cartilage-like graft material with mechanical properties that approach native values (Fig. 1)⁴. We have also demonstrated that the application of dynamic compressive loading via custom bioreactors can regulate the expression of genes responsible for the synthesis of cartilage matrix proteins (Fig. 2)⁵. Current work with this HA hydrogel will utilize the addition of novel degradable linkages to allow for optimal physical properties and improved matrix diffusion in developing constructs⁶.

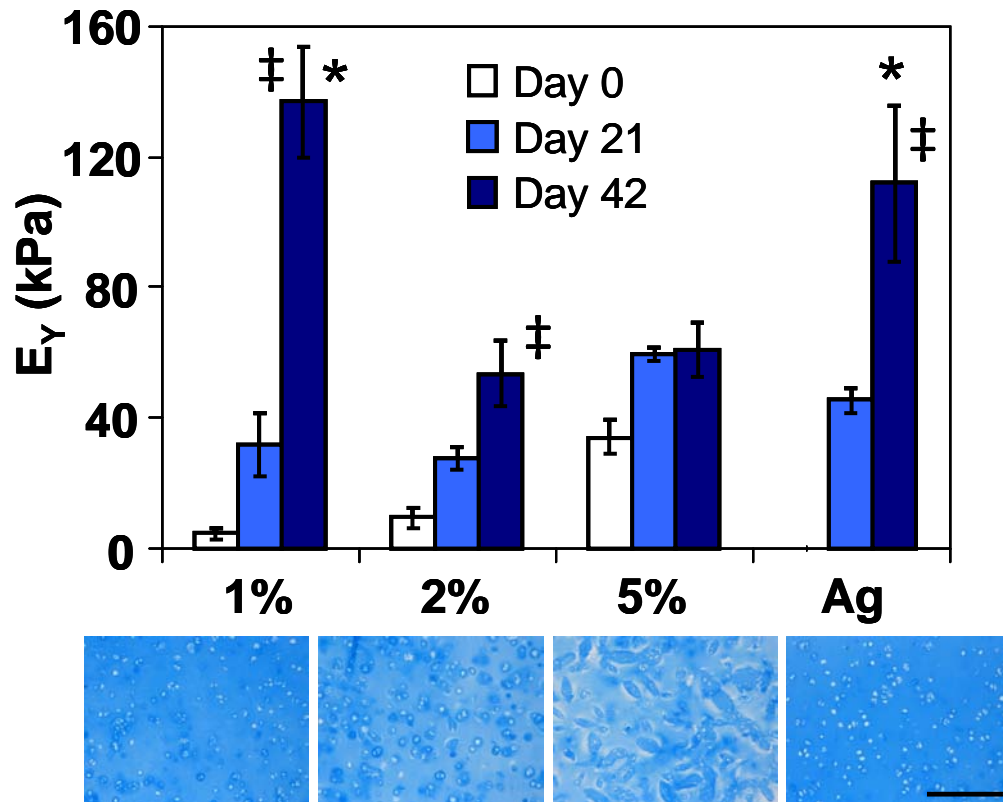


Figure 1. Equilibrium compressive modulus (E_Y) of HA and agarose (Ag) hydrogels through 6 weeks of culture (mean \pm SD; $n=4$; * indicates $p<0.05$ vs. 2% and 5% formulations; ‡ indicates $p<0.05$ day 0). Alcian blue staining showed even proteoglycan distribution in 1% HA and Ag constructs while greater aggregation occurred in 2% and 5% HA.

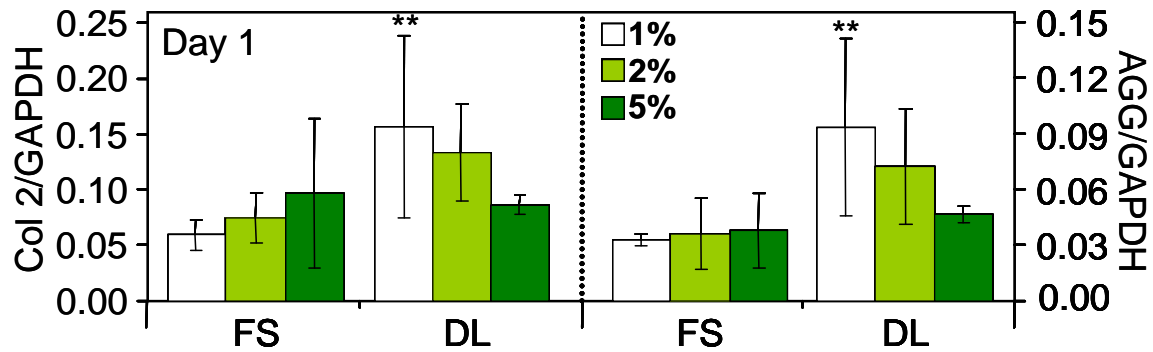


Figure 2. Type II collagen (left) and aggrecan (right) expression (per GAPDH) on day 1 for 1, 2, and 5% macromer density MSC seeded HA hydrogels subjected to dynamic compressive loading (DL) or cultured in free-swelling conditions (FS). (** $p<0.05$ vs FS control)

Recent Publications:

1. Burdick JA, Chung C, Jia X, Randolph MA, Langer R. Controlled degradation and mechanical behavior of photopolymerized hyaluronic acid networks. *Biomacromolecules* 2005;6(1):386-91.
2. Chung C, Burdick JA. Influence of Three-Dimensional Hyaluronic Acid Microenvironments on Mesenchymal Stem Cell Chondrogenesis. *Tissue Engineering Part A* 2009;15(2):243-254.
3. Erickson IE, Huang AH, Chung C, Li RT, Burdick JA, Mauck RL. Differential Maturation and Structure-Function Relationships in Mesenchymal Stem Cell- and Chondrocyte-Seeded Hydrogels. *Tissue Engineering Part A* 2009;15(5):1041-1052.
4. Erickson IE, Huang AH, Sengupta S, Kestle S, Burdick JA, Mauck RL. Macromer density influences mesenchymal stem cell chondrogenesis and maturation in photocrosslinked hyaluronic acid hydrogels. *Osteoarthritis and Cartilage* 2009;17(12):1639-1648.
5. Erickson IE, Kestle S, Farrell MJ, Burdick JA, Mauck RL. Macromer Density Mediates Mesenchymal Stem Cell Response to Dynamic Compression in Photo-Crosslinked Hyaluronic Acid Hydrogels. 56th Annual Meeting of the Orthopaedic Research Society. New Orleans, Louisiana; 2010.
6. Chung C, Beecham M, Mauck RL, Burdick JA. The influence of degradation characteristics of hyaluronic acid hydrogels on in vitro neocartilage formation by mesenchymal stem cells. *Biomaterials* 2009;30(26):4287-4296.

Personnel:

Alice Huang

Isaac Erickson
Megan Farrell
Minwook Kim
Sydney Kestle
Jason Burdick, PhD

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