Photopatterning Hyaluronic Acid into Mechanically Robust Hydrogels Based on Melt-Assembled Networks of Sphere-Forming Block Copolymers

Jackson Lewis, Travis Bailey
Colorado State University

Statement of Purpose: Glycosaminoglycans (GAGs) are naturally occurring long-chain polysaccharides known for their lubricating properties, shock absorption, and their role in the wound-healing cascade. Hyaluronic Acid (HA) is one of the most commonly used GAGs in the medical and cosmetic industry today. Integrating this material into a mechanically robust hydrogel platform can increase biocompatibility and reduce autoimmune reactions when the hydrogel is used for medical applications. Our unique hydrogel system is comprised of AB diblock and ABA triblock copolymer and has been tuned to form a highly homogeneous network of 20nm spheres (A blocks) which are tethered mechanically during melt-state self-assembly. Through increasing the triblock copolymer content in this hydrogel platform to levels above 40 mol% we have been able to produce single network systems able to compete mechanically with soft tissues, as well as being applicable to perform in other high-load bearing and cyclic loading applications. We have recently been able to photopattern HA into our tough hydrogel platform to further augment the surface properties independently of the bulk hydrogel characteristics.

Methods: AB diblock copolymer was synthesized through subsequent anionic polymerization of the A block followed by the B block. The triblock copolymer was synthesized by coupling the 2 AB diblock copolymer species. The diblock and triblock copolymer were then blended in different amounts and heated in the melt in order to achieve self- assembly into a morphology composed of spherical domains of A block surrounded by a coronal layer of B block. The structured system was then vitrified to its solid form preserving the morphology. The hyaluronic acid was derivatized with fluorescein and methacrylate. Functionalization was confirmed via ^{1}H NMR
This functionalized HA was then dissolved in an aqueous solution containing a water-soluble photodegradable free radical initiator. The block copolymer solid was then swollen in this solution for 24 hours. The resultant hydrogel was exposed to UV light, initiating the crosslinking of methacrylate groups of the HA. The hydrogel was then rinsed of free HA. Fluorescence microscopy was used to confirm the presence of the HA network following the extraction of the free material.

Results: In Figure 1A the dry polymer and the swollen hydrogel are compared to show the change in size post swelling. It was determined gravimetrically that the hydrogel consists of ~14g of solution/g of polymer. Figure 1B shows the hydrogel under a 365nm lamp after the hydrogel had been rinsed in DI water for 60 hours removing all uncrosslinked HA from the hydrogel. It is clear that the functionalized HA which had been exposed to UV light in order to be crosslinked stays inside of the hydrogel while the functionalized HA which had not been exposed to UV light leaves the hydrogel upon rinsing. The CSU logo in Figure 1 confirms the photo-patterning capability of this synthetic approach.

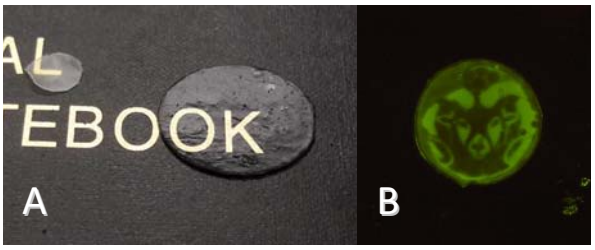

Figure 1. **A** Dry Polymer vs Swollen Hydrogel. **B** Photopatterned, fluorescently-tagged HA in hydrogel after 60 hour rinse in DI water.

Conclusions: Although prior groups have been successful at incorporating hyaluronic acid into a gel platform through random crosslinking events, yielding a gel which is biologically friendly these gel systems are often brittle and weak and would have difficulty performing in mechanically demanding environments[1,2,3]. This hydrogel system possesses high mechanical robustness while allowing for an easy incorporation of glycosaminoglycans by trapping them in the primary hydrogel network through methacrylate mediated crosslinking. This system may expand the use of these glycosaminoglycan incorporated hydrogels into an arena of mechanically demanding environments such as soft tissue replacements and tissue engineering scaffolds.

References:

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