A New Approach to Regenerative Cartilage Tissue Engineering Using Temperature-Sensitive Therapeutic Hydrogels

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Injury and diseases that affect articular cartilage present a daunting challenge in orthopedic medicine. During the onset of injury or disease, low oxygen environments decrease healthy cartilage cell growth and regeneration. Ultimately, this environment reduces the efficacy of traditional biomaterial scaffolds to provide a regenerative interface. Our research group has developed a therapeutic injectable hydrogel that provides a regenerative interface for cartilage tissue engineering via a cell-protective mechanism. Using Poly(N-vinylcaprolactam)[PVCL] a smart biomaterial that changes its molecular orientation upon temperature change along with its mechanical properties in conjunction with other natural products. This hydrogel composite, containing PVCL-hyaluronic acid-therapeutic (PVC-HA-TH) affords a robust hydrogel with tunable (lower critical solution temperature) [LCST] parameters near physiological temperature. Hydrogels were synthesized and used *in vitro* static cell culture studies and *in vivo* studies. Using 3D printing, hydrogels were also fabricated to compare the effect of material properties on cell proliferation and metabolism on extra cellular matrix (ECM) proteins. Fetal bovine chondrocytes were harvested and seeded [or 3D bioprinted] into various formulations of PVCL-HA-TH under normoxia (21%) and hypoxia (1%) low oxygen conditions. Chondrocyte cell viability at 1% O_2 levels remained higher than that of 20% O_2 levels in PVCL-HA for each time point. PVCL-HA hydrogels reached a maximum of 89% on the third day of observance. Higher cell viability was also noted on meHA samples at 1% O_2 levels than at 20% O_2 levels, with the peak value at 74% on the first day of observance. Animal studies were performed for 30 days after injection of therapeutic hydrogels into the defective knee joint confirm higher amounts of chondrocyte cloning within the murine joint. This work shows promise in providing a cyto-protective biomaterial construct that will begin to regenerate diseased articular cartilage.

This work was partially supported by the NSF GOALI Grant #1606226; subaward#127300.