

## 2006 CORS Founder's Medal

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### **EVALUATION OF GENIPIN CROSS-LINKED FIBRIN GELS FOR TISSUE ENGINEERING OF HUMAN ARTICULAR CARTILAGE**

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**PURPOSE:** The objective of this project is to determine the suitability of modified fibrin hydrogels as scaffolds for articular cartilage tissue engineering. The attractive feature of the fibrin system is that the gel precursors are available in autologous form. We have previously demonstrated that genipin, a naturally occurring cross-linking agent, stabilizes the fibrin gel. **METHODS:** Human articular chondrocytes were isolated from articular cartilage harvested from consenting patients undergoing total knee arthroplasty. The human cells were encapsulated into fibrin gels where gelation was induced by combining fibrinogen, thrombin, and genipin. The resulting gels were evaluated for extracellular matrix (ECM) production, mechanical properties, cell viability, and biodegradation. **RESULTS:** No breakdown of the gels was detected during 5 weeks of cell culture. After several weeks in culture, histology indicates significant proteoglycan production by encapsulated cells, and collagen II and aggrecan were detected in this ECM by immunostaining. There was a greater accumulation of cartilage-like ECM in the gels cross-linked with genipin. Dynamic compression tests performed at 0.1 Hz for 10 cycles using an MTS machine indicate that accumulation of ECM was associated with increased stiffness of the material. Cell viability was assessed using live/dead staining, and was found to be >50% after 24 hours and at 1 week in culture. The presence of genipin cross-linking did not significantly affect cell viability. Real-Time RT-PCR indicated that encapsulated chondrocytes show an increase in Sox9, collagen II and aggrecan expression over 5 weeks and that this is further increased in the presence of genipin. The gene expression results agreed with the enhanced ECM seen under these conditions by histology and immunostaining. The fibrin material was also implanted subcutaneously into rats and after 30 days the material was removed, sectioned and evaluated. Immunostaining indicated that while there was evidence of biodegradation, the material did not appear to cause an inflammatory response. **CONCLUSIONS:** Modified fibrin hydrogels show potential as cellular scaffolds for articular cartilage tissue engineering. An in vivo orthopaedic model must now be developed to fully evaluate the potential of the fibrin gel. **Funding:** Other Education Grant