

STEM CELLS FOR CARTILAGE REGENERATION

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INTRODUCTION: Damage and loss of articular cartilage leads to focal lesions that disrupt the distribution of loads across the joint, causing acute pain, disability and potentiating degenerative joint disease. Tissue engineering of neocartilaginous implants from stem cells is a possible solution for this pathology. However, there are many unresolved issues, including the type of stem cell and scaffold(s) to be used and how close to the native tissue the initial implant should be for successful repair and regeneration.

METHODS: Tissue engineering requires some combination of cells, scaffolds and bioactive factors. Cells with osteogenic, adipogenic and chondrogenic potential have been isolated from many postnatal tissues including bone marrow, synovial tissue, fat and periosteum. Methods for their isolation, expansion and differentiation have been developed. We have experimented with scaffolds of various types, examining cell behavior and matrix production with the addition of various bioactive factors. Some of the tissue-engineered constructs have been tested in models of human skeletal tissue pathologies.

RESULTS: *In vitro* chondrogenesis of mesenchymal stem cells was first accomplished by our group utilizing scaffold-free pellet culture and a defined culture medium (1,2). Tissue engineering was used for scaling this technology for clinical applications. We have worked with scaffolds including sponges and polymerizable scaffolds of various types and stem cells of different sources. In PEG-based semi-interpenetrating networks (3), we noted that as the stem cells differentiated, collagen localization remained pericellular in all the scaffold

chemistries we explored, preventing interterritorial fibril assembly and resulting in a neocartilage construct with inferior mechanical properties. We have now developed bioresponsive scaffolds designed to degrade with timing corresponding to stem cell differentiation and matrix elaboration, which enable interterritorial matrix assembly and a structure with superior mechanical properties.

DISCUSSION & CONCLUSIONS: By use of an implant that is initially liquid, the implant is injectable, and can fill a pathological defect, being polymerized *in situ*. Alternatively, the implant can be polymerized *in vitro* and the cells stimulated to produce a cartilaginous implant. Providing the ability to explore both delivery options is a potentially important attribute of bioresponsive scaffolds as it is unclear which option will be more successful in the clinical situation. Furthermore, the ability to tune the implants to the stem cell types used is a significant advantage of these types of implants and offers the ability to more fully test the tissue-forming capacity of each cell source.

REFERENCES: (1) Johnstone et al (1998) *Exp Cell Res* 238, 265-272. (2) Yoo et al (1998) *J Bone Joint Surg Am* 80, 1745-1757. (3) Buxton et al (2007) *Tissue Eng* 13, 2549-2560.

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