Injectable Scaffolds for Osteochondral Tissue Regeneration

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Over 27 million people in the United States suffer from osteoarthritis, and costs of non-steroidal anti-inflammatory drugs run to about $4 billion per year[1]. Injuries sustained to articular cartilage are especially challenging to heal due to the tissue's heterogeneous and avascular nature. Although current treatment methods, including arthroscopic lavage, microfracturing and cartilage grafting, are fairly effective in alleviating symptoms associated with cartilage defects, they have low long-term success rates and fail to promote regeneration of natural cartilage tissue. Research in the field of tissue engineering has long sought to enable rapid regeneration of bone and cartilage defects through combination of scaffolds, cells, and biomolecular signals.

In particular, the structure of the scaffold plays a critical role in guiding tissue development. Scaffolds for osteochondral injuries must not only be biocompatible, bioresorbable, and able to withstand the mechanical forces that these tissues are subjected to but also guide the complex and heterogenous repair of a multi-tissue defect. As such, the major focus thus far has been in constructing implantable scaffolds, which can be readily designed to offer appropriate mechanical properties and enable 3D spatiotemporal control over the defect repair process. However, use of such scaffolds requires open surgery, simple tissue defects, and has been unable to effectively promote the integration of the new tissue with the old.

Thus, it has become of high interest to discover minimally invasive methods using injectable polymeric biomaterials capable of gelling *in situ* as scaffolds to stimulate osteochondral tissue regeneration. Hydrogels are a versatile class of polymeric materials well suited to this task, and their physical properties can be altered based on their chemical composition. Such injectable, *in situ* gelling materials can readily conform to complex defects, are able to deliver and maintain cell populations due to high water content and ease of nutrient transport,[2] and can provide a synthetically-tuned extracellular matrix that promotes cell differentiation and proliferation.

Thermoresponsive hydrogels, such as those based on poly(*N*-isopropylacrylamide) (pNiPAAm), have been especially promising due to their ability to solidify without addition of often cytotoxic crosslinkers, initiators, or catalyst molecules. Recent research has seen further advancement of these materials through controlled elimination of gel syneresis after injection and solidification and the successful delivery and maintenance of primary stem cells *in vitro* for application in craniofacial bone defects[3-4]. The next grand challenge in the development of injectable scaffolds is to endow them with spatiotemporally-controlled signaling to guide the regeneration of heterogeneous and multi-tissue defects.[5]

References:

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