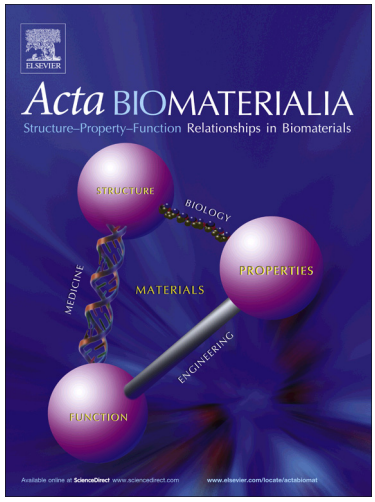

Full length article

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Cartilage Tissue formation through assembly of microgels containing mesenchymal stem cells

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Abstract

Current clinical approaches to treat articular cartilage degeneration provide only a limited ability to regenerate tissue with long-term durability and functionality. In this application, injectable bulk hydrogels and microgels containing stem cells can provide a suitable environment for tissue regeneration. However insufficient cell-cell interactions, low differentiation efficiency and poor tissue adhesion hinder the formation of high-quality hyaline type cartilage. Here, we have designed a higher order tissue-like structure using injectable cell-laden microgels as the building blocks to achieve human bone marrow-derived mesenchymal stem cell (hBMSC) long-term maintenance and chondrogenesis. We have demonstrated that a 4-arm poly(ethylene glycol)-*N*-hydroxysuccinimide (NHS) crosslinker induces covalent bonding between the microgel building blocks as well as the surrounding tissue mimic. The crosslinking process assembles the microgels into a 3D construct and preserves the viability and cellular functions of the encapsulated hBMSCs. This assembled microgel construct encourages upregulation of chondrogenesis markers in both gene and glycosaminoglycan (GAG) expression levels. In addition, the regenerated tissue in the assembled microgels stained positively with Alcian blue and Safranin O exhibiting unique hyaline-like cartilage features. Furthermore, the immunostaining showed a favourable distribution and significantly higher content of type II collagen in the assembled microgels when compared to both the bulk hydrogel and pellet cultures. Collectively, this tissue adhesive hBMSC-laden microgel construct provides potential clinical opportunities for articular cartilage repair and other applications in regenerative medicine.

Keywords:

cartilage tissue engineering, microgels, mesenchymal stem cells, cell encapsulation

Statement of Significance

A reliable approach to reconstruct durable and fully functional articular cartilage tissue is required for effective clinical therapies. Here, injectable hydrogels together with cell-based