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Editorial

Osteoarthritis: Insights in Cartilage Tissue Integration

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Articular cartilage is a lubricant substrate that serves as a cushion between the bones of diarthrodial joints. Several factors such as aging, disease and abnormal loading conditions applied to the joints can lead to degeneration of articular cartilage. Among the over 100 different types of common degenerative conditions, osteoarthritis is the most commonly reported cause, where the cartilaginous layers gradually wear away to increase the friction coefficient of the articular surface, concomitant pain and loss of mobility [1]. Self-repair of articular cartilage is limited due to its avascular nature. Although some surgical treatments for cartilage defects are currently available, autologous chondrocyte implantation (ACI) is the only cell-based surgical therapy approved in the United States [2]. Alternatively, tissue engineering approaches which involve the use of a combination of cells, biomaterials and bioactive molecules to grow functional tissue substitutes may offer a long-term solution to cartilage degeneration [3]. While ACI is only considered for patients with minor cartilage lesions, it becomes more effective in treating relatively large defects when combined with tissue engineering matrices. The approach is commonly known as matrix-assisted chondrocyte transplantation (MACT).

Tissue grafts need to integrate with host native tissues to support their continuing development after the implantation. However, it has been demonstrated that fibrocartilage which is biochemically and mechanically inferior to healthy articular cartilage usually forms at the implant-cartilage interfaces [4]. Clinically, fibrin glue composed of fibrinogen is the standard material used to anchor cells and grafts to cartilage defect sites [5]. Although fibrin glue enhances initial adhesion of the implant to native cartilage, stable integration has not been achieved due to the high degradation rate of fibrin glue and thus it is considered as a delivery

vehicle rather than a support substrate [6]. The quality of naturally established tissue integration relies on a variety of factors including the developmental stage of the implant, architecture and composition of the implant and the adjacent tissues, choices of scaffolding materials and cell sources for tissue-engineered constructs [7]. Properties of biocompatible materials used as a support substrate in MACT have been shown to modulate integration of the implant with native cartilage. For example, a recent study utilized biocompatible agarose to examine the effects of hydrogel stiffness on in-situ cartilage integration using an in-vitro tissue explant model [8]. The results suggest that an optimal range of substrate mechanics that yields superior integration strength without compromising the development of neocartilage can be identified and that overly high hydrogel stiffness may compromise tissue integration due to a dense polymer network and thereby a limited void space that impede chondrocyte migration.

Furthermore, cell motility is another contributing factor to tissue integration since it is believed that when migrating from the implant to native tissues, cells simultaneously synthesize extracellular matrix (ECM) components at the interfacial regions that eventually fill the gaps between the two compartments. Inclusion of cell adhesion molecules or peptides like Arg-Gly-Asp (RGD) in the network of biocompatible substrates allows more extensive cell movement and thus may further facilitate tissue integration in MACT. Recently, the use of decellularized ECM as a scaffolding material or an ingredient is of particular interest and some successful ECM-based clinical cases have been reported to repair human tissues [9]. The main advantage of such approaches includes that (i) removal of cells and nucleic acids minimizes the possibility to elicit adverse immune response after the transplantation and (ii) retention of growth factors and structural and functional proteins entrapped within the original tissue supports cell adhesion, migration and growth [9]. Although decellularized cartilage ECM particles which contain primarily type II collagen in the absence of chondrocytes and glycosaminoglycans have been incorporated into biomaterials to regenerate articular cartilage [10], their concentration needs to be further optimized before being applied to the MACT procedures.

In short, implanted tissue grafts or tissue engineering matrices need to integrate strongly with native cartilage to support the development of the regenerating tissue since poor integration can cause an altered property of the implant and ultimately its degradation. Therefore, properties of biomaterial substrates should be carefully designed when fabricating three-dimensional platforms suitable for treatment of osteoarthritis via MACT.

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Conflicts of interests

The author declares no financial conflicts.

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