SMGroup

SM Journal of Orthopedics

Editorial

Tissue Engineering in Cartilage Repair: A Perspective

Daping Wang[1]*

[1]*Department of Orthopedics, Shenzhen Key Laboratory of Tissue Engineering, Shenzhen Second People's Hospital (The 1st Hospital affiliated to Shenzhen University), PR China*

Article Information

Received date: Dec 03, 2015
Accepted date: Dec 03, 2015
Published date: Dec 04, 2015

***Corresponding author**

Daping Wang, Department of Orthopedics, Shenzhen Key Laboratory of Tissue Engineering, Shenzhen Second People's Hospital (The 1st Hospital affiliated to Shenzhen University), PR China, Email: 825343512@qq.com

Editorial

Cartilage is a special avascular tissue with sparse chondrocytes imbedding in the dense Extracellular Matrix (ECM). Cartilage injuries can be caused by trauma, osteoarthritis, obesity, meniscus injury, joint line change and chronic joint instability. Cartilage has inferior self-healing capacity due to the lack of ECM and the blood supply, in which one for the chondrocyte migration and another for proliferation. Therefore replacement is the best way for cartilage repair. Tissue engineering is a novel strategy for cartilage replacement and consists of three key elements, i.e. cells, signaling molecules and scaffolds. Here we will present the recent progress of cartilage tissue engineering from these three parts.

Cells

Autologous cartilage is the best source for seed cells. However, the need for a second operation and the limitation in large area impair restrict its application on clinic. In recent years, Mesenchymal Stem Cells (MSCs) arise as a new star for the seed cell development.

MSC attributes comprise its abundance in various tissue sources (bone marrow, adipose tissue, umbilical cord, cord blood, others), self-renewal and a vast differentiation potential towards chondrogenesis. In addition, MSCs produce a variety of ECM macromolecules and signaling molecules. With these advantages, MSCs and differentiated MSCs are widely used in cartilage repair alone or with biomolecule scaffolds. Many groups have reported the chondrogenic induction of MSCs. The resulting differentiated tissue can be classified as cartilage in which it expresses many typical biomolecules of hyaline cartilage, such as type II collagen, aggrecan and so on.

However, so far none of these studies has regenerated a fully functional articular hyaline cartilage without exhibiting a hypertrophic phenotype. The failure of articular cartilage formation may be due to the intrinsic inability of MSCs to differentiate into articular cartilage or a reflection of poor understanding of the underlying MSC biology. Based on several mechanism studies, we conclude that precise induction process or cell optimization will contribute to chondrogenic induction in future. Besides, as reported, embryonic stem cells can break the restrictions of MSCs, which will provide a new possibility of articular cartilage regeneration.

Signaling Molecules

During the chondrogenic process, several signaling molecules like transforming growth factor (TGF-β) get involved at different specific stages and levels. The differentiation of MSCs into chondrocytes requires a very precise combination of all these factors.

Here we take the TGF-β family as an example to explain the roles of signaling molecules in chondrogenesis. The TGF-β family includes several ligands such as activin A, Growth and Differentiation Factors (GDFs), TGF-β, and Bone Morphogenetic Proteins (BMPs). They are widely expressed in chondrocytes and constitute the class of growth factors almost exclusively involved in the chondrogenic process. Among the whole family, TGF-β1 initiates the condensation of MSCs and is one of the most important factors during the early stages of chondrogenesis. BMPs induce the differentiation of MSCs into mature chondrocytes, as well as the differentiation of proliferative chondrocytes to hypertrophic chondrocytes.

As different signaling molecules play various roles in each stage of differentiation, precise control of dose and timing is essential for cartilage tissue engineering.

Growth factors have been applied in numerous tissue-engineering studies. One of the problems for its application is that the adsorption or encapsulation of growth factors into polymeric scaffold will cause the burst release that might be toxic to cells. Covalent immobilization can overcome this problem to some extent. However, it may influence the conformation of growth factors and result in reduced bioactivity. Growth factors mimicking peptides or small molecules will provide

an opportunity to tackle these problems. As reported Peter, et al. applied the TGF-β mimicking peptide CM-10 on microsphere, in which the conjugated microsphere can modulate the stem cell fate to chondrocytes.

Scaffolds

Current cartilage repair methods involve drilling holes into the bone marrow to free stem cells, which as sometimes kept in position with the use of hydrogels. Scaffolds that can assist with organization of the cartilage are needed. Tissue engineering provides a strategy to create a scaffold to stimulate cartilage regeneration. There are two mainstreams of tissue engineering strategies associated with these tissue-regenerating scaffolds: scaffolds themselves that directly enable the stimulation of in situ tissue regeneration; and scaffolds pre-processed with seeded cells and the subsequent pre-grown tissue *in vitro* before implantation. The scaffolds have the ability to restore, maintain, or improve the cartilage function. An ideal tissue-engineered scaffold should mimic both the structure and mechanical properties of the targeted tissue. Generally, the scaffold should be:

a. Biodegradable and its degradation products must be non-toxic and biocompatible, which is one of the most important principles of material selection for cartilage implants. The degradation rate should be controlled to match new tissue ingrowth.

b. The scaffold should have the ability to bond to cartilage and induce chondrogenesis. It requires the surface chemistry of the scaffold to enable the stimulation of cell attachment, migration, proliferation and differentiation. Ideally, the scaffold surface should also contain some active functional group for biomolecule attachment.

c. The scaffold should act as a template to direct cell ingrowth in three dimensions for the formation of effective construction. An interconnected pore network with appropriate porosity is required to encourage the transport of nutrients, oxygen and metabolic wastes.

d. Mechanical properties similar to the host tissue are required, especially for resisting load bearing in articular cartilage.

e. The scaffold should meet international regulations for clinical use and should be easy to produce commercially and to be sterilized.

Common commercial scaffolds used for cartilage repair in clinic mainly are hydrogels of one or more compositions (e.g. hyaluronic acid, chondroitin sulfate, collagen and alginate). Membranes such as type I/III collagen are also used as a defect cover in the case of Autologous Chondrocyte Implantation (ACI), or as a scaffold template for Matrix-Induced Autologous Chondrocyte Implantation (MACI). However, one of the main problems regarding the usage of these scaffolds is the unsatisfactory mechanical property. Besides, as for hydrogels the immobilization into the defect is of difficulty. In addition, injectable hydrogels are highly preferred since minimally invasive surgery becomes possible.

As a consequence, the optimization of cartilage scaffolds is essential. Introducing the inorganic component into the polymeric matrix to fabricate hybrid scaffolds will be a promising strategy for improving mechanical properties. The modification of specific functional groups of scaffold to form bonds with the surrounding tissue can enhance the immobilization. Therefore, in the future work numerous studies have to be performed to create a novel tissue-engineered scaffold, which can simultaneously fulfill various clinical requirements for cartilage repair.