Synovial stem cell therapy for meniscal regeneration

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Indications for surgical meniscal repair are limited, and failure rates remain high. As a result, partial meniscectomy is often the treatment of choice. However, removal of the meniscus leads to accelerated osteoarthritis. Thus, new techniques designed to restore meniscal structure and function following injury are needed.

Mesenchymal stem cells (MSCs) are multipotent cells present in mature individuals and readily accessible from peripheral connective tissue sites such as bone marrow, periosteum, adipose, and the synovial lining of major joints. Among them, synovium-derived MSCs (synovial MSCs) are an attractive cell source for meniscal regeneration because they have high proliferative and chondrogenic potentials1. We first investigated whether intra-articular injection of synovial MSCs enhanced meniscal regeneration in a rat model of massive meniscectomy. The anterior half of the medial meniscus was excised, and undifferentiated synovial MSC suspension was injected intra-articularly. The results demonstrated that synovial MSCs adhered to sites of meniscal injury, differentiated into meniscal cells directly, and promoted meniscal regeneration without mobilization to distant organs2. We next investigated whether local administration of synovial MSCs enhanced meniscal regeneration in a rabbit model of partial meniscectomy. A 1.5-mm cylindrical defect was created in the avascular portion of the anterior horn of the medial meniscus, and synovial MSC suspension was placed directly into the meniscal defect for 10 min. Synovial MSCs adhered to sites of meniscal injury, differentiated into cells resembling meniscal fibrochondrocytes, and enhanced both quality and quantity of meniscal regeneration3. In order to allow clinical application of our method, we further examined whether administration of synovial MSCs promoted healing after meniscal repair of extended longitudinal tear of avascular area in a pig model. A longitudinal tear lesion was created in
medial menisci and sutured, and then a synovial MSC suspension was administered for 10 min. The result demonstrated that transplantation of synovial MSCs promoted morphological and biomechanical healing after meniscal repair with induction of synovium into the longitudinal tear in the avascular zone of meniscus. Our method has the following advantages: 1) the synovial tissues can be harvested easily from patient’s own knee joint by arthroscopically, 2) the cells can be expanded using patient’s own serum therefore minimizing the risk for transmission of infectious diseases or immunoreactions, 3) there is no requirement for scaffolds, and 4) the cells can be transplanted arthroscopically.

Based on these basic results, as a first step for clinical application, we have a plan to launch the clinical trial of transplantation of synovial MSCs in combination with surgical suture repair for the treatment of degenerative tear of the meniscus.

References:
(2) Horie M, Sekiya I, Muneta T, et al. Intra-articular Injected synovial stem cells differentiate into meniscal cells directly and promote meniscal regeneration without mobilization to distant organs in rat massive meniscal defect. Stem Cells 2008