Cartilage injury is a frequent problem, with recovery limited by incomplete natural healing mechanisms complicated by progression to osteoarthritis (OA), which leads to pain and dysfunction. This lack of effective healing of chondral defects has led to a need to develop new therapies to restore the articular surface to near normal.

Among the cell-based therapy, the most frequently employed technique is autologous chondrocyte implantation (ACI), with further advancements employing collagen membranes and third generation approaches utilizing cells seeded within bio-scaffolds rather than injection as a cell suspension. However, in a systematic review there was insufficient evidence to indicate superiority of ACI to non-cell based therapy with relatively short-term follow-up and most studies demonstrating no convincing differences (1). Recently, the isolation of mesenchymal stem cells (MSCs) from a variety of tissues and their promise in in vitro and in animal models has led to their relatively recent implementation in humans.

There are several methods of stem cell transplantation for cartilage repair. Among the techniques, a simpler, scaffold-free approach in which MSCs are delivered as a suspension by intra-articular injection has several potential advantages, including reduced recovery time and less cost (2-5). From a therapeutic perspective, intra-articular injection may be better matched to the pathogenesis of OA (6).

A crucial requirement for intra-articular therapy for OA is the delivery of MSCs to the defect site and engraftment. Previous studies have shown that intra-articularly injected MSCs can mobilize into injured tissues and participate directly in tissue repair, and also have beneficial paracrine effects that can induce a host repair response to replace the injured tissue (7, 8). One of the engraftment enhancing techniques is pretreatment of recipient cartilage using chondroitinase (9-11). Mesenchymal stem cell injection has been utilized as an adjunct to other arthroscopic procedures like mosaicplasty, microfracture or debridement. The exact mechanisms by which implanted MSCs retard the progression of OA are not known. However, it is clear that the implanted MSCs engraft into the defect site and are involved in tissue repair. In addition, MSCs can exert a great effect on local tissue repair by modulating the local environment and activating of endogenous progenitor cells (12).

Because MSCs can be receptive to transduction with various viral vectors, the limitations of current
MSC-based therapies for advanced or late OA might be overcome by the adaptation of MSC-based gene-transfer technologies (13, 14). Recently, the clinical application of genetically modified chondrocytes or MSCs has begun (15).

However, the complication rate and the problems of MSC-based therapy have received much attention. The safe cellular dose for OA therapy should be clarified, though no neoplastic complication was detected. Also, it is necessary to determine whether one injection will be sufficient to reach the desired result.

The potential use of MSCs in intra-articular injection therapy for chondral defects and OA has generated much enthusiasm, due to their trophic anti-inflammatory and other paracrine effects. Many clinical and animal studies have produced convincing data suggesting the prospect of the widespread clinical application of this therapy. However, we still have problems which must be resolved before the clinical application of the intra-articular injection of MSCs. Moreover, it is crucial to increase our understanding of the mechanisms by which MSCs affect the progression of OA or contribute to the pathogenesis of the disease.