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# Cartilage repair by amniotic fluid stem cell exosomes

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Mesenchymal stromal cells from the amniotic fluid (AFSCs) have been shown to favour tissue repair and regeneration after transplantation in rodent models of inflammatory-based disease. The benefits of transplanted amniotic cells were observed despite cell engraftment in injured tissue, thus suggesting these cells produce bioactive factors able to mediate these effects through paracrine signaling. It is increasingly more evident that the bioactive factors included into extracellular vesicles produced by amniotic cells (i.e. exosomes) can trigger tissue repair and regeneration through the resolution of inflammation by acting on different inflammatory mediators. Articular osteochondral defects are often associated with severe joint pain and progressive loss of joint function. The cartilage tissue engineering associated to stem cell-related therapies is becoming very interesting since adult articular cartilage has limited intrinsic capacity for regeneration upon injury.

Based on this state of the art, the main aim of this study was to explore the efficacy of the secreted exosomes, compared to their AFSC source, in animal model of osteoarthritis to mimic a chronic and degenerative process, a paradigm condition in which immune-related mechanisms are prominently involved and lead to irreversible joint damage.

In this study, osteochondral defects were created on rats knees with monoiodoacetate injection. After 3 weeks, the defect was treated with 100 $\mu$g exosomes or 5*105 cells derived from three amniocentesis. After 2 weeks exosome treatment was repeated. Analyses were performed by histology, immunohistochemistry, and behavioral scoring up to 4 weeks after the treatment.

Generally, exosome-treated defects showed enhanced behavioral test and improved histological scores than the AFSC-treated defects. Indeed by 4 weeks, TGFβ- rich exosome samples induced a complete restoration of cartilage with characteristic features including a hyaline cartilage with good surface regularity, showing extracellular matrix with GAG and collagen II, and complete bonding to adjacent cartilage. In contrast, there were only fibrous repair tissues found in the PBS-treated defects and initial cartilage close to fibrous tissues in AFSC-treated samples.

This study demonstrates for the first time the efficacy of human AFSC exosomes in cartilage repair, and a positive correlation with the content of TGFβ.

Key words

Exosomes stem cells, osteochondral defects.