

**THE STUDY OF THE THERAPEUTIC EFFECT OF GROWTH FACTORS AND  
SYNOVIUM-DERIVED MESENCHYMAL STEM CELLS INCAPSULATED IN  
HEPARIN-CONJUGATED FIBRIN HYDROGEL  
ON OSTEOCHONDRAL DEFECTS IN RABBITS**

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**Introduction.** Restoring of knee and hip joints osteochondral defects are still unsolved problem in traumatology and orthopedics. Because of the limited regeneration ability of cartilage and bone tissues after trauma or disease it leads to progressive loss of joint mobility or total loss ability to work, which in some cases even leads to disability.

Methods of stimulating the subchondral bone such as arthroplasty are used to create controlled microdamages in bone. However fibrous cartilage emerged after this does not reproduce the structural organization and functions of native hyaline cartilage.

The purpose of present study was to investigate the effect of synovial mesenchymal stem cells (MSCs), chondro- and osteoinductive growth factors (TGF-P1, BMP-4) and heparin-conjugated fibrin (HCF) hydrogel on regeneration of osteochondral defects in rabbits.

**Methods.** MSCs were isolated from synovium of Flemish giant rabbits. MSCs were characterized by CFU-assay, multi lineage differentiation and immunocytochemistry assays. HCF hydrogel was prepared by activating heparin and conjugating the activated heparin with fibrinogen to prepare heparin-conjugated fibrinogen. Osteochondral defects (4 mm in diameter) were performed under general calypsal anesthesia (5 mg/kg) using a kit for mosaic chondroplasty. HCF hydrogels containing MSCs and/or growth factors were examined in 7 combinations. Regeneration of osteochondral defects in control and experimental groups were analyzed macroscopically and histologically 90 days after HCF hydrogels implantation.

**Results.** *In vivo* studies revealed that application of HCF hydrogel with MSCs to the osteochondral defect formed fibrous cartilage tissue. Implantation of HCF hydrogel with MSCs and/or one of the growth factors (TGF-P1 or BMP-4) improved regeneration, however complete repair of cartilage layer and subchondral bone tissue was not observed after 90 days. Combined administration of synovial MSCs, BMP-4 and TGF-P1 encapsulated in HCF hydrogel completely restored osteochondral defect with hyaline-like cartilage and the subchondral bone tissue forming.

**Conclusion.** Thus, our study showed that combined application of synovium-derived MSCs, TGF-P1 and BMP-4 encapsulated in HCF hydrogel significantly promote regeneration of osteochondral defects in rabbits and will be a promising tissue engineering technique for cartilage and bone regeneration.