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Mechanically induced chondrogenesis of human bone marrow derived stem cells

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Bone marrow derived mesenchymal stem cells (MSCs) have been shown to offer great promise in regenerating defects of the musculoskeletal system. Beside growth factors, mechanical load is known to regulate the phenotypic fate decision in these cells. So far, a number of studies have shown beneficial effects of load on chondrogenesis of MSCs. However, the proper mechanical input still remains unknown. This study aimed to compare the chondrogenic response of compression and shear on MSC differentiation, while varying the cell number on the upper-surface of the construct in the absence of exogenous chondrogenic stimuli. In this set of experiments, human MSCs will be seeded into fibrin-polyurethane (PU) composite scaffolds. Human bone marrow derived MSCs were seeded into three-dimensional PU scaffolds (4 x 8 mm) at a cell density of 4 x 106 per scaffold. Constructs were cultured in Dulbecco's modified Eagle's Medium (DMEM) with no exogenous transforming growth factor-β (TGF-β). Scaffolds were exposed to 15 loading cycles over 3 weeks, thereby assigned to 4 groups: Group A was exposed to compression and shear 4 milions MSC cells seeded into the scaffold. Group B was the free-swelling 4 milions MSC cells seeded into the scaffold (unloaded) control. Group C was exposed to compression and shear 3.6 milions MSC cells seeded into the scaffold plus 400 thousands MSC cells seeded on the top. Group D was the free-swelling 3.6 milions MSC cells seeded into the scaffold plus 400 thousands MSC cells seeded on the top (unloaded) control. Measurements included DNA, glucosaminoglycan (GAG), Elisa analysis, histology, himmunohistochemistry and mechanical competence. In addition, mRNA expression of chondrogenic markers (collagen type-II (Col 2), Aggrecan (AGG), osteogenic markers (collagen type-I (Col 1), alkaline phosphatase (ALP) and hypertrophic markers (collagen type-X (Col 10)) were assessed. Mechanical load and shear led to an increase in all the chondrogenic genes investigated with the greatest effect in group C. On mRNA level, AGG and Col 2 were upregulated to a greater extend in loaded groups compared to no loaded groups. This was reflected in the histological analysis, where only the group C showed a matrix rich in glucosaminoglycan staining. These results highlight that Group C was exposed to compression and shear 3.6 milions MSC cells seeded into the scaffold plus 400 thousands MSC cells seeded on the top demonstrated to mechanically induce in vitro chondrogenesis of MSCs. This is important knowledge for the repair of musculoskeletal disorders, whereby the same cell type (MSC) can induce bone repair as well as cartilage repair depending on the mechanical cues. Furthermore, this insight provides valuable information to optimise rehabilitation procedures to be used after implantation of MSCs for cartilage repair.

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