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Differentiation potential and ectopic cartilage formation capacity of human mesenchymal stem cells derived from bone marrow, adipose tissue and synovium

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Introduction:

Mesenchymal stem cells (MSC) are suitable candidates for the cell-based reconstruction of different tissues including cartilage and have been isolated from different sources such as synovium, adipose tissue and bone marrow. These cells were assumed to be similar with regard to self-renewal, multidifferentiation potential and surface epitopes. For the clinical application of MSCs for articular cartilage repair, functional suitability and phenotypic stability are crucial factors. In this study, we compared the *in vitro* differentiation capacity of MSC derived from bone marrow, adipose tissue and synovium and their ectopic cartilage formation capacity.

Materials and Methods:

MSC were isolated from adipose tissue (ATSC), bone marrow (BMSC) and synovium (SMSC) and were cultured under chondrogenic, osteogenic and adipogenic conditions. Differentiation was evaluated based on histochemical staining,

immunohistology and gene expression analysis. After 5 weeks of chondrogenesis, MSC were transplanted subcutaneously into SCID mice. Four weeks later, explants were analysed by histology.

Results:

ATSC and SMSC showed reduced chondrogenic differentiation potential compared to BMSC and required combined application of TGF-beta 3 plus BMP-6 for successful chondrogenic differentiation. Chondrogenesis was always associated with up-regulation of hypertrophic markers like Col X. *In vivo*, explants derived from ATSC and BMSC remained positive for proteoglycans and Col II and underwent calcification. SMSC-derived explants showed a more heterogenic differentiation pattern: some explants were positive for proteoglycans and Col II, while others were positive for proteoglycans but negative for Col II. Remarkably, explants derived from two of five SMSC populations lost the Col II revealed at transplantation time, while proteoglycans

persisted. These Col II negative SMSC transplants were negative for calcification.

Discussion and Conclusions:

Our findings indicate that adipose tissue, bone marrow and synovium provide heterogenous MSC populations. SMSC, like ATSC, required more stringent conditions for chondrogenesis when compared with BMSC. None of the *in vitro* differentiated ATSC and BMSC populations were able to form stable ectopic cartilage with resistance to vascular invasion and calcification. Transplants underwent alterations related to endochondral ossification rather than adopting a chondrogenic phenotype typical for articular cartilage. Since calcification was confined to Col II positive areas in SMCS explants, the persistent presence of Col II may be relevant for mineralization.

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