multifunctional NP platform has the potential to advance translation of stem cell-based therapies, by improving stem cell function and consistency via engineering and magnetic selection of cells, and providing tools to monitor cells in a clinically relevant manner.

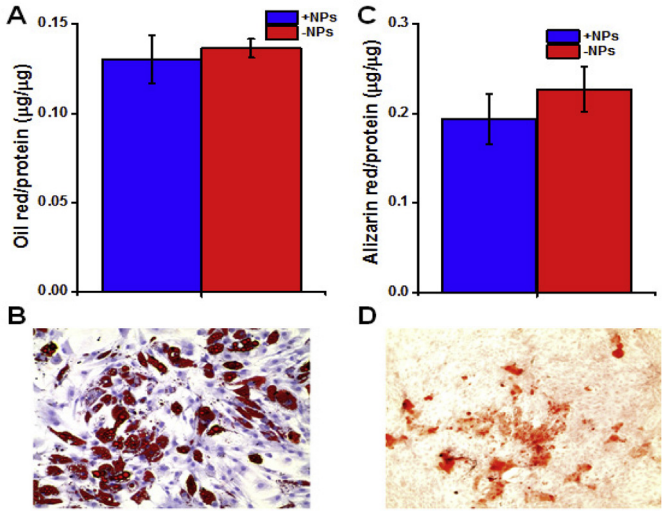

Fig. l: Multipotency of magPLGA NPs loaded MSC. (A) Quantified oil red stain for adipogenesis and (B) image of adipocytes differentiated from magPLGA loaded MSCs. (C) Quantification of Alizarin red stain for osteogenesis of magPLGA loaded and unloaded NPs. (D) Image of Alizarin red stained osteocytes differentiated from magPLGA NP loaded cells.

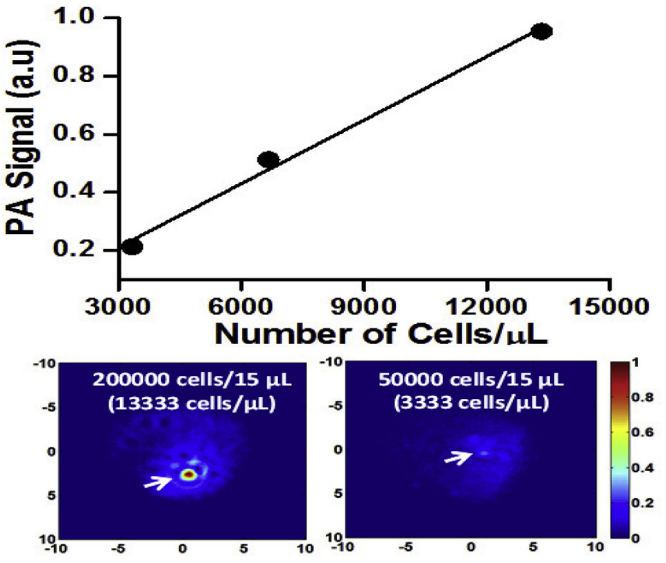

Fig. 2: Photoacoustic imaging of magPLGA-loaded. MSCs. Alinear correlation exists between cell number and PA signal. R2 = 0.95.

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HUMAN UMBILICAL CORD BLOOD-DERIVED MESENCHYMAL STEM CELLS AND HYALURONIC ACID HYDROGEL COMPOSITE PROMOTES THE ARTICULAR CARTILAGE REPAIR IN A RABBIT MODEL

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Purpose: Human umbilical cord blood-derived mesenchymal stem cells (hUCB-MSCs) have gained great interest as a promising cell source for regenerative medicine due to non-invasive collection, readily availability, high expansion capacity, and low immunogenicity. We investigated the feasibility of transplanting hUCB-MSCs and a hyaluronic acid (HA) hydrogel composite to repair full-thickness articular cartilage defects and determine whether the transplanted cells disappeared from the defect site.
Methods: Full-thickness osteochondral defects (3 mm in diameter and 3 mm depth) were created in the trochlear groove of the femur. A composite of hUCB-MSCs (0.5 × 107 cells/mL) and 4% HA hydrogel was transplanted into the full-thickness defect in the experimental knee (right knee), whereas 4% HA hydrogel without hUCB-MSCs was transplanted into the control knee (left knee). Animals were sacrificed at 8 and 16 weeks post-transplantation. The articular cartilage defect repair was evaluated grossly and histologically. Histological images were assessed with the modified O'Driscoll score. The mouse anti-human nuclei monoclonal antibody was applied to tissues for cell tracking analysis.
Results: Transplanting hUCB-MSCs and a HA hydrogel composite resulted in overall superior cartilage repair tissue with better quality than HA alone or no treatment. Cellular architecture and collagen arrangement at 16 weeks were similar to those of surrounding normal articular cartilage tissue. The histological scores also revealed that cartilage repair in experimental knees were better compared to control knees. The grafted cells were tracked by immunohistochemistry using anti-human nuclei antibody after transplanting the cells. Anti-human nuclei antibody staining revealed gradual decrease of the transplanted cells at the region of the cartilage defect in 2, 4, and 8 weeks post-transplantation.
Conclusions: This study demonstrated that hUCB-MSCs and a 4% HA hydrogel composite resulted in favorable cartilage repair grossly and histologically compared to HA only and defect only in a rabbit model. The transplanted cells disappeared in the repair tissue over time, which supported the paracrine action of transplanted MSCS for cartilage repair rather than direct differentiation. These findings suggest that transplanting hUCB-MSCs and a HA hydrogel composite can be a novel therapeutic modality to treat full-thickness cartilage defects.

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DIFFERENCES IN THE RESPONSE OF MESENCHYMAL STEM CELLS FROM HEALTHY DONORS AND OA PATIENTS TO EXOGENOUS GDF5 DURING CHONDROGENIC DIFFERENTIATION

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Purpose: The first osteoarthritis (OA) susceptibility locus reported as achieving compelling, genome-wide significance was to the growth differentiation factor 5 gene GDF5, with the genetic risk mediating reduced expression of this anabolic gene. In a previous study, we reported that chondrocytes derived from OA patients do not respond in a predictable manner to exogenous supplementation with GDF5 protein. Stem cell based therapies are emerging as a potential means for cartilage regeneration in OA. Hence, we chose to study the response of healthy donor and OA patient derived mesenchymal stem cells (MSCs) to exogenous GDF5 protein during chondrogenic differentiation.
Methods: Bone marrow derived MSCs from three healthy donors (isolated from the iliac crest) and four OA patients (isolated from the femoral head) were expanded and differentiated to chondrocytes in the presence or absence of wildtype recombinant human GDF5 protein (100 ng/ml) for 7 days using the Transwell culture system. We also studied a variant form of GDF5 protein (100 ng/ml) that binds preferentially to BMPR-IA, an alternative Type I receptor, which is more abundantly expressed than BMPRIB in chondrocytes. Cartilage discs were harvested at days 3 and 7, RNA was extracted and cDNA was synthesised. The wet mass of the discs was also measured at both time points. Cartilage marker gene expression was analysed by quantitative PCR (qPCR).
Results: The wet mass observed in cartilage discs derived from healthy donors was higher than that from OA patients at day 3 and 7, after both GDF5 treatments. The expression of the relevant GDF5 receptor genes BMPRII, BMPRIA and BMPRIB was confirmed by qPCR. Treatment with the two types of GDF5 protein resulted in gene expression changes in anabolic markers (ACAN and SOX9), catabolic markers (ADAMTS4, ADAMTS5, MMP1 and MMP13) and hypertrophic markers (COL1A1 and RUNX2). We observed consistent changes in gene expression in response to GDF5 in healthy donor and in OA patient MSCs. In healthy MSCs, SOX9 showed a consistent upregulation at day 7 in response to both types of exogenous GDF5 proteins. In OA MSCs, MMP13 and the bone specific RUNX2 transcript were both upregulated at day 3 in response to both GDF5 treatments. There was however no significant trend in gene expression of any of the target genes that persisted through the time course studied. Furthermore, the only consistency observed between the healthy donor and OA patient MSC groups was