Figure 1. Effects of LOR on the quantity of the cartilage catabolism end products glycosaminoglycan (GAG) and nitric oxide (NO) in supernatants. Exosome-stimulated cultures stimulated with pro-inflammatory cytokines were subsequently treated with DMSO (control) or LOR as shown.  \(N=22;^{*} P<0.05, ^{**} P<0.01, ^{***} P<0.001 \) vs. DMSO by one-way ANOVA.


AB0071

THERAPEUTIC EFFECTS OF BONE MARROW MESENCHYMAL STEM CELLS DERIVED EXOSOMES ON OSTEOARTHRITIS

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Background: Mesenchymal stem cells (MSCs) have shown chondroprotective effects in clinical models of osteoarthritis (OA)1, 2.

Objectives: The study aimed to investigate the therapeutic potential of exosomes from human bone marrow MSCs (BM-MSCs) in alleviating OA.

Methods: The anterior cruciate ligament transection (ACLT) and destabilization of the medial meniscus (DMM) surgery were performed on the knee joints of 30 OA rats. BM-MSCs were harvested from human bone marrow MSCs (BM-MSCs) in non-invasive OA models. In vitro, BM-MSCs were stimulated with pro-inflammatory cytokines (IL-1 \( \beta \), TNF-\( \alpha \)) to observe the functional and molecular alterations. In addition, exosomal RNA was investigated in conditioned media to explore the biological contents accounting for anti-OA effects of BM-MSCs-derived exosomes.

Results: Based on the observation in the OA rat model, both of BM-MSCs and BM-MSCs-derived exosomes alleviated cartilage degradation, reduced joint damage and restored the trabecular bone of OA rats. In addition, in vivo assays showed that BM-MSCs-exosomes could maintain the chondrocyte phenotype by increasing collagen type II synthesis and inhibiting IL-1 \( \beta \) by increasing collagen type II synthesis and inhibiting IL-1 \( \beta \) damage and restored the trabecular bone of OA rats. In addition, lncRNA MEG3 were investigated in chondrocytes to explore the biological contents accounting for anti-OA effects of BM-MSCs-derived exosomes.

Conclusion: The exosomes from BM-MSCs exerted beneficial therapeutic effects on OA by reducing the senescence and apoptosis of chondrocytes, suggesting that MSCs-derived exosomes might provide a candidate therapy for OA treatment.


AB0072

A MULTICOMPONENT MEDICATION PROMOTES CHONDROGENESIS AND REDUCES MMP-13 IN PRIMARY ARTICULAR CHONDROCYTES FROM KNEE OSTEOARTHRITIS PATIENTS IN VITRO

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Background: HE-1100 is a multicomponent medicinal product. Initial preclinical data potentially suggest a preventive effect on cartilage degradation.

Objectives: This study aims to understand the mode of action of HE-1100 on OA chondrocytes in vitro.

Methods: Primary chondrocytes were obtained from 10 knee osteoarthritis (OA) patients undergoing knee replacement surgery. The cultures were treated with 20% (v/v) HE-1100 or placebo. Samples were collected for subsequent RNA extraction using standard methods. The reads were generated with Illumina NextSeq5000 sequencer and aligned to the human reference genome (UCSC hg19) to generate the transcriptome. Differential expression analysis between HE-1100 and placebo was made in R using the DESeq2 package to identify the differentially expressed genes in the OA-associated regulatory pathways. The protein production of the selected genes was quantified by ELISA in 10 independent human OA chondrocytes cultures.

Results: According to the DESeq2 analysis, HE-1100 significantly modified the expression of 13 genes in OA chondrocytes by at least 10% with an adjusted p-value < 0.05: EGFR (+93%), FOS (+87%), NLR3A1 (+43%), DUSP1 (+18%), ZFP36 (+18%), ZFPS6L1 (+14%), NFkBZ (+16%) and CYR61 (+14%) were upregulated and ATFP7P (-10%), TNXP1 (-11%), C10orf10 (-12%), CLEC3A (-12%) and MMP13 (-18%) were downregulated after 24 h HE-1100 treatment. HE-1100 significantly increased (2.3-fold +/-1.2 after 24 h, p=0.0444 and 2.3-fold +/-1.0 after 72 h, p=0.0239) the CYR61 protein production by human OA chondrocytes. After 72 h, HE-1100 slightly but not significantly increased aggrecan production by 14 % (p=0.1117) and significantly increased type II collagen pro-peptide production by 27 % ± 0 % (p=0.1474). For both time points CYR61 protein by OA chondrocytes was positively and significantly correlated with aggrecan (r=0.66, p=0.0004) and type II collagen pro-peptide (r=0.64, p=0.0008) production. In alginate beads culture, pro-MMP-13 was significantly decreased by HE-1100 treated cultures from day 7 to day 14 (from -16 to -25 %, p<0.05) and from day 17 to 21 (-22 %, p=0.0331) in comparison to controls.

Conclusion: HE-1100 significantly modified the expression of DUSP1, C10orf10, ZFP36/L1 and CLEC3A, which are pathway mediators involved in MMP-13 expression and activation. Further, long-term (28 days) treatment with HE-1100 significantly reduced the production of pro-MMP-13, the inactive precursor of the metalloproteinase MMP-13 involved in type II collagen degradation. HE-1100 also promoted extracellular matrix formation probably through CYR61 production, a growth factor well correlated with type II collagen and aggrecan production.


AB0073

BOSWELLIA SERRATA EXTRACT AND CURCUMIN INCREASE GDF15 PRODUCTION BY HUMAN PRIMARY OSTEOARTHRITIS CHONDROCYTES: A NEW MECHANISM OF ACTION

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Background: Boswellia serrata extract (BSE) and curcumin are used to relieve symptoms in osteoarthritis (OA). Objectives: This study aims to better understand the mode of action of these compounds on OA chondrocytes in vitro.

Methods: Therapeutic plasmatic concentrations of the different components of BSE correspond to an in vitro range from 25 to 100 µg/ml of total BSE (100 µg/ml of BSE corresponds to 9.2 µM of 11-keto-β-boswellic acid (KBA), 5.2 µM of acetylKBA, 22 µM de oBA, 34 µM de βBA, 4.4 µM de acetylβBA and 13.2 acetyl βBA), and between 2 to 10 µM for bioavailability increased curcumin. BSE (5-100 µg/ml) and curcumin (0.04 to 4 µg/ml corresponding to 0.1 to 10 µM) were tested separately on primary chondrocytes from 3 OA patients. Lactate Deshydrogenase LDH, nitrite (NO\(_x\)), interleukin (IL)-6 and Growth Differentiation Factor (GDF)15 were quantified in 72-h treated supernatant using enzyme activity, Griess reaction and ELISAs, respectively.

Results: No mortality was observed at the tested concentrations. BSE and curcumin both decreased concentration-dependently NO\(_x\) and IL-6 production, and increased GDF15 production. For NO\(_x\) production, the decrease was observed from 0.2 µg/ml of curcumin and 10 µg/ml of BSE. For IL-6 production,