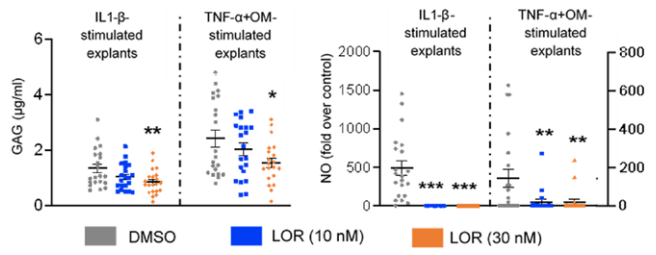

Figure 1. Effects of LOR on the quantity of the cartilage catabolism end products glycosaminoglycan (GAG) and nitric oxide (NO) in supernatants. Knee cartilage explant cultures stimulated with pro-inflammatory cytokines were subsequently treated with DMSO (control) or LOR as shown. N=22; *P<0.05, **P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

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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].
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) anddestabilization of the medial meniscus (DMM) surgery were performed on the knee joints of a rat OA model, followed by intra-articular injection of BM-MSCs or their exosomes. The beneficial effects were evaluated by histological staining, OARSI scores and micro-CT. Furthermore, BM-MSCs-derived exosomes were administrated to primary human chondrocytes to observe the functional and molecular alterations. In addition, lncRNA MEG3 were investigated in chondrocytes to explore the biological contents accounting for anti-OA effects of BM-MSCs-derived exosomes.
Results: Based on the observation in the rat OA model, both of BM-MSCs and BM-MSCs-derived exosomes alleviated cartilage destruction, reduced joint damage and restored the trabecular bone of OA rats. In addition, *in vitro* assays showed that BM-MSCs- exosomes could maintain the chondrocyte phenotype by increasing collagen type II synthesis and inhibiting IL-1β- induced senescence and apoptosis. Furthermore, exosomal lncRNA MEG3 also reduced the senescence and apoptosis of chondrocytes induced by IL-1β, indicating that lncRNA MEG3 might partially account for the anti-OA effects of BM-MSC 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.
References:
[1] Mckinney J M, Doan T N, Wang L, et al. Therapeutic efficacy of intra-articular delivery of encapsulated human mesenchymal stem cells on early stage osteoarthritis[J]. Eur Cell Mater, 2019, 37: 42-59.
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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: EGR1 (+93%), FOS (+87%), NR4A1 (+43%), DUSP1 (+18%), ZFP36 (+18%), ZFP36L1 (+14%), NFKBIZ (+16%) and CYR61 (+14%) were upregulated and ATF7IP (-10%), TXNIP (-11%), C10orf10 (-12%), CLEC3A (-12%) and MMP13 (-18%) were downregulated after 24h HE-1100 treatment. HE-1100 significantly increased (2.3 fold +/-1.2 after 24h, p=0.0444 and 2.3-fold +/-1.0 after 72h, p=0.0239) the CYR61 protein production by human OA chondrocytes. After 72h, HE-1100 slightly but not significantly increased aggrecan production by 14 ± 19 % (p=0.1117) and significantly increased type II collagen pro-peptide production by 27 ± 20 % (p=0.0147). For both time points CYR61 production 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.
References: /
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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 relief 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 αBA, 34 µM de βBA, 4.4 µM de acetylαBA and 13.2 acetyl βBA), and between 2 to 10 µM for bioavaibility-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_2), interleukin (IL)-6 and Growth Differentiation Factor (GDF)15 were quantified in 72h-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_2 and IL-6 production, and increased GDF15 production. For NO_2 production, the decrease was observed from 0.2 µg/ml of curcumin and 10 µg/ml of BSE. For IL-6 production,