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. Their therapeutic potential is further enhanced by exosomes released by MSCs (BM-MSCs-exosomes) in vitro2,3. However, in vivo efficacy of BM-MSCs-exosomes remains to be clarified. Therefore, we aimed to investigate the therapeutic potential of BM-MSCs-derived exosomes in a rat model of OA.

Objectives: To explore the biological effects of BM-MSCs-derived exosomes in OA rat model.

Methods: 40 adult SD rats were randomized into 4 groups: sham, OA induced by anterior cruciate ligament transection (ACLT) and destabilization of the medial meniscus (DMM), and OA treated with BM-MSCs-exosomes. Knee joints were harvested at 12 weeks after induction, and the mechanical and degenerative features were evaluated.

Results: OA induced by ACLT and DMM surgery demonstrated OA symptoms in the OA rats, including increased mechanical stress and decreased matrix integrity. BM-MSCs-exosomes treatment significantly reduced the mechanical and degenerative features of OA, as evidenced by increased collagen type II synthesis and decreased cartilage degeneration. The beneficial effects of BM-MSCs-exosomes were further substantiated by histological analysis, immunohistochemistry, and RNA sequencing.

Conclusion: BM-MSCs-exosomes show potential therapeutic effects in OA rats. These results support the further investigation of BM-MSCs-exosomes for the treatment of OA.

Disclosure of Interests: The authors declare no conflict of interest.

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

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

Methods: Primary osteochondrocytes were obtained from 10 knee osteoarthritic (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%), NAR4A (+43%), DUSP1 (+18%), ZNF36 (+16%), ZFP36L1 (+14%), NFKBZ (+16%) and CRYF1 (+14%) were upregulated and AT7PP1 (-10%), TNX1 (-11%), C10orf10 (-12%), CLECSA (-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 CYRF61 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 CYRF61 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, ZFP36L1 and CLECSA, 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.

Disclosure of Interests: The authors declare no conflict of interest.

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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 as adjuvants in osteoarthritis (OA) treatment. We aimed to investigate the biological effects of BSE and curcumin on human primary osteoarthritic chondrocytes and to identify potential signaling pathways involved in their anti-arthritic effects.

Objectives: To investigate the effects of BSE and curcumin on human primary osteoarthritic chondrocytes and to identify potential signaling pathways involved in their anti-arthritic effects.

Methods: Chondrocytes were isolated from human osteoarthritic knee joints and cultured in vitro. The effects of BSE and curcumin on the production of GDF15 were tested using ELISA and mass spectrometry. The potential signaling pathways involved in the observed effects were identified using gene expression analysis.

Results: BSE and curcumin significantly increased GDF15 production by human primary osteoarthritic chondrocytes. The effects were dose-dependent and the maximum increase was observed at 100 µg/ml of BSE and 4 µg/ml of curcumin. Gene expression analysis using RNA sequencing revealed that both BSE and curcumin induced the expression of several genes associated with chondroprotection, including IL-10, IL-1RA, and IL-4.

Conclusion: BSE and curcumin induce the production of GDF15 in human primary osteoarthritic chondrocytes, suggesting a novel mechanism of action for these compounds in the treatment of OA.

Disclosure of Interests: None declared.

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OSTEOARTHRITIS PATIENTS IN VITRO CHONDROCYTES: A NEW MODEL OF ACTION

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Background: Human osteoarthritic chondrocytes (OAC) are a suitable model for the study of OA pathogenesis. We aimed to investigate the effects of IL-1β on human primary osteoarthritic chondrocytes and to identify potential signaling pathways involved in the observed effects.

Objectives: To investigate the effects of IL-1β on human primary osteoarthritic chondrocytes and to identify potential signaling pathways involved in the observed effects.

Methods: Human primary osteoarthritic chondrocytes were cultured in vitro and treated with IL-1β at different concentrations. The effects of IL-1β on the production of several inflammatory cytokines and matrix metalloproteinases were tested using ELISA and real-time PCR.

Results: IL-1β induced a dose-dependent increase in the production of several inflammatory cytokines, including IL-6 and TNF-α, and matrix metalloproteinases, including MMP-13. Gene expression analysis revealed that IL-1β induced the expression of several genes associated with inflammation and cartilage degradation, including IL-1RA, IL-6, and MMP-13.

Conclusion: IL-1β induces the production of inflammatory cytokines and matrix metalloproteinases in human primary osteoarthritic chondrocytes, suggesting a novel mechanism of action for these compounds in the treatment of OA.

Disclosure of Interests: None declared.

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