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 exosomes from BM-MSCs exerted beneficial therapeutic effects in OA rat 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, IncRNA MEG3 was 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 IncRNA MEG3 also reduced the senescence and apoptosis of chondrocytes induced by IL-1β, indicating that IncRNA MEG3 might partially account for the anti-OA effects of BM-MSC exosomes.

Conclusion: The exosomes from BM-MSCs exerted beneficial therapeutic effects in 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. Eur Cell Mater. 2019; 37: 42-59.

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AB0073

BOSWELLA 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 of deBSE, 34 µM of deBSE, 4.4 µM of deacetyloxyA and 13.2 acetylate), and between 2 to 10 µM for bioavailability-functional and bioavailability-growth factors. CSE (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 dehydrogenase (LDH), nitrite (NO2), interleukin (IL)-6 and Growth Differentiation Factor (GDF15) 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 NO2 and IL-6 production, and increased GDF15 production. For NO2 production, the decrease was 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.

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