therapeutic potential of exosomes from human bone marrow MSCs (BM-MSCs) in alleviating OA.

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

Methods: The anterior cruciate ligament transaction (ACL-T) and destabilization 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.

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-MSCs-derived 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:

Disclosure of Interests: None declared.

DOI: 10.1136/annrheumdis-2020-eular.6346
the decrease was observed from 1 µg/ml for curcumin and 10 µg/ml for BSE. For GDF-15, the increase was observed from 2 µg/ml for curcumin and 50 µg/ml for BSE. Maximal effect was observed at 4 µg/ml for curcumin: -67% NO$_2$ (p=0.0001) and -71% IL-6 (p=0.0001) and +84% GDF15 (p=0.0001) and at 100 µg/ml for BSE: -40% NO$_2$ (p=0.0003), -70% IL-6 (p=0.0003) and +73% for GDF15 (p=0.0017).

Conclusion: At therapeutic plasmatic concentrations, BSE and curcumin decreased the production of NO$_2$ and IL-6, two inflammatory mediators. Furthermore, BSE and curcumin enhanced GDF-15 production, an anti-inflammatory growth factor, GDF15 was first identified that Macrophage inhibitory cytokine-1 or NSAID-activated gene-1 (by a prostanoi-independent manner), and is known as a regulator of inflammatory, cell repair and apoptosis pathways. GDF-15 has pro-apoptotic and anti-tumorigenic activity in vitro and in vivo. It could represent a new pathway explaining the beneficial effects of BSE and the curcumin on synovium inflammation and cartilage degradation.

Disclosure of Interests: christelle sanchez: None declared, Jérémie Zappia: None declared, Yvan Dierckxsens Shareholder of: Tilman SA, Employee of: Tilman SA, Jean-Pierre Delcour: None declared, Yves Henrotin Grant/research support from: HEEL, TILMAN

DOI: 10.1136/annrheumdis-2020-eular.3457

AB0074 KRÜMPPEL-LIKE FACTOR 10 IS A IMPORTANT MODULATORY FACTOR OF CHONDROCYTE HYPERTROPHY IN DEVELOPING SKELETON

J. Y. Ko, E. Lee, J. Kim, G. I. Im, Research Institute for Integrative Regenerative Biomedical Engineering, Dongguk University, Goyang, Korea, Rep. of (South Korea)

Background: To investigate the functional role of KLF10 as a modulator of chondrocyte hypertrophy in developmental skeleton, the developmental characteristics in the long bone of KLF10 knockout mice and characteristics of MSCs from KLF10 KO mice were investigated regarding chondrogenesis and osteogenesis. Delayed long bone growth and delayed formation of primary ossification center were observed in an early embryonic stage in KLF10 KO mouse along with very low Ihh expression in epiphyseal plate. While the chondrogenic potential of mMSCs appeared normal or slight decreased in KLF10 KO mice, osteogenesis and hypertrophy were extensively suppressed. KLF10 was found to be a mediator of chondrocyte hypertrophy in developing skeleton. Suppression of KLF10 may be considered as a new strategy for preventing hypertrophy in cartilage regeneration using MSCs.

Objectives: Investigated the functional role of KLF10 to present new insights into the transcriptional network regulating skeletal development and provide a novel strategy for preventing aberrant hypertrophic differentiation in cartilage regeneration strategies using MSCs.

Methods: Generation of KLF10 KO mice and genotyping / Skeletal preparations, embryo heights, and mineralized bone length measurements / Histological and Fluorescent Immunohistochemical Analysis / ALP staining and activity / Alizarin red staining / Von Kossa staining and calcium salts quantification / Isolation and Establishment of Mouse Cional MSC Lines / Chondrogenic pellet culture and differentiation of mMSCs / DNA Quantification and GAG Contents Analysis / qPCR Analysis / Statistics

Results: The overall results showed that mMSCs from KLF10 KO mice have significantly decreased osteogenic potential with very low Ihh expression while an increase in chondrogenic potential was not significant. In addition to Ihh promoter demonstrated in our previous study, KLF10 can activate Runx2 expression through its proximal-promoter region. Thus, KLF10 may indirectly stimulate Ihh expression upstream of Runx2 or directly bind to Ihh promoter and activate Ihh expression. As shown in this and our previous study, KLF10 also enhances Wnt/β-catenin signalling in MSCs. KLF10 modulates β-catenin sub-cellular localization and enhances Wnt signalling in osteoblasts.

Conclusion: In conclusion, primary ossification in KLF10 KO mice was critically delayed during early endochondral bone development. KLF10 KO inhibited hypertrophy via reduced Ihh expression in developing skeleton. TGF-β-induced hypertrophy was inhibited during chondrogenesis of KLF10 KO mMSCs. Our findings present new insights into the transcriptional-network system of skeletal development and provide a novel strategy for suppressing hypertrophy in cartilage tissue engineering.

AB0075 SYNOVIAL TISSUE MACROPHAGES ARE DOMINANTLY ALTERNATIVELY ACTIVATED IN PATIENTS WITH MATURE OSTEOARTHRITIS

G. Laskarin, T. Kehler, D. Legovic, V. Šantić, B. Curko-Cofek, M. Rogozinica, D. Rukavina, Faculty of Medicine, University of Rijeka, Department of Physiology and Immunology, Rijeka, Croatia, 2Hospital for Medical Rehabilitation of Health and Lung Diseases and Rheumatism "Thalassotherapia-Opatija"; Opatija, Croatia, 3Faculty of Medicine, University of Rijeka, Department of Medical Rehabilitation, Opatija, Croatia; 4Orthopaedic University Hospital - Lovran, Lovran, Croatia; 5Clinical Hospital Centre Rijeka, Clinical Department of Laboratory Diagnostics, Rijeka, Croatia, 6Hospital for Medical Rehabilitation of Heart and Lung Diseases and Rheumatism "Thalassotherapia-Opatija"; Rijeka, Croatia; 7Croatian Academy of Sciences and Arts, Department of Biomedical Sciences in Rijeka, Opatija, Croatia

Background: Macrophages are abundant inflammatory cell type in the synovial membrane of knee osteoarthritis (OA) (1). Their quantity is associated with radiographic severity of knee OA and joint symptoms (2), while their functions are set in response to micro-environmental signals (3). Classically activated macrophages M1 support T helper 1 (Th1) driven pro-inflammatory reactions, while alternatively activated macrophages M2 strengthen Th2 inflammatory processes (3).

Objectives: To investigate activation status of synovial tissue macrophages in patients with mature OA in terms of M1 / M2 polarization.

Methods: Synovial tissue samples (6) with abundant lymphocyte infiltration were obtained during alloarthroplasty. Double immunofluorescence labeling was performed on paraffin-embedded synovial tissue sections using primary rabbit anti-macrophage CD68 mAb and mouse anti-human antibodies directed toward CD3, arginase-1, TNF-alpha and IL-15. CD206 and CD163 were single labelled.

Results: CD68+ macrophages mostly co-expressed arginase-1 (4/6 samples), indicating their M2 orientation. Macrophages were placed in lining synovial tissue and nearby tissue-resident CD3+ cells. M2 markers CD206 and CD163 were