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% NO2 (p<0.0001), -71% IL-6 (p<0.0001) and +80% GDF15 (p<0.0001) and at 100 µg/ml for BSE: -40% NO2 (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 NO2 and IL-6, two inflammatory mediators. Furthermore, BSE and curcumin enhanced GDF-15 production, an anti-inflammatory growth factor. GDF15 was first identified as Macrophage inhibitory cytokine-1 or NSAID-activated gene-1 (by a prostanoïd-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, Jérémy 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 SA, Jean-Pierre Delcour: None declared, Yves Henrotin

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**Background:** To investigate the functional role of KLF10 as a modulator of chondrocyte hypertrophy in developing 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 Clonal MSC Lines / Chondrogenic pellet culture and differentiation of mMSCs / DNA Quantification and GAG Contents Analysis / Rq-PCR 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 out 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 mouse 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.

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**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 alopexithrapy. Double immunofluorescence labeling was performed on paraffin-embedded synovial tissue sections using primary rabbit anti-macrophage CD68 mAb in combination with mouse anti-human antibodies directed toward CD3, arginase-1, TNF-α 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...
found in the area of macrophage interaction with T cells. CD68+ cells co-expressing TNF-alpha or IL-15 M1 markers were in minority in these synovial tissues. Lymphocyte infiltration was less abundant in remaining (2/6) synovial tissue samples.

Conclusion: Mature synovial tissue macrophages, equipped dominantly with arginase-1 are M2 oriented and might support Th2 immune response in surrounding T cells.

References:


Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.3896

AB0076 SPATIAL VARIATIONS OF BONE MICROARCHITECTURE AND MINERALIZATION IN HIP OSTEOARTHRITIS AND OSTEOPOROSIS

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Background: The pattern of changes in bone microarchitecture and mineralisation are distinctly different in osteoarthritis (OA) and osteoporosis (OP). However, the pathogenesis of OA is closely related with OP, making subchondral bone a promising target for OA treatment [1]. A detailed comparison of subchondral bone in OA and OP may help understand the relationship of the two diseases.

Objectives: To carry out a comprehensive analysis of regional and compartmental variations in subchondral bone architecture and mineralisation in OA and OP.

Methods: Femoral heads were collected from patients undergoing hip arthroplasty surgeries for hip OA (N=16) or osteoporotic fracture (N=7). For OP group, osteochondral plugs were collected from fixed sites: anterior, posterior and superior. For OA group, an optimised sampling procedure, based on a new macroscopic grading method and modified OARSI macroscopic grading system, was used to collect plugs from regions with varying severity of cartilage degradation. Plugs were scanned by micro CT (voxel size 4.88µm). Regions of interest for cortical plate (Ct) and trabecular bone (Tb) were segmented from reconstructed images using semi-automatic approach. Densitometric (tissue and bone mineral density: TMD and BMD) and architectural parameters (cortical plate thickness (Ct.Th), trabecular bone volume fraction (BV/TV), trabecular thickness (Tb.Th), etc.) were measured using commercially available software. Unmatched inter-group regional comparisons were made between OA microscopic grades (1 to 4) and OP. Matched intra-sample regional analysis was made between ‘mild’ (Grade 1 and/or 2) and ‘severe’ (Grade 3 and/or 4) OA. TMD was also subjected to paired comparison between cortical (Ct.TMD) and trabecular (Tb.TMD) compartments. Correlations between densitometric and architectural parameters were also explored.

Results: Regional analysis showed that Tb.TMD in OA Grade 3 and 4 was significantly lower than in OP and Grade 1 and 2, while Tb.TMD in OP was not significantly different from OA Grade 1 and 2 (Fig 1A, F). Ct.TMD in OA Grade 4 was significantly lower than in OP, but no difference was found in other comparisons (Fig 1B, G). For BMD of trabecular bone (Tb.BMD) and architectural parameters including BV/TV and Ct.Th, values for OA Grade 3 and/or 4 were significantly higher than OP and Grade 1 and/or 2, but the difference between OP and Grade 1 and 2 was not significant (Fig 1C-E, H-J). Compartmental analysis showed that Ct.TMD was significantly lower than Tb.TMD in all groups (Table I). Tb.TMD was inversely correlated with Tb.BMD and BV/TV in both OA and OP; Ct.TMD and Tb.TMD were inversely associated with Ct.Th and Tb.Th respectively in OA (Table II).

Conclusion: In both OA and OP, material density (TMD) of cortical plate was lower than trabecular bone. In hip OA, densitometric and architectural changes of subchondral cortical and trabecular bone were related to severity of cartilage degradation. In OA trabecular bone, the decrease in material density was compensated by increased bone volume, leading to higher apparent density (BMD); while in OP, loss of bone volume was correlated with, but not compensated by increased mineralisation, leading to lower apparent density.

References:

Table 1. Componental comparison of TMD

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<tr>
<td></td>
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<tr>
<td>Ct.TMD</td>
<td>1.19 ± 0.07</td>
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<td>Tb.TMD</td>
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Table 2. Correlation analysis

<table>
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<tr>
<td>Tb.BMD - BV/TV</td>
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Acknowledgments: China Scholarship Council

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.703

AB0077 CONTRIBUTION OF NOTUM TO THE DEVELOPMENT OF OSTEOARTHRITIS

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Figure 3. Regional comparisons of densitometric and architectural parameters. Left panel: unmatched inter-group (one-way ANOVA) analysis. Right panel: matched intra-sample regional analysis. Significance level is indicated by * as follows: P = 0.05; ** P = 0.01; *** P = 0.001; **** P = 0.0001.