in Micro-CT data analysis was found between PEMFs group and gene knockouts, although a slight increase could be observed in $TNF\alpha^{-/-}$ mice when compared to the PEMFs group. Negative effects on bone and cartilage was proved by testing key cytokines in anabolism and catabolism. PEMFs treatment and gene knockouts corrected the negative effects by targeting mediators in molecular pathways like Wnt and RANK. The differences in mRNA and protein level changes between PEMFs and gene knockouts were minor.

Study Design

PEMFs exposure system (Version 1.0)

Patent No. CN201058179Y

PEMFs exposure system (Version 2.0)

Conclusions: PEMFs alleviated surgeries induced bone loss and cartilage degeneration by promoting anabolism and inhibiting catabolism possibly in a similar mechanism to $TNF-\alpha$ and IL-6 gene knockouts, which imply that $TNF-\alpha$ and IL-6 may become new potential targets for PEMFs in treating degenerative bone diseases.

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SAT0070

ROLE OF C/EBPβ IN 1,25D-INDUCED ACTIVATION OF RANKL EXPRESSION

S. Jo¹, Y.L. Lee¹, I.-H. Sung², T.-H. Kim¹. ¹Rheumatology, Hanyang University Hospital For Rheumatic Disease; ²Orthopaedics, Hanyang University Seoul Hospital, Seoul, Korea, Republic Of

Background: 1 alpha 25-dihydroxyvitamin D3 (1,25D) is the active form of vitamin D3, which is responsible for osteoblast activation, subsequently bone formation. Although recent studies have shown that 1,25D stimulates RANKL expression in osteoblast differentiation¹, its molecular mechanism of action is not fully understood.

Objectives: The aims of this study were to evaluate cellular response of human bone-derived cells to 1,25D treatment by observing expression during osteoblast differentiation

Methods: In this study, MG63, SaOS2, and primary bone-derived cells (BdCs) were cultured and isolated to further elucidate the effect of 1,25D on osteoblasts. Those were incubated in osteogenic medium (ascorbic acid, beta-glycerol phosphate, and dexamethasone) for 1, 3, and 7 days with or without 20 μM 1,25D. The

osteoblast activity and differentiation status were evaluated by intercellular Alkaline Phosphatase (ALP) activity, ALP staining, Alizarin Red S (ARS) staining, and hydroxyapatite staining. In this situation, C/EBPβ gene manipulation with siRNA or overexpression system were subjected to report assay of human RANKL promoter, quantitative PCR(qPCR), immunoblotting and immunostaining of osteoblastic gene expression (alkaline phosphatase, osteocalcin, vitamin D3 receptor, RANKL, and C/EBPβ etc.)

Results: 1,25D promotes osteoblast differentiation and expression of osteogenic markers in three different cells. Intriguingly, treatment of 1,25D to those cells are accompanied by stabilising C/EBPβ proteins and stimulating RANKL expression. Moreover, Overexpression of C/EBPβ significantly increases RANKL mRNA and protein. In contrast, suppression of C/EBPβ decreases RANKL expression. Thus, C/EBPβ is a key mediator involved in 1,25D induced RANKL expression.

Conclusions: our preliminary data indicated that human bone-derived cells response to vitamin D3 promoted RANKL expression via activation of C/EBPβ, and enhanced osteoblast activity and differentiation. This study provides insight into the molecular mechanism of RANKL expression and osteoblast activation in human bone-derived cells response to 1,25D.

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SAT0071

SUBCHONDRAL OSTEOGENESIS BUT NOT CARTILAGE DAMAGE IS PREVALENT IN KNEE JOINTS OF PREMATURELY AGEING MITOCHONDRIAL DNA MUTATOR MICE

J. Geurts¹, S. Nasi², T.A. Prolla³, G.C. Kujoth³, U.A. Walker⁴, T. Hügle². ¹Spine and Surgery and Biomedical Engineering, University Hospital Basel, Basel; ²Rheumatology, University Hospital Lausanne, Lausanne, Switzerland; ³Medical Genetics, University of Wisconsin, Madison, USA; ⁴Rheumatology, University Hospital Basel, Basel, Switzerland

Background: Mitochondrial dysfunction has been demonstrated in ageing and osteoarthritic tissues. However it remains unclear whether dysfunctional mitochondria are directly implied in the pathogenesis of osteoarthritis.

Objectives: We investigated knee joints of prematurely ageing mitochondrial DNA mutator mice (*Polg*^{D275A}) to evaluate a causal relationship between mitochondrial dysfunction and different features of osteoarthritis.

Methods: Bone structural parameters and chondrocyte were evaluated in knee joints of mice displaying increased mtDNA mutations rates and accelerated ageing, due to expression of a proofreading-deficient mtDNA polymerase, using micro-computed tomography and histopathological analysis.

Results: Homozygous mutants displayed osteopenia of the epiphyseal trabecular bone and subchondral cortical plate in comparison to wild type controls and heterozygous mutants. Osteopenia was associated with a strong increase of osteoclast numbers (0.88±0.30/mm bone perimeter) compared to heterozygous (0.25±0.03/mm) and wild type mice (0.12±0.04/mm). New bone formation was not observed. Wild type mice displayed only low grade cartilage degeneration (OARSI grade ≤1) due to loss of cartilage proteoglycans. Increased tibio-femoral chondropathy was not apparent in hetero- and homozygous mitochondrial DNA mutator mice.

Conclusions: Mitochondrial dysfunction and premature ageing in mice with somatically acquired mtDNA mutations predisposes to enhanced subchondral bone resorption as potential early step of osteoarthritis, but not to cartilage damage or new bone formation. This phenotype potentially corresponds to an osteoporotic osteoarthritis phenotype in humans.

Disclosure of Interest: None declared

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SAT0072

MIRNA-146A IS A KEY PLAYER IN BONE METABOLISM AND OSTEOPOROSIS

V. Saferding¹, M. Hofmann¹, J.S. Brunner¹, M.F. Militaru¹, A. Puchner¹, S. Hayer¹, M. Timmer², R. Stange², J.S. Smolen¹, S. Blüml¹. ¹Medical University Of Vienna, Vienna, Austria; ²University Muenster, Muenster, Germany

Background: Micro RNAs (miRNAs) play a crucial role in the regulation of bone metabolism. MiR-146a, an important anti-inflammatory miRNA, was found to negatively impact osteogenesis and bone regeneration *in vitro*, by controlling the differentiation of mesenchymal stem cells. But to date the role of miR-146a in bone