arthritis. Especially CD11b⁺CD11c⁺ and monocyte derived inflammatory seem to play a role in inflammatory arthritis, suggesting that they could be an important therapeutic target.

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Disclosure of Interest None declared.

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EXTRACELLULAR MATRIX ATTENUATED MATRIX-DEGRADING EFFECTS OF VISFATIN DURING ADIPOGENIC MSC DIFFERENTIATION

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Career situation of first and presenting author Student for a master or a PhD.

Introduction Osteoporosis (OP) is the most common age-related disorder characterized by bone loss and correlates with increased bone marrow adiposity due to a shift of osteogenic towards adipogenic differentiation of bone marrow mesenchymal stem cells (MSC). Therefore, bone marrow adipocytes are in direct contact with the altered bone matrix in OP. Adipose tissue is metabolically active. Therefore, adipocyte-derived factors such as adipokines might influence MSC differentiation.

Objectives We analyzed the presence of adipokines (visfatin, resistin and leptin) in bone tissue and their effects on MSC differentiation under standard culture vs. spongiosa.

Methods RNA and MSC were isolated from spongiosa of femoral heads of osteoarthritis patients after hip replacement surgery, or after osteoporotic femoral neck fracture. Adipogenic MSC differentiation was performed with/without adipokines and visfatin inhibitor Apo866 as well as SB203580 p38-MAPK inhibitor. For the transfer and differentiation of MSC on cancellous bone, bone fragments were purified and sterilized. Gene expression was evaluated by Realtime PCR. Protein production was analyzed by ELISA.

Results Visfatin and leptin levels were increased in OP bone vs. non-osteoporotic OA bone, however, resistin was reduced. Visfatin induced the secretion of proinflammatory factors during adipogenesis in standard cell culture as well as on cancellous bone. Visfatin-induced cytokine release was markedly reduced during differentiation on spongiosa (e.g. 14d IL6, x-fold: standard culture 151±110, spong. 40±30, n=7). Significantly elevated MMP13 mRNA as well as protein expression induced by visfatin could be observed during adipogenesis in standard cell culture as well as on

spongiosa, however visfatin-mediated MMP13 expression was reduced on cancellous bone (e.g. 21d, x-fold: standard culture 81±89, spong. 13±21, n=7). The visfatin inhibitor Apo866 inhibited the visfatin-induced cytokine release. However, the MMP13 expression was not influenced during adipogenesis in culture (n=4). In contrast to Apo866, the p38-MAPK inhibitor did not reduce cytokine release during adipogenesis.

Conclusions Visfatin and leptin levels were elevated in osteoporotic bone. Therefore, visfatin-mediated increase of MMPs and proinflammatory cytokines during adipogenic differentiation might influence bone turnover at the adipose tissue/bone interface. Our results support the idea that the extracellular matrix attenuates visfatin-mediated detrimental effects during adipogenesis. The observed visfatin-mediated effects most likely depend on different signaling pathways.

Disclosure of Interest None declared.

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OSTEOCYTE-DERIVED PODOPLANIN IS AN IMPORTANT REGULATOR OF BONE REMODELLING IN THE KBXN SERUM TRANSFER MODEL OF RHEUMATOID ARTHRITIS

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Introduction Osteocytes derive from bone-forming osteoblasts and are located deep inside the bone matrix. They are encysted in cavities (lacunae) and form dendritic extensions to develop a dense sentinel network inside the bone. Osteocytes are not passive cells. They modulate bone remodelling through regulation of both osteoclast and osteoblast activity. Immature osteocytes express the transmembrane glycoprotein podoplanin (PDPN/gp38)¹ which is important for dendrite elongation and osteocyte function.² Moreover it has been reported that PDPN expression is regulated by inflammatory cytokines including TNFα, IL-6, IL-22, TGF-β1, IFN-γ³ and is highly expressed in synovial tissues from RA patients.⁴ However the role of PDPN in osteocytes during inflammatory disease has not previously been investigated.

Objectives In this study we investigated the effect of osteocyte-specific deletion of PDPN in the KBxN serum transfer (ST) mouse model of rheumatoid arthritis.

Methods Dmp1 Cre mice were crossed with PDPN^{fllox/fllox} mice to generate osteocyte specific conditional knockout mice as well as appropriate PDPN^{fllox/fox} controls. KBxN ST arthritis was used to study the effect of PDPN deletion on mouse arthritis progression. PDPN expression was assessed by immunohistochemistry. Osteoclast numbers were calculated by TRAP staining. Loss of cartilage and pannus formation was evaluated by Safranin-O and H and E staining. Standard microCT and synchrotron microCT analysis was used to assess bone density parameters, osteocyte location and bone erosions.

Results PDPN is expressed in osteocytes at sites of bone erosions in inflamed joints of KBxN ST mouse model. Osteocyte-specific PDPN deletion has no effect on trabecular and cortical bone density parameters in mouse tibiae under resting