of most common therapies used in RA patients and has been shown to have beneficial effects on RA-associated cardiovascular pathologies in these patients.¹ Initial studies in the collagen-induced arthritis (CIA) model revealed an increase in cardiac fibrosis marker galectin-3, both locally in perivascular adipose tissue (PVAT) and systemically in blood plasma during inflammatory arthritis and correlated with impaired vascular function.²

Objectives This study aims to investigate the impact of anti-TNF treatment on galectin-3 expression and vascular function during CIA.

Methods Male DBA/1 mice underwent CIA induction and received either Enbrel or phosphate buffered saline (PBS) by intravenous injection. Vascular function was determined by measuring the constriction response of the thoracic aorta at termination using a myograph. Galectin-3 was measured locally in thoracic PVAT by immunohistochemistry and quantitative polymerase chain reaction (qPCR), and systemically by ELISA.

Results Anti-TNF treatment during CIA resulted in a decrease in arthritis severity and progression compared to PBS treated mice, and partially restored vascular function. Galectin-3 expression was significantly reduced in thoracic PVAT, but not in blood plasma, in CIA mice treated with Enbrel.

Conclusions In conclusion, decreased galectin-3 expression in Enbrel treated mice is associated with an improvement in arthritis-associated disease activity including arthritis clinical score, joint swelling and vascular function.

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P098

VISFATIN IN BONE METABOLISM OF OSTEOPOROSIS AND OSTEOARTHRITIS PATIENTS

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Introduction Osteoporosis predominantly affects elderly people and is characterised by bone loss, increased fracture risk and reduced regeneration ability. Age-related bone loss correlates with increased bone marrow adiposity due to a shift of osteogenic towards adipogenic differentiation of bone marrow-derived mesenchymal stem cells (MSC). Adipose tissue is metabolically active. Through the release of adipokines with immunomodulatory properties adipose tissue might influence differentiation of bone marrow-derived MSC and contribute to bone loss in osteoporosis.

Objectives Thus we analysed the presence of adipokines (visfatin, resistin and leptin) in the bone marrow cavity and their effects on MSC differentiation.

Methods MSC and RNA were isolated out of spongiosa from femoral heads (hip replacement surgery of osteoarthritis patients (OA) or after osteoporotic femoral neck fracture (FF). Adipogenic as well as osteogenic MSC differentiation was performed with/without adipokines. For the transfer and differentiation of MSC on cancellous bone, cell-free bone fragments were prepared and sterilised. Proinflammatory factors were measured by immunoassays. Gene expression was evaluated by Realtime PCR. Matrix mineralization was assayed using Alizarin red S staining.

Results While resistin was reduced, visfatin and leptin levels were increased in FF bone vs. non-osteoporotic OA bone (FF mean visfatin 7.77 ± 1.86 , $n=11$; OA 2.25 ± 0.36 , $n=13$, $p=0.002$). In contrast to leptin and resistin, visfatin induced the secretion of proinflammatory factors (IL-6, IL-8, MCP-1) during both, osteogenic and adipogenic differentiation, (e.g. adipogenic differentiation IL-6, 21d; control: 270.3 ± 140.2 pg/ml; visfatin: $3,223 \pm 600.4$ pg/ml, $p=0.0006$, $n=12$). In osteogenically differentiated cells matrix mineralization was significantly increased, while collagen type 1 expression was downregulated (d21: -4.2 -fold/ $p=0.0001$; $n=7$) after visfatin stimulation. The expression of MMP2, -13, TIMP1 and -2 (e.g. d21: -2.4 -fold; -3.2 -fold; -3.2 -fold; -4.3 fold, respectively) was also reduced by visfatin during osteogenesis. Interestingly, visfatin significantly induced MMP13 expression (e.g. d21: 104-fold) during adipogenic differentiation under cell culture conditions. However, when differentiated on autologous cancellous bone, visfatin-induced MMP13 expression, as well as IL-6 and IL-8 release was markedly reduced (e.g. MMP13 21d: 13.8-fold, $p=0.0156$, $n=7$).

Conclusions Taken together, visfatin expression was not only elevated in osteoporotic bone, it induced release of proinflammatory factors and dysregulated the MMP/TIMP balance during MSC-differentiation. Therefore visfatin might influence bone remodelling specifically at the bone/adipose tissue interface. The visfatin-mediated increase of matrix mineralization and the observed reduction of organic component of ECM – Coll.1, essential for the bone plasticity might contribute to bone fragility and therefore to the pathogenesis of osteoporosis.

Disclosure of interest None declared

P099

INTENSIVE 24-WEEK PHYSIOTHERAPY PROGRAMME IN PATIENTS WITH IDIOPATHIC INFLAMMATORY MYOPATHIES – PRELIMINARY DATA FROM A SINGLE-CENTRE CONTROLLED STUDY

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Introduction Presence of muscular inflammation, followed by atrophy in idiopathic inflammatory myopathies (IIM) leads to impaired function, reduced muscle strength, endurance and aerobic capacity, decreasing quality of life. Data on the efficacy of non-pharmacologic care in IIM is very limited due to variety in studied interventions/outcomes.

Objectives To address the limitations of existing studies, and evaluate the effect of a controlled, long-term (24 week intervention, 24 week follow-up), intensive (1 hour physiotherapy twice weekly, and home-exercise for 1 hour 5x weekly), tailored physiotherapy program to improve muscle strength, endurance and deep stabiliser system, and quality of life/disability in cohorts with a substantial number of IIM patients.

Methods All patients fulfilled the Bohan and Peter 1975 diagnostic criteria, had muscle involvement, and were consecutively recruited between 2014–2016. At months 0,3,6,12 all patients were assessed by a physician (physical examination, MITAX, MYOACT, and MDI), and a physiotherapist blinded to intervention (MMT-8 – muscle strength test, FI-2 – muscle endurance test), patients filled out patient reported outcomes (PRO)/questionnaires (HAQ, SF-36, Beck's depression inventory-II (BDI-II), PROs assessing nutrition and fatigue), body composition was analysed using densitometry (iDXA Lunar) and bioelectric impedance (BIA2000-M), and patients provided blood for routine laboratory analysis and biobanking. Normality of data was tested and inter-group analysis performed with 2-way ANOVA and intra-group analysis by Friedman's test with Dunn's post hoc test.

Results 27 IIM patients were recruited into the intervention group (IG) and 27 patients into the control group (CG). Compared to observed statistically significant deterioration in CG over the period of months 0–6, we found statistically significant improvement in FI-2, MMT8, HAQ, BDI-II. Only numerical improvement in IG compared to numerical deterioration in CG, which has not reached statistical significance, was observed in SF-36 and fatigue PROs.

Conclusions Our physiotherapy program led to a significant improvement in muscle strength, endurance, and function. Additionally, patients expressed a decrease in the level of depression. The improvements were clinically meaningful in a substantial proportion of patients.

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P100

THE LINK BETWEEN ANGIOGENESIS AND OSTEOGENESIS IN SPONDYLOARTHRITIS

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Introduction Spondyloarthritis is characterised by inflammation, extensive angiogenesis and pathological osteogenesis. Transmembrane (tm) TNF transgenic (tg) mice¹ that overexpress tmTNF exhibit features of SpA, including chronic inflammation and pathological osteogenesis. tmTNF ligation to TNF receptor 2 in endothelial cells (ECs) can induce signal transduction pathways, that may promote these processes. Of note, angiogenesis and osteogenesis are coupled by EC differentiation towards a type H (CD31^{hi} endomucin^{hi}) phenotype.²

Objectives To investigate the link between pathological angiogenesis and osteogenesis in tmTNF tg mice and the potential contribution of noncanonical NF-κB signalling in ECs to this process and infiltration of immune cells into the bone marrow (BM).

Methods Vertebrae and ankles from 6 and 12 weeks and 8 months old tmTNF tg mice or sex-matched non-tg littermates

(n=18) were prepared by cutting 60 μm thick cryosections for confocal imaging.

Results tmTNF tg mice exhibited ectopic osteogenesis which was not observed in non-tg littermates. Immunostainings showed that type H vessels are in the vicinity of the ectopic osteogenesis and osterix⁺ osteoprogenitors. At six weeks of age, osterix⁺ cells are located throughout the ectopic lesion, while at eight months, osterix⁺ cells are only present at the border of the lesion. Furthermore, there is increased osteogenesis and a different vessel architecture within the vertebrae of tmTNF tg mice compared to non-tg littermates that progresses with age. Non-tg littermate vertebrae only have physiological osteogenesis, which is in the metaphysis and periosteum. In addition, tmTNF tg mice also exhibit altered bone marrow (BM) architecture containing extensive lymphoid aggregates, which predominantly consisted of B220⁺ B cells.

Conclusions tmTNF overexpression in mice leads to development of type H vessels associated with ectopic osteogenesis. In addition, extensive lymphoid aggregates develop in the BM. Current studies are aimed at identification of signalling pathways in ECs that contribute to these processes.

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P101

DOT1L INHIBITION INCREASES DERMAL FIBROBLAST PROLIFERATION BUT HAS NO EFFECTS ON IN VITRO OR IN VIVO COLLAGEN DEPOSITION IN MODELS OF FIBROSIS

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Introduction Fibrosis is a key process in Systemic Sclerosis, a devastating disease that is not well understood. The role of epigenetic disease mechanisms is increasingly explored. DOT1L, the unique H3K79-methyltransferase, methylates histone 3 at the Lysine residue at position 79, and regulates gene expression. Inhibition of DOT1L has cell-type specific effects on Wnt-signalling, a pathway suggested to play an important role in fibrosis.

Objectives To study the role of DOT1L in fibrosis.

Methods Primary cell cultures of fibroblasts, isolated from healthy human skin and treated with DOT1L-inhibitor EPZ-5676 or vehicle for 14 days, were stimulated with TGFβ 5 ng/ml after starvation. Smooth muscle alpha 2 actin (ACTA2) gene expression was measured by RT-qPCR. Efficiency of DOT1L-inhibition was analysed with Western Blot for dimethylated H3K79. Picrosirius Red staining measured collagen I and III deposition. Proliferation was analysed with 5-Bromo-2'-deoxy-uridine (BrdU) labelling. 7–9 week old Col1a2; Cre-ERT²; DOT1L^{fl/fl} mice were injected intraperitoneally with tamoxifen (1 mg/day, 5 days) to induce a fibroblast-specific DOT1L knockout. Bleomycin (0.1 mg) or vehicle was injected subcutaneously (5 days/week, 4 weeks). Injected skin was analysed by OH-prolin assay for collagen content, and by histology for dermal thickness measurement.

Results The DOT1L-inhibitor EPZ-5676 reduced H3K79 dimethylation in all samples. TGFβ increased expression of ACTA2