confirmed increased carotid plaque formation, increased cIMT. Biologics may beneficially influence some parameters in the intracranial vessels.

Disclosure of interest None declared

P095 PLASMA LEVELS OF HSP90 ARE INCREASED IN PATIENTS WITH SYSTEMIC SCLEROSIS WITH MORE SEVERE ORGAN INVOLVEMENT

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Introduction Our previous study demonstrated that Hsp90 is overexpressed in the skin of patients with systemic sclerosis (SSc), in cultured SSc fibroblasts and preclinical models of SSc. We showed that Hsp90 is a regulator of TGF- β signalling and its inhibition prevents the stimulatory effects of TGF- β on collagen synthesis and dermal fibrosis in three preclinical models of SSc.¹

Objectives The aim of this study was to evaluate Hsp90 in the circulation of SSc patients and characterise its potential association with skin changes and SSc-related features.

Methods A total of 91 patients (78 females; mean age 52.7; disease duration 6.0 years; diffuse cutaneous (dc)SSc/limited cutaneous (lc)SSc=38/53) who met the ACR/EULAR 2013 criteria for SSc and 85 age-/sex- matched healthy controls (HC) were included. Plasma Hsp90 was measured by ELISA. Data are presented as median (IQR).

Results Plasma Hsp90 levels were increased in SSc patients compared to HC [12.5 (9.6–17.9) vs. 9.9 (7.9–12.6) ng/mL, $p=0.001$], but no difference between lcSSc and dcSSc were detected [13.1 (9.4–18.1) vs. 11.5 (9.5–17.5) ng/mL, $p=0.316$]. Hsp90 levels in all patients positively correlated with CRP ($r=0.313$, $p=0.006$). Furthermore, Hsp90 was increased in patients with interstitial lung disease (ILD) compared to those without ILD [12.8 (10.2–17.9) vs. 10.3 (8.6–16.6) ng/mL, $p=0.045$] and was negatively associated with functional parameters of ILD: FVC ($r=-0.299$, $p=0.011$), FEV1 ($r=-0.256$, $p=0.031$), DLCO ($r=-0.303$, $p=0.009$) and SpO₂ ($r=-0.317$, $p=0.038$). In addition, only in patients with dcSSc, Hsp90 levels positively correlated with the mRSS ($r=0.437$, $p=0.006$). Hsp90 concentrations were not significantly affected by other main clinical parameters of SSc.

Conclusions We demonstrated higher plasma levels of Hsp90 in SSc patients compared to healthy controls. Concentrations of extracellular Hsp90 increase with higher inflammatory activity, with deteriorated lung functions in ILD and also with the extent and severity of the skin involvement in patients with diffuse cutaneous SSc. These data further highlight the role of Hsp90 as a significant regulator of fibroblast activation and tissue fibrosis in SSc.

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P096 SYNOVIAL TISSUE REMODELLING AS A MEANS OF TISSUE MEMORY

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Introduction The synovium demonstrates a distinct cellular structure with a densely packed synovial lining layer that sits on top of a loosely organised sublining layer. In rheumatoid arthritis (RA), this tissue hosts the inflammatory reaction and undergoes drastic structural changes. We hypothesise that this inflammatory remodelling results in tissue dysfunction, thereby perpetuating the inflammatory process. To explore the relationship between tissue structure and function, we use a 3D human synovial organoid culture system to model healthy and diseased synovium.

Methods FLS from RA patients were resuspended in Matrigel and cultured as 3D organoids for an extended period of time. This allows FLS to re-establish a synovial tissue-like structure. To mimic inflammation, 3D synovial organoids were challenged with TNF. A re-stimulation experiment was designed in which synovial organoids were exposed to TNF for 10 days, followed by a 3 day wash out phase. Thereafter, the organoids were re-stimulated with TNF. To prevent TNF-driven remodelling, Marimastat, a broad MMP inhibitor, was added during the first TNF stimulation. For selected experiments, synovial tissue-like structure was assessed by HE staining in paraffin embedded sections of synovial organoids. qPCR and RNA Seq were used in gene expression profiling. IL-6, IL-8 and MMP3 protein production was determined by ELISA.

Results TNF-stimulated synovial organoids demonstrated lining layer hyperplasia and cellular condensation in the sublining layer. After TNF-stimulation, gene expression of MMP1, MMP3 and IL-6 and protein production of IL-6, IL-8 and MMP3 was upregulated. Upon re-stimulation of synovial organoids with TNF, protein levels of IL-6, IL-8 and MMP3 were significantly increased when compared to previous stimulations. In order to explore whether this effect is due to TNF-induced structural changes, tissue remodelling was blocked using Marimastat. IL-6 protein level was reduced in 21%. To further explore the increased TNF response upon re-stimulation, epigenetic mechanisms are currently being tested.

Conclusions TNF stimulation has a direct effect on synovial organoids function and structure. TNF-driven tissue remodelling is associated with an increased in IL-6, IL-8 and MMP3 expression response upon re-stimulation. Inhibition of TNF-induced remodelling partially prevents this effect. Additional epigenetic mechanisms may account for tissue memory.

Disclosure of interest None declared

P097 ANTI-TNF TREATMENT IMPROVES VASCULAR FUNCTION VIA SUPPRESSION OF GALECTIN-3 EXPRESSION DURING INFLAMMATORY ARTHRITIS

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Introduction The link between rheumatoid arthritis (RA) and cardiovascular disease (CVD) is well established but not yet fully understood. Anti-TNF treatment, e.g. with Enbrel, is one

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.