differences disappeared. Adverse events were mostly mild and comparable between groups.

Conclusion: Six-week treatment with low-dose oral prednisolone led to a substantial improvement of symptoms in patients with painful hand OA and signs of inflammation. This trial provides evidence that local inflammation is a suitable target for drug-treatment in hand OA.

Acknowledgement: The HOPE study was supported by a grant from the Dutch arthritis foundation (ReumaNederland).

Disclosure of Interests: Féline Kroon: None declared, Marion Kortekaas: None declared, Annelies Boonen: None declared, Stefan Böhringer: None declared, Monique Reijniere Grant/research support from: Funding from the Dutch Arthritis Foundation.

The funding source had no role in the design and conduct of the study., Frits Rosendaal: None declared, Naghmeh Riyazi: None declared, Mirian Starmans: None declared, Franktien Turkstra: None declared, Jende van Zeben: None declared, Cornelia Allaart: None declared, Margreet Kloppenburg Grant/research support from: Pfizer, IMI-APPROACH (Grant Agreement n° 115770), Consultant for: GlaxoSmithKline, Merck-Serono, Abbvie, Levicept, Pfizer

DOI: 10.1136/annrheumdis-2019-eular.997

THURSDAY, 13 JUNE 2019

Systemic sclerosis, myositis and related syndromes – etiology, pathogenesis and animal models

OP0181

MOLECULAR CHARACTERIZATION AND STRATIFICATION OF IDIOPATHIC INFLAMMATORY MYOPATHIES: ON THE BASIS OF SKELETAL MUSCLE TRANSCRIPTOME STUDY

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Background: Idiopathic inflammatory myopathies (IIM) are a group of complicated heterogenous autoimmune diseases, to date, little is known about its skeletal muscle transcriptomic features.

Objectives: Here, we performed skeletal muscle RNA-sequencing (RNA-seq) to discover the global muscle transcriptional signature of IIM based on myositis-specific antibodies (MSA) profiles and investigate the potential molecular pathway of IIM.

Methods: Muscle specimen were taken from 60 patients with IIM, 6 patients with non-IIM myopathies and 9 healthy controls. The serum and PBMC samples were also obtained from the IIM patients at the time of muscle biopsy. For RNA-seq, IIM was dissected into eight groups based on their MSA profiles: MSA and ANA negative (n = 4), anti-synthetase antibodies positive (n = 13), -MDA5 positive (n = 6), -NXP-2 positive (n = 7), -TIF-1γ positive (n = 10), -SRP or anti-HMGCR positive (n = 6), -Mi-2 positive (n = 7), MSA negative but anti-Ro-52 positive (n = 7). RNA from muscle specimen were extracted according to manufactory guide and sequenced using Illumina HiSeq2500. Quantitative real-time reverse transcription-polymerase chain reaction (qRT-PCR) was performed on sequencing cohorts and expanding cohorts to validate the results of RNA-seq. Immunohistochemistry was also performed on muscle biopsy to determine the MxA expression in different MSA subgroups.

Results: To define the global muscle signature of IIM, all IIM samples were compared to NC and total of 1637 transcripts were differentially expressed (log2 Fold Change > 1, Padj < 0.05). Unsupervised hierarchical clustering of these differentially expressed transcripts (DETs) revealed a prevalent interferon (IFN) signature and showed that 68 interferon-stimulated genes (ISGs) were significantly up-regulated in IIM. Then these 68 ISGs were used to cluster different MSA subgroups and distinct ISG expression was found. The mRNA expression levels of several ISGs (MX1, IFIH1, LAMP3, CMPK2, HERC6) in sequencing cohorts and expanding cohorts also confirmed the diverse ISG expression between different MSA subgroups. An IFN signature scoring system was established to quantify the IFN activity and subsequently IIM could be classified into IFN-Dominant, IFN-Moderate and IFN-Weak respectively based on the IFN intensity and different MSA subgroup. Moreover, the IFN-Dominant group showed much higher MxA expression on muscle biopsy than the IFN-Moderate and IFN-Weak group by immunohistochemistry.

Conclusion: We revealed a prominent IFN signature and MSA-based ISG expression heterogeneity in IIM through muscle transcriptomics. Preliminary

results showed that the IFN muscle signature may play a predominant role in some subgroups but not all IIM groups in the pathogenesis of IIM.

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Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.854

OP0182

SYNTHETIC PEPTIDES TARGETING CD206 INHIBIT PATHOGENIC MACROPHAGES IN SYSTEMIC SCLEROSIS

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Background: In systemic sclerosis, activated macrophages having M2-like properties are believed to contribute to the fibrotic pathology by secreting profibrotic factors such as TGFβ. Certain synthetic peptides (10-12mers) studied here coopt the mechanism used by macrophages to detect bacteria by binding to certain regions of CD206, a receptor highly expressed in the M2 macrophages, and repolarise them to an M1 phenotype.

Objectives: We aimed to determine the macrophage activation signature in SSc, assess CD206 as a biomarker of ongoing fibrotic activity, and measure the effect of the peptides on macrophage activation and macrophage-fibroblast cross-talk. Methods: sCD206 was assayed in plasma (n=50 healthy, 50 limited SSc, 50 diffuse SSc), and suction blister fluid (BF) obtained over active lesions by ELISA. sSIGLEC (monocyte interferon signature) and IL-31 (Th2 signature) were assayed for comparison. Cell surface CD206 and DAMP receptor P2X7, were assayed by flow cytometry. The macrophage activation signature was investigated further by qPCR for inflammatory M1, as well as M2-like gene expression (IFNγ, Arg1, CD2106). Macrophage-fibroblast cross talk was assessed using media transfer following heat activation to SSc dermal fibroblasts assayed by qPCR for collagen I. The macrophage secretome was determined by Luminex and ELISA.

Results: CD206 was significantly elevated in SSc BF (SSc median sCD206 42, HC 31 pg/ml, p<0.041). Plasma sCD206 was raised in diffuse versus limited SSc (P<0.0103) and was correlated with ESR (R=0.364, p<0.009) and sSIGLEC (R=0.244, p<0.05), but not disease duration or IL-31. By flow cytometry both CD206 and P2X7 were highly expressed by SSc macrophages (mean fluorescence SSc, 776.1 SD=409.1, 724.4 SD=455.3 vs HC 632.2 SD=73.7, 472.9 SD=25.4), correlating with modified Rodnan Skin Score (mRSS) (p<0.05, r=0.51). Double positive P2X7 and CD206 cells were seen in a subgroup with higher mRSS. Four RP peptides (RP182, 185, 832 & 837) were assessed for effect on growth of SSc and control macrophages. In general, the RP peptides selectively inhibited SSc macrophage growth, with RP185 and RP832 reaching significance (p<0.05) for 1 and 10μM concentrations at 96 hours. Pro-fibrotic cross-talk leading to elevated fibroblast collagen I, was characteristic of 4 out of 9 SSc macrophage cell lines examined. A mixed activation signature was identified by qPCR of the fibroblast-stimulating macrophages (elevated Arginase1, CD206 and IFNγ) but not the non-fibroblast inducing cell lines. Pre-treatment of the pro-fibrotic SSc macrophages with RP832, but not the others, eliminated the pro-fibrotic cross-talk (fibroblasts treated with SSc macrophage media mean collagen I, 1995 (SEM 149), RP832 treated macrophages 1551 (SEM 133) p<0.038 relative expression units, paired t test), and suppressed the macrophage activation signature (reduced mean Arg1 p<0.030, CD206 p<0.058, IFNγ p=0.058, paired t test). Secretome analysis confirmed the mixed activation signature of SSc macrophages including elevated total TGFβ, PDGF-BB, sCD40L as well as inflammatory factors IL-6, IL-1β, TNFα and type I cytokine IFNγ. Treatment with RP 832c reduced TGFβ in 6 out of 9 SSc macrophage cell lines but this did not reach statistical significance.

Conclusion: A macrophage activation signature is identified in SSc patients, in proportion to the severity of disease. A mixed activation signature with inflammatory as well as pro-fibrotic M2-like properties is seen. RP peptides, which target the cells via CD206, reduce the activation signature and inhibit pro-fibrotic cross talk in these cells.

Disclosure of Interests: : Henry Lopez Shareholder of: Murigenics, Riptide Bioscience, Employee of: Pfizer, Kimti Kumar: None declared, George Martin