immune-regulating response when exposed to an inflammatory environment through the secretion of soluble mediators and cell-cell contact mechanisms. Several molecules are implicated in ADSC-mediated immunomodulation such as PGE₂, IDO, IL-6, TGF- β and TSG6. However, while ADSC have shown remarkable results *in vitro* and in animal models, their efficacy in clinical applications has yet to be fully elucidated.

Objectives Considering the diversity of the local inflammatory microenvironment in the joints of RA patients and to further explore the behaviour of ADSC within their microenvironment, we aimed to study the effect of synovial fluid (SF) collected from patients with RA on ADSC proliferation and immune-modulating properties.

Methods ADSC isolated from 6 healthy subjects were cultured for 24 hours in the presence or absence of RASF (diluted to 5%) obtained from 10 different RA patients or a control SF obtained from a patient undergoing non-inflammatory rheumatism related surgery. ADSC proliferation was assessed by an MTT colorimetric assay. After SF treatment, ADSC were harvested for RNA extraction and subsequent RT-qPCR to quantify the gene expression of COX2, IL6, IDO, TSG6, TGF- β . To evaluate the inflammatory status of SF, pro-inflammatory cytokines present in SF were first identified using an antibody-based membrane array and then quantified by ELISA or CBA.

Results RASF differentially affected the proliferation of ADSC with 2 out of 10 inducing ADSC proliferation whilst the remaining inhibited proliferation. Gene expression of COX2, IDO, IL-6, TSG6 and TGF- β was simultaneously induced in only 4 of the 10 RASF included in this study. We thus investigated if these four RASF had any particular inflammatory signature that could explain their effect on ADSC. Higher concentrations of one or more of the following markers IL-6, TNF α , MCP1, ICAM1, IL1 α were detected in these SF compared to others, which correlates with a more potent pro-inflammatory environment. Conversely, RASF that had no effect on ADSC gene expression presented a less inflammatory profile. Recombinant cytokines and neutralisation assays are underway to determine which specific molecules mediated the SF effect on ADSC.

Conclusions Proper licensing of ADSC to an anti-inflammatory phenotype is usually done *in vitro* by stimulation with high concentrations of pro-inflammatory cytokines which do not necessarily reflect the concentrations present in the synovial fluid. This study sheds further light on how ADSC respond to local inflammatory stimuli in order to better direct their immunomodulatory ability and efficacy in clinical therapy.

Acknowledgements *N. Alaaeddine and J.-L. Davignon are joint senior authors

Disclosure of interest None declared

P122

TREATMENT WITH RITUXIMAB TO DEMAND IN RHEUMATOID ARTHRITIS. EFFECTIVENESS ANALYSIS

¹U Julia*, ²MJ Fobelo, ³M Guzman. ¹Rheumatology Unit; ²Pharmacy Unit, Valme University Hospital, Seville, Spain

10.1136/annrheumdis-2018-EWRR2018.137

Introduction Rituximab (RTX) is a chimeric anti-CD20 monoclonal antibody that has been shown to be effective in the treatment of rheumatoid arthritis (RA). At present we have different treatment regimens in terms of the time of

administration, every 6 months or on demand and with respect to the dose used: cycles of 1000 mg x 2 or 500 mg x 2.

Objectives Our objective was to analyse the effectiveness on-demand treatment regimen of RTX in RA

Methods Retrospective observational study on RA with RTX treatment between January 2006 and February 2015 was carried out. Administration was performed if DAS28 >3.2. The median time of retreatment and the number of patients portrayed at 8, 12, 16, 20 and 24 months were calculated

Results 57 patients were included, mean age 55 years, 70% women; 93% FR+, 31.6% ACPA + and 63.2% with erosive disease. The median time of evolution of RA at the start of RTX 8.1 years. All patients had high activity at the start of RTX [median DAS28=5.6; HAQ=1.75]. Prior to RTX, all patients were treated with another biological (24.5% with two or more). 56% of patients were receiving DMARDs.

The median time of retreat was 7 months.

The number of patients portrayed was: at 8 months 55.8%, at 12 months 69.4%, at 16 months 80%, at 20 months 81.3% and at 24 months at 88.6%. Those not evaluated in each quarter are those who are discontinued RTX before two years of follow-up (four due to inefficacy and one due to adverse reaction) or, at the time of completing the study, have not completed two years of treatment. The effectiveness considered as the median number of cycles received at two years was 2.

Conclusions Although the median time to retreatment was seven months, there are some patients who remain unplastered for about two years. 80% of the patients had been portrayed at 16 months, half with 1 cycle of RTX and the other half with 2. The pattern on demand even allowed to decrease the doses of concomitant DMARDs. A subsequent individualised analysis of patients will allow us to evaluate the possible characteristics that can affect the effectiveness of the pattern on demand

Disclosure of interest None declared

P123

THE IFN TYPE I GENE EXPRESSION IN A CARDIOVASCULAR DISEASE CONTINUUM OF RHEUMATOID ARTHRITIS

^{1,2}AN Burska*, ¹G Harrison, ^{1,2}EM Hensor, ¹LA Bissell, ³G Fent, ⁴I Sadreev, ^{1,2}YM El Sherbiny, ⁵H Donica, ^{1,2}EM Vital, ³S Plein, ^{1,2}MH Buch. ¹Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds; ²NIHR- Leeds Biomedical Research Centre (NIHR-LBRC), Leeds Teaching Hospitals NHS Trust, Chapel Allerton Hospital; ³Leeds Institute of Cardiovascular and Metabolic Medicine; ⁴Leeds Institute of Cancer and Pathology, University of Leeds, Leeds, UK; ⁵Department of Biochemical Diagnostics, Medical University of Lublin, Lublin, Poland

10.1136/annrheumdis-2018-EWRR2018.138

Introduction Rheumatoid Arthritis (RA) patients have a prominent increase in cardiovascular (CV) comorbidity not fully explained by traditional risk factors.¹ Interferons type 1 (IFN-1) have been associated with premature CV disease (CVD) in SLE² and are implicated in several aspects of atherosclerosis and acute coronary syndromes.³ In RA a subpopulation of patients also display an IFN-1 signature in the blood,⁴ which is associated with response to biologics. The IFN-1 signature association with CVD in RA remains unclear.

Objectives To analyse expression of interferon type 1 response genes (ISGs) along a CVD continuum in patients with RA using a well phenotyped cohort of RA patients whereby

cardiovascular changes were assessed by Cardiac Magnetic Resonance Imaging (CMR).

Methods PBMCs samples from 60 RA patients (mean (90% CI) age 62.4 (60.2, 64.6)y.o, sex F/M 42/18, disease duration 153.3 (121.3, 185.2) mths and n=18 healthy controls (HC); age 42 (37.8,46.0) y, F/M 12/6 were obtained. RA patients were stratified based on CMR into: no CVD (RA CMRneg n=13) and abnormal CMR (RA CMRpos n=26), and RA with clinical CVD (no CMR, defined as history of cerebrovascular disease or ischaemic heart disease) (RA CVD n=21). qPCR of ISGs was performed using TaqMan Gene Expression Assays on Biomark (Fluidigm). Factor scores were created using the set of 51 genes measured in 78 subjects.

Results All routinely used biomarkers were associated with RA diagnosis (ACPA, RF, TJC, SJC, CRP, DAS28). Total cholesterol and LDL levels were higher in RA than in HC group ($p=0.051$ and $p=0.015$). Three IFN-1 scores were present in the dataset (IFN Score 1, 2 and 3) and were composed of 19, 21 and 7 genes respectively. IFN-1 score 2 showed significant differences between HC and RA CMRpos groups (mean difference and 90% CI: 0.52 (0.09, 0.96)) and HC and RA CVD (0.57 (0.10, 1.03)) as well as all RA patients with CVD (CMRpos and RA CVD) ((0.54 (0.16, 0.93); $p<0.05$ for all comparisons). IFN-1 Score 3 showed trend for a difference between RA CMRneg and CMRpos patients (0.37 (0.03, 0.70); $p=0.071$). There was no statistical difference between HC and RA CMRneg groups.

Conclusions An IFN-1 score 2 emerged as a possible factor characterising progression along a CVD continuum in RA patients, from no CVD to subclinical and clinical CVD; also distinguishing between HC and RA with subclinical and clinical CVD. These results warrant further evaluation in a larger cohort to confirm the findings.

REFERENCES

1. Kaplan MJ. *Curr. Opin. Rheumatol* 2006;**18**(3):289–297.
2. Somers EC, et al. *PloS One* 2012;**7**(5):e37000.
3. de Winther MPJ. *Arterioscler. Thromb. Vasc. Biol* 2016;**36**(2):217–218.
4. van der Pouw Kraan TC, et al. *Ann. Rheum. Dis* 2007;**66**(8):1008–1014.

Disclosure of interest None declared

P124

ALTERED CD4+ T CELL DNA METHYLATION IN EARLY RHEUMATOID ARTHRITIS

¹AD Clark*, ¹N Naamane, ^{2,3}N Nair, ¹AE Anderson, ¹AJ Skelton, ¹J Diboll, ^{2,3}J Massey, ^{2,3}S Eyre, ^{2,3}A Barton, ¹JD Isaacs, ⁴LN Reynard, ¹AG Pratt. ¹National Institute for Health Research Newcastle Biomedical Research Centre, Newcastle upon Tyne Hospitals NHS Foundation Trust and Newcastle University, Newcastle upon Tyne; ²Arthritis Research UK Centre for Genetics and Genomics, Centre for Musculoskeletal Research, Institute of Inflammation and Repair, University of Manchester; ³NIHR Manchester Musculoskeletal BRU, Central Manchester NHS Foundation Trust, Manchester; ⁴Institute of Genetic Medicine, Newcastle University, Newcastle upon Tyne, UK

10.1136/annrheumdis-2018-EWRR2018.139

Introduction Over 100 genetic variants associated with rheumatoid arthritis (RA) to date explain a relatively small proportion of its heritability. Epigenetic factors, including variation in DNA methylation, may in part account for this, impacting gene expression at a cellular level.

Objectives Seeking insights into disease pathogenesis and discriminatory biomarkers of clinical value, we undertook an epigenome-wide association study (EWAS) of DNA methylation

in CD4 +T cells of untreated RA and control patients attending a UK early arthritis clinic.

Methods A cohort of 44 treatment-naïve RA patients were recruited from the Newcastle Early Arthritis Clinic (NEAC) along with a comparator cohort of 53 matched disease controls with arthritis. CD4 +T cells were isolated from fresh peripheral blood by positive selection, and DNA/RNA extracted from lysates. DNA methylation was quantified on the Illumina Human MethylationEPIC array, and gene expression measured using the Illumina 12HT BeadChip. Following methylation data pre-processing, functional normalisation and probe filtering, 715,279 CpGs were considered. Batch effects were corrected using the ComBat function and a moderated T-statistic identified differentially methylated positions (DMPs) between RA patients and disease controls. Differentially methylated regions (DMRs; clusters of DMPs) were also sought using the DMRcate function. Linear Discriminant Analysis (LDA) combined with a Stepwise Forward Selection (SFS) procedure was used to identify the most discriminatory CpGs for downstream independent validation.

Results Between RA and non-RA patients we identified a total of 263 DMPs in CD4 +T cells, of which 159 were hypomethylated in RA patients (adjusted p -value <0.05 , $\Delta\beta>5\%$), as well as 14 DMRs. One DMR in particular, comprising 4 intronic CpG sites in the *CD151* gene that were hypomethylated in RA patient CD4 +T cells, was notable for the strong association between *CD151* expression and methylation. This suggests a mechanism whereby altered DNA methylation during early disease determines pathogenically relevant gene expression. We assessed the ability of our differentially-methylated CpG sites to discriminate patients by diagnosis through evaluating the performance of a classification algorithm. LDA classification based on CpGs selected by SFS achieved an area under the receiver operating characteristic (ROC) curve of 0.82 (95% confidence interval: 0.80–0.85).

Conclusions The CD4 +T cell methylation landscape in age- and sex-matched early inflammatory arthritis patients has unique features in early RA, indicating a possible role for DNA methylation in conferring susceptibility to this condition. A further application of these data may be in predicting outcome in undifferentiated arthritis, though further work is required to explore this.

Disclosure of interest None declared

P125

CHONDROCYTES DERIVED FROM MESENCHYMAL STEM CELLS DIFFERENTIATED IN THE PRESENCE OF PLASMA-DERIVED EXTRACELLULAR VESICLES FROM OSTEOARTHRITIC PATIENTS EXPRESS DISEASE-RELATED GENES

BCH Pieters, CEJ Waterborg*, OJ Arntz, AB Blom, PM van der Kraan, FAJ van de Loo. *Experimental Rheumatology*, Department of Rheumatology, Radboud University Medical Centre, Nijmegen, Netherlands

10.1136/annrheumdis-2018-EWRR2018.140

Introduction Osteoarthritis (OA) is an age-related musculoskeletal disease and the most common form of arthritis characterised by low grade synovial inflammation and articular cartilage degeneration. OA has many risk factors such as genetic predisposition, age and gender, but also joint specific (e.g. trauma) and systemic (obesity, hormones). Also many different cell types have been implicated in the pathogenesis of OA and interplay between these cells contribute to the dynamic events