RA, n=13), RA CMRpos (subclinical CVD-RA, n=54), and RA with clinical CVD (defined as history of cerebrovascular disease or ischaemic heart disease) (RA-CVD n=25). qPCR of ISGs was performed using TaqMan Gene Expression Assays on Biomark (Fluidigm) with compatible reagents. Factor analysis of Ct values from 51 genes was used to create scores by calculating median dCt for genes loaded by each factor.

Results: RA cohort median(IQR) age 63 (13.3) yrs, 69% female, disease duration 148.7 (215.3) mths; HC age 43 (16.5) y, 62% female. Three IFN-I factors (IFN Score 1, 2, 3) were present in the dataset and were composed of 19, 21 and 7 genes respectively. The Jonckheere-Tepstra test showed significant increases in expression of Score 2 across the 4 groups ($p=0.002$), consistent with a continuum, and multiplicity-corrected post-hoc analysis identified differences between HC and subclinical CVD ($p=0.034$), HC and RA-CVD ($p=0.004$); as well as between no CVD-RA and subclinical CVD-RA ($p=0.034$); and subclinical CVD-RA with RA-CVD ($p=0.029$). Scores 1 and 3 did not show consistent directional trends across all studied groups. In no CVD-RA expression of Score 1 and 2 positively correlated with CRP ($\rho=0.744$, $p=0.002$ and $\rho=0.659$, $p=0.010$ respectively). Score 1 with Low-Density Lipoproteins ($\rho=0.527$, $p=0.044$), Framingham 10y risk ($\rho=0.595$, $p=0.019$) and Score 3 with Pulse Wave Velocity ($\rho=0.584$, $p=0.022$). In subclinical CVD-RA score 3 expression negatively correlated with Left Ventricular mass ($\rho=-0.381$, $p=0.005$), in RA-CVD score 3 expression positively correlated with Glucose ($\rho=0.724$, $p=0.042$), Triglycerides ($\rho=0.821$, $p=0.023$) and Total Cholesterol/High-Density Lipoprotein ratio ($\rho=0.505$, $p=0.039$).

Abstract AB0047 – Figure 1

Conclusions: An IFN-I score (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. IFN- γ is involved in metabolic disturbances associated with CVD development in RA. These results warrant further evaluation to confirm the findings in a larger cohort.

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Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.4195

AB0048 SERUM CXCL13 LEVELS IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND ITS CORRELATION TO DISEASE ACTIVITY AND LUPUS NEPHRITIS

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Background: Systemic lupus erythematosus (SLE) is a complex autoimmune disease that is characterised by the production of pathogenic autoantibodies against nuclear structures.¹ B lymphocyte chemoattractant (BLC) or CXC motif ligand 13 (CXCL13) play an important regulatory role of B1 and B2 cell trafficking for activation of autoreactive T helper cells.² CXCL13 can induce trafficking of the CXCR5⁺ T lymphocyte subset designated as follicular helper T lymphocytes which are specifically involved in production of autoantibodies during the development of lupus.³

Objectives: To detect serum CXCL13 levels in SLE patients and determine its relation to the disease activity and lupus nephritis

Methods: The study included 32 SLE patients and 20 healthy individuals as a control group. Patients' group was further subdivided according to disease activity and renal involvement. Serum samples from all studied individuals were analysed for the concentrations of CXCL13 by ELISA.

Results: There was a high statistically significant increase ($p<0.001$) in the mean of serum CXCL13 on comparing its levels in SLE patients [242 (121.5–855.6) pg/ml] versus control group [73.8 (22.8–120.3) pg/ml], and on comparing its levels in lupus nephritis patients [542.4 (171–855.6) pg/ml] versus other patients without lupus nephritis [212.9 (121.5–580.5) pg/ml]. Moreover, CXCL13 Concentrations were correlated with SLEDAI ($r=0.771$, $p<0.001$) and double-stranded DNA titres ($r=0.374$, $p<0.05$).

Conclusions: Our data suggest that CXCL13 has an important role in pathogenesis of SLE and lupus nephritis. Also, pharmacological regulation of CXCL13 and its receptor CXCR5 may be a useful therapy in lupus nephritis.

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Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.7326

AB0049 EVALUATION OF CASPASE-3, CASPASE-9, CASPASE-14 AND PANNEXIN-1 LEVELS IN BEHÇET'S DISEASE

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Background: Behçet's disease (BD) is a rheumatic disease in which various systemic findings such as especially recurrent oral ulcers, and genital ulcers, eye involvement, skin lesions, gastrointestinal involvement, neurological involvement, vascular involvement and arthritis can be seen.¹ The pathogenesis of the disease has not yet been fully understood. Caspases play a central role in apoptotic signal transduction. They are cysteine bound aspartate specific proteases.² There are three main types of caspases, the initiator caspases, the effector caspases and the inflammatory caspases. Pannexin-1 is a high-conduction voltage-gated channel protein that is commonly found in many organs and tissues including sensory systems and both neuronal and non-neuronal cell types.³

Objectives: The aim of this study is to examine the role of initiator, effector and inflammatory caspases in BD and the levels of pannexin duct protein, which is thought to be active in inflammation in BD and to compare clinical findings with healthy individuals.

Methods: Between January 2017 – June 2017, forty-six patients diagnosed with BD admitting to Cumhuriyet University Medical Faculty, Department of Internal Medicine Rheumatology and forty-four healthy volunteers without any rheumatic, systemic and metabolic diseases enrolled in this study. Clinical findings of all patients were recorded. The blood from a peripheral vein using suitable blood tubes was withdrawn to measure serum caspase-3, caspase-9, caspase-14 and pannexin-1 levels. Blood tests were examined by Elisa method in Cumhuriyet University Department of Biochemistry.

Results: The mean serum caspase-3 level was measured as 12.04 (11.25–43.69) pg/ml in BD group and 12.1 (11.19–484.3) pg/ml in healthy control (HC) group. There was no statistically significant difference between two groups ($p=0.143$). The mean serum levels of caspase-9 in the BD group were measured as 22 (5.14–29.33) pg/ml and 22.01 (11.23–850) pg/ml in the HC group. There was no statistically significant difference between the two groups ($p=0.593$). The mean serum caspase-14 level was 6 (5.2–8.21) pg/ml in the BD group and 6.15 (5.7–353) pg/ml in the HC group. There was no statistically significant difference between the two groups ($p=0.053$). The mean serum pannexin-1 levels were 6.36 (4.21–527.2) pg/ml in the BD group and 255.8 (5.38–2000) pg/ml in the HC. Serum pannexin-1 levels were statistically significant higher in the HC group ($p<0.0001$) (figure 1).

Abstract AB0049 – Figure 1. Serum levels of caspase-3, caspase-9, caspase-14 and pannexin-1 in patients with behçet's disease and healthy controls

Conclusions: Serum caspase-3, caspase-9 and caspase-14 levels were not statistically significant different between BD and HC groups. Serum pannexin-1 levels were statistically significant lower in the BD group.

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Acknowledgements: We would like to thank to "Cumhuriyet University Scientific Projects Unit (CUBAP)" for funding this project.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.3897

AB0050

BIOMAP® PHENOTYPIC PROFILING OF TWO BATCHES OF ORIGINATOR ETANERCEPT REVEALS EQUIVALENT ACTIVITY SIGNATURES CONSISTENT WITH CONSERVED BIOLOGICAL ACTIVITY

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Background: The BioMAP® platform is a complex human primary cell-based system for modelling tissue and disease states that is used to characterise drug activities based on the analyses of 148 clinically relevant biomarker readouts.

Objectives: To confirm that the BioMAP phenotypic signatures of two originator etanercept (ETN) samples remained comparable over time.

Methods: Two different ETN samples (ETN_1 and ETN_2) were independently profiled with a 5 year interval across a panel of 12 disease-relevant systems (3C and 4 hour [endothelial inflammation]; LPS [monocyte activation]; SAg [T cell activation]; BT [B cell activation]; BF4T and BE3C [epithelial inflammation]; CASM3C [vascular inflammation]; HDF3CGF, KF3CT, and MyoF [tissue remodelling, fibrosis]; Mphg [macrophage activation]). BioMAP systems consist of human primary cells or cocultures from healthy donors cultured in the presence of cytokines and growth factors. Protein levels, measured using immune-based methods or functional assays for cell viability and proliferation, were used to generate a BioMAP activity profile for each sample. ETN activities were annotated if they differed from the vehicle control and had an effect size >20%. The profiles of the 2 samples were compared using Pearson's correlation.

Results: BioMAP phenotypic profiling of ETN_1 versus ETN_2 samples at 10 µg/mL revealed similar signatures across 148 biomarkers in 12 disease-relevant systems. The Pearson's correlation coefficient was 0.781, which is above the determined threshold for mechanistic similarity ($r \geq 0.7$). Key efficacy-related anti-inflammatory and immunomodulatory activities were commonly inhibited in multiple systems including tumour necrosis factor alpha (LPS and BT), interleukin (IL)-2 (BT), vascular cell adhesion molecule 1 (MyoF and Mphg), IL-8 (SAg and MyoF), and E-Selectin (SAg and Mphg). The profiles of ETN samples at 1 µg/mL in the SAg system modelling T cell activation responses also revealed statistically significant similarity in signatures ($p < 0.01$) in both magnitude and direction across all biomarker activities (figure 1).

Abstract AB0050 – Figure 1. SAg system profile of ETN_1 and ETN_2 samples at 1 µg/mL.

Conclusions: The BioMAP phenotypic signatures of the ETN_1 and ETN_2 samples profiled in independent experiments using different primary cell pools remained comparable, which was consistent with conserved ETN mechanisms of action. The BioMAP platform represents a useful orthogonal approach for assessing ETN activity.

Disclosure of Interest: A. O'Mahony Employee of: Eurofins DiscoverX, E. L. Berg Employee of: Eurofins DiscoverX, H. Jones Shareholder of: Pfizer, Employee of: Pfizer, B. Fitzpatrick Shareholder of: Pfizer, Employee of: Pfizer, B. Hassett Shareholder of: Pfizer, Employee of: Pfizer, S. Vicik Shareholder of: Pfizer, Employee of: Pfizer, L. Marshall Shareholder of: Pfizer, Employee of: Pfizer, K. Roshak: None declared, E. Choy Grant/research support from: Novimmune, Pfizer, Roche, UCB, Consultant for: Abbott Laboratories, Amgen, Biogen, BMS, Celgene, Chugai Pharma, Eli Lilly, GSK, Hospira, Janssen, MedImmune, Napp, Novimmune, Novartis, Pfizer, Regeneron, Roche, R-Pharm, Sanofi

DOI: 10.1136/annrheumdis-2018-eular.2335

AB0051

THE INFLUENCE OF ANTI-INFLAMMATORY LIPOXIN A4 ON GENERATION OF CYTOKINES BY PBMCs OF PATIENTS WITH PSORIATIC ARTHRITIS

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Background: Psoriatic arthritis (PsA) is affecting up to 40% of the patients with psoriasis. The pathogenesis of PsA is not completely understood. One of the hypothesis suggest that repeated micro injuries and trauma and lack of proper inhibition of inflammation lead to chronic inflammation spreading to surrounding tissue and other joints and ligaments. One of the mediators which lead to inhibition of inflammation in healthy conditions are derivatives of arachidonic acid – lipoxins.

Objectives: The aim of the study was to assess if the influence of lipoxin A4 on inhibition of synthesis of pro-inflammatory cytokines by peripheral blood mononuclear cells (PBMCs) of patients with psoriatic arthritis.

Methods: The study group consisted of 10 patients with psoriatic arthritis and 5 healthy controls. The peripheral blood mononuclear cells from patients with PsA and healthy controls were isolated and were stimulated with lipopolysaccharide (LPS) with or without 200 nM of lipoxin A4 for 24 hours. The supernatants were collected after 24 hour stimulation. The levels of IL-1b, IFN-gamma, TNF alpha, MCP-1, IL-6, IL-8 and IL-33 were assessed by cytometric bead array system.

Results: Incubation of cells with LPS, increased production of all cytokines assessed either in patients with psoriatic arthritis or in healthy controls. In PBMCs from healthy controls incubation of cells with lipoxine A4 decrease production of proinflammatory cytokines (IL-1b, MCP-1, IL-8, IL-6, IL-33 and TNF-alpha; $p < 0.05$). However in patients with psoriatic arthritis addition of lipoxine A4 did not inhibit LPS – induced proinflammatory cytokines release (IL-1b, MCP-1, IL-6, IL-8, IL-33 and TNF-alpha, $p < 0.05$).

Conclusions: Our study demonstrated that modulation of Inflammation by lipid mediators in patients with psoriatic arthritis is dysregulated.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.7577