Objectives:

1. To investigate the role of OAS–RNase L pathway in PsA;
2. To quantify the hypothesised increased OAS–RNase L activity.

Methods: To further explore the gene expression data, we developed a highly sensitive ELISA and fluorescence resonance transfer (FRET) assay to access and compare the RNase L activity in plasma and serum derived from PsA (n=10), PsO (n=10) patients or healthy control donors (n=5).

Results: We found that RNase L activity was 2–3 fold higher in PsO and 3–5 fold in PsA compared to normal control (figure 1). Consistent with the gene expression analysis of upregulated type I IFN inducible genes, we also observed amplification of the downstream pro-inflammatory pathway consisting of RNase L dimer (active) and the produced cleaved RNA, which further induce IFN- β production and other inflammatory signalling.

Abstract AB0045 – Figure 1. RNASEL_Activity

Conclusions: The proportionally increased activation of OAS/RNase L in psoriatic arthritis merits further investigation into this pathway as a potential disease activity biomarker. RNase L is an easily quantifiable enzyme that could categorise disease severity and progression in daily routine lab ordered by primary physician. The timely diagnosis is key to improved function and quality of life in PsA patients.

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AB0046 TOFACITINIB IMPAIRS MONOCYTE-DERIVED DENDRITIC CELL DIFFERENTIATION IN RHEUMATOID ARTHRITIS AND PSORIATIC ARTHRITIS

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Background: Tofacitinib (Pfizer) is an oral Janus kinase inhibitor, recently approved for the treatment of rheumatoid arthritis (RA). Although its mechanism

of action has been explored in circulating cells, in particular neutrophils and lymphocyte, its effect on dendritic cells development remains still to be elucidate. Monocyte-derived dendritic cells are a subset of inflammatory DC derived from circulating monocytes and have a key role in inflammation and infection.

Objectives: The aim of this project is to evaluate the effect of Tofacitinib on inflammatory monocyte-derived dendritic cells (Mo-DC) from RA and PsA patients, and in particular on the ability of monocyte to differentiate into dendritic cells, an important step in innate immunity.

Methods: Mo-DC were isolated from blood of RA and psoriatic arthritis (PsA) patients by magnetic separation. Monocyte were plated in presence/absence of GM-CSF/IL-4 cocktail for 7 days, to acquire immature dendritic cell phenotype. To evaluate the effect of Tofacitinib on Mo-DC differentiation, monocyte were treated with 1 μ M Tofacitinib (or DMSO as control) for 15 min prior to cytokine stimulation. CD209 (immature DC marker) and CD14 (monocyte marker) were evaluated by flow cytometry in the CD11c positive population. Phagocytosis was investigated by the analysis of dendritic cell uptake of soluble antigens through two different mechanisms: non-specific macropinocytosis (using Lucifer Yellow), and receptor-mediated endocytosis (using DQ^{TM} Ovalbumin).¹ Western blot analysis was utilised for analysis of NOX5 and Actin protein expression on the total cell lysate.

Results: The pre-treatment of Mo-DC with Tofacitinib inhibited Mo-DC differentiation in RA and PsA patients, as shown by reduced CD209 surface marker expression, and a mirrored increase of CD14 marker. The decreased ability of monocyte to differentiate into dendritic cells was translated into a function impairment of phagocytic ability, as observed by the decreased uptake of both DQ^{TM} Ovalbumin (receptor-mediated endocytosis) and Lucifer Yellow (micropinocytosis) PsA cells treated with Tofacitinib. Low phagocytosis was observed in RA patients. NOX5 has previously been shown to play a key role in Mo-DC differentiation,² therefore we sought to investigate whether Tofacitinib could exert its effect on Mo-DC development through modulating NOX5. NOX5 protein expression was significantly decreased in Mo-DC pre-treated with Tofacitinib in PsA, and to a lesser extent in RA patients.

Conclusions: Together, these observations suggest a novel mechanism of action of Tofacitinib in RA and PsA, by inhibiting Mo-DC development, which may alter migration of DC to the joint and subsequent activation of the immune response.

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Cytokines and inflammatory mediators

AB0047 EXPRESSION OF IFN TYPE I RESPONSIVE GENES IN A CARDIOVASCULAR DISEASE CONTINUUM OF RHEUMATOID ARTHRITIS

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Background: Rheumatoid Arthritis (RA) patients have a prominent increase in cardiovascular disease (CVD) not fully explained by traditional risk factors¹. Interferons type 1 (IFN-I) have been associated with premature CVD in SLE² and are implicated in several aspects of atherosclerosis and acute coronary syndromes³. A subpopulation of RA patients also display a peripheral blood IFN-I signature from 25% to 65%⁴, associated with clinical response to biologics⁵. The IFN-I signature association with CVD in RA remains unclear.

Objectives: To analyse expression of interferon type 1 response genes (ISGs) along a cardiac MRI (CMR) phenotyped CVD continuum in patients with RA.

Methods: PBMC samples from 94 RA patients and 21 healthy controls (HC) were obtained. RA patients were stratified based on CMR into: RA CMRneg (no CVD-

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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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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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).