(SYBR Green technology). $2^{-\Delta\Delta Ct}$ method was used for analysis. 10 healthy donors were used as controls.

Results: Expression levels of miR-124-3 p were upregulated in the plasma of 33 (97.06%) of the patients when compared to controls. Receiver operating characteristic curve analysis was conducted in order to evaluate the diagnostic accuracy of the expression levels of the studied miRNA in the plasma. Area under the curve for miR-124-3 p was 0.879 (95% CI=0.740–1.00), $p=0.303 \times 10^{-3}$. When the relative quantification (RQ) cut value was 2.89, the sensitivity was 91.2% and the specificity was 80%. Levels of miR-124-3 p in plasma correlated with the diagnosis ($p=0.106 \times 10^{-3}$), with markers of inflammation – ESR ($p=0.0497$) and CRP ($p=0.047$) as well as with the immunological activity – the presence of RF ($p=0.007$), RF IgM ($p=0.004$), RF IgG ($p=0.004$), RF IgA ($p=0.005$) and anti-CCP antibodies in the serum ($p=0.025$).

Conclusions: In contrary to the literature data that report levels of miR-124 to be decreased in RA synovial fibroblasts we found increased expression of miR-124-3 p in the plasma of RA patients which might reflect the pathophysiological response to the inflammation, the effect of the treatment regimen or the presence of miR-124a gene promotor hypermethylation in the synovial tissue which might downregulate miR-124 locally.^{1,2} To our knowledge this is the first study to evaluate the diagnostic accuracy of plasma levels of miR-124 in RA patients as well as the possibility of using miR-124 as biomarker for disease activity but larger set is needed to confirm these results in the clinical practice.

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AB0014 GENETIC INFLUENCE OF DIFFERENT MEASURE FOR TUMOUR NECROSIS FACTOR INHIBITORS RESPONSE IN RHEUMATOID ARTHRITIS

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Background: The genetic studies of tumour necrosis factor inhibitors (TNFi) response in patients with rheumatoid arthritis (RA) have largely relied on the changes in complex disease scores as a measure of treatment response. It is expected that genetic architecture of such complex score is heterogeneous and not very suitable for pharmacogenetic studies.

Objectives: We aimed to select the most optimal phenotype for TNFi response using heritability estimates using genome-wide association studies (GWAS) in the Korean population.

Methods: Disease Activity Scores based on 28 joint counts (DAS28) and Clinical Disease Activity Index (CDAI) were assessed at baseline, and after 6 months in 370 Korean RA patients who started TNFi due to moderate or high disease activity. Genotypes were generated on the Illumina HumanOmni2.5Exome array (2.5 million variants) in TNFi-treated Korean patients with RA. We estimated heritability using a linear mixed-modelling approach (GCTA) for the TNFi drug-response phenotype Δ DAS28, Δ CDAI and its separate components, such as Δ swollen joint count (SJC), Δ tender joint count (TJC), Δ erythrocyte sedimentation rate (ESR), Δ visual-analogue scale of general health (VAS-GH) and Δ provider global assessment of disease activity (PrGA). Furthermore, a multivariate GWAS approach was implemented, analysing separate DAS28 and CDAI components simultaneously.

Results: The highest heritability estimates were found for Δ PrGA ($h^2=0.76$) and Δ TJC ($h^2=0.73$); lower heritability was found for Δ DAS28 ($h^2=0.32$) with estimates for Δ ESR ($h^2=0.66$), Δ SJC ($h^2=0.62$), Δ CDAI ($h^2=0.60$) and Δ VAS-GH ($h^2=0.53$) (all p -value<0.005).

Conclusions: Our results indicate that multiple SNPs together explain a substantial portion of the variation in change in provider global assessment of disease

activity in TNFi-treated patients with RA. In conclusion, optimal phenotype based on heritability suggests the use of changes in clinical disease activity index (CDAI) including provider global assessment than DAS28 in pharmacogenetic study.

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AB0015 THE EFFECT OF RARE CODING VARIANTS ON RESPONSE OF TNF INHIBITORS TREATMENT IN RHEUMATOID ARTHRITIS

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Background: Although pharmacogenetic studies of TNF inhibitors (TNFi) response presented the estimates of high heritability, only few loci with suggestive weak common association as biomarkers for TNFi response have been identified. **Objectives:** We aimed to identify novel functional rare variants associated with response to etanercept using targeted exon sequencing in Korea.

Methods: Disease activity scores were assessed at baseline and after 6 months in 156 Korean RA patients who started etanercept due to moderate or high disease activity. We analysed targeted exon sequencing data of 399 genes selected from a multifaceted approach. We conducted a single-marker association test ($MAF \geq 1\%$) and a gene-based analysis [optimal sequence kernel association test (SKAT-O)] of rare variants ($MAF < 1\%$). In addition, we performed gene set analyses of TNF pathway genes.

Results: We identified that clinical factors seem to influence the therapeutic good response of etanercept including male, high disease activity score at baseline, BMI. After stringent quality control, we analysed 14 024 variants of 399 genes in 156 RA patients. We identified two novel significant functional SNPs [rs16942564, rs61734378 (exon of AKAP13)] associated with response to etanercept, surpassing study-wide significant threshold ($p < 3.0 \times 10^{-5}$) in single variant association tests. Using a gene-based approach, we found two genes with nominal burden signals ($p < 0.001$) which did not reach study-wide significance. In the gene set enrichment test, we found no evidence for enrichment of association at genes involved in the TNF pathway.

Conclusions: We were unable to identify rare coding variants with large effect of 399 targeted genes. Our study suggests that rare coding variants of RA risk associated genes do not contribute to heritability of response to etanercept therapy.

Disclosure of Interest: None declared

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AB0016 CHROMATIN LOCALIZATION OF SURVIVIN IN CD4+ T-CELLS OF PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Oncoprotein survivin emerged as an important player in the pathogenesis of rheumatoid arthritis (RA). Results of genome-wide study suggest that survivin may take part in transcription stimulation of the RA-specific genes.

Objectives: To identify and describe survivin-dependent differences in transcription pattern between CD4+ T-cells of RA patients and healthy subjects focusing in particular on a subset of genes involved in maturation of Th1 and Th17 cells.

Methods: CD4+ T-cells were isolated from PBMC of 3 RA patients and 5 non-smoking and 2 smoking healthy controls using a positive selection and activated by Pam3cys+Concanavalin A+LPS. Chromatin immunoprecipitation (ChIP) was done using rabbit polyclonal anti-Survivin, purified DNA was prepared into libraries using ThruPLEX (Rubicon) and sequenced using HiSeq 2000 (Illumina). Resulting fastq sequencing files were mapped to the human reference genome (hg38) using the STAR aligner. Peaks were associated with the closest transcription start site. Enriched peak regions ($p < 10^{-5}$) were identified in survivin-ChIP samples above background ("input") using the Homer software. The peaks were analysed using gene ontology (GO) technique as implemented in GOrilla and GSEA software. The genes, scored high in RA and not present/low in any controls or vice versa were identified. The enriched GO groups were searched for presence of Th1/Th17 regulating genes.

Results: We identified 11 145 survivin-bound chromatin sequences. Out of them, GO technique indicated 770 genes in RA samples (7.3%) and 766 genes in healthy controls (19.5%) which were annotated and enriched ($-\log_5$) in GO

terms. In the screening for genes regulating maturation of Th1/Th17 cells, CBLB, IRF1, STAT3, SGK1 and TNFSF14 were identified among the genes enriched in RA samples, while EGR3 and ETS1 were enriched only in healthy controls. Additionally, transcription factors Ezh2, Rad21, Ctbp2 and Suz12 were identified as common for both RA and healthy groups genes, associated with significant GO enrichment.

Conclusions: This study confirms the role of survivin as a transcription mediator in CD4 +T cells and is suggested to influence multiple genes involved in RA pathology.

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AB0017 VITAMIN D LEVEL AND MIRNA 22 AND 125b GENE EXPRESSION IN BEHÇET'S DISEASE PATIENTS

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Objectives: To investigate serum levels of vitamin D and its effect on microRNA 22 and 125b gene expression in Behçet's disease (BD) patients and to evaluate their relation to clinical characteristics and disease activity.

Methods: Fifty-one BD patients and 45 matching controls were studied. Disease activity was assessed using BD Current Activity Form (BDCAF). Serum vitamin D3 was measured by ELISA. MicroRNAs were assayed by reverse transcription-quantitative polymerized chain reaction (RT-qPCR).

Results: Patients mean age was 34.3±8.6 years and disease duration 65.3±52.4 months. The BDCAF was 2.4±1.3. Vitamin D level was significantly lower (29.7 ±14.4 ng/ml) in patients than in control (40.1±17.8 ng/ml)(p<0.001) especially males (25.8±7.5 ng/ml) compared to females (48±23.7 ng/ml)(p<0.001). There was no relation between 25(OH)D levels and disease activity or with the presence of clinical manifestations. There was a 3.8±1.5 fold increase in miRNA125b while miR-22 showed no significant difference (0.38±0.46) but was significantly reduced in those receiving steroids (0.21±0.27) compared to those not (0.66±0.58) (p=0.003). There was no significant difference in the frequency of miR-22 or miR-125 expression according to the presence of clinical manifestations, medications received or disease activity. The fold change in miR-125b significantly correlated with vitamin D (r=0.54, p<0.001) but not with BDCAF (p=0.64).

Conclusions: Vitamin D level is decreased in BD patients and significantly correlated with the fold change of miR-125b especially in males thus representing a possible therapeutic target. The miR-22 expression did not change but was notably downregulated by steroids. Further longitudinal studies on a larger sample are recommended to validate the present results.

Disclosure of Interest: None declared

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AB0018 CLINICAL STATUS AND GENE EXPRESSION IN CLASS IV LUPUS NEPHRITIS

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Background: Lupus nephritis (LN) is one of the most frequent and serious complications in the patients with systemic lupus erythematosus. Several studies have identified risk factors for poor kidney prognosis in patients with SLE, including age, sex, hypertension, decreased estimated GFR (eGFR), proteinuria, and renal pathologic types.¹ Biopsy allows classifying the type of renal involvement, assessing its activity, and thus guiding the therapeutic behaviours. It has been shown that structural changes and inflammatory infiltrate associated with LN contribute to a hypoxic state which induces angiogenesis.² Herein, it was hypothesised that differential expression of angiogenic genes could classify Lupus

Nephritis Patients (LNP) with the same histological score but different "clinical status".

Objectives: To investigate if there is a differential angiogenic gene expression in biopsies of LNP under the same histological classification but different "clinical status" measured by eGFR.

Methods: Twenty four kidney biopsies samples classified according to ISN/RPS scoring system as Class IV from 24 LNP were divided into eGFR <60 ml/min (n=10, age: 31.00±10.93, range: 17–46) and eGFR >60 ml/min (n=14, age: 32.64 ±11.34, range: 21–64). RNA was isolated using TRIzol-Chloroform technique and then was reverse-transcribed using random primers. Gene expression level of pro-angiogenic factors: VCAM-1, VEGF, TGF-β and ANGPT-1 were evaluated using Quantitative Real Time PCR (QPCR). The threshold cycle (Ct) scores were averaged for calculations of relative expression values. The Ct scores were normalised by subtracting β2Microglobuline (β2M) control, or ΔCt=Ct, gene- Ct,β2M. To test for differential gene expression between groups, a two sample T-test was performed to compare the ΔCt in the two groups.

Results: ΔCt is inversely proportional to the gene expression level. Significant differences between groups was found in VEGF-A gene (p=0.0326), where the greatest expression corresponding to eGFR <60 ml/min group. However, there were not statistically significant differences in VCAM-1, ANGPT1 and TGF-β expression (table 1). Particularly TGF-β, a proangiogenic and profibrotic gene showed a uniform expression level in both groups.

Abstract AB0018 – Table 1. Levels of gene expression and laboratory parameters in eGFR <60 ml/min and eGFR >60 ml/min expressed as ΔCt values.

Gene	eGFR<60 ml/min n=10	eGFR>60 ml/min n=14	p value
VCAM-1	5,021±1768	6,248±3264	0,3165
VEGF-A	3,414±1161	4,651±1409	0,0326
TGF-β	6,168±1011	6,699±1351	0,3421
ANGPT1	10,330±2294	9,891±2113	0,5007

Conclusions: In the present cross-sectional study, increased levels of VEGF-A were observed in biopsies Class IV from LNP with eGFR <60 ml/min. These findings suggest a differential gene expression that may be associated with an impaired renal function, reflected by eGFR.

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AB0019 THE ROLE OF THE IL2-IL21 RS6822844 POLYMORPHISM IN THE PREDISPOSITION TO THE ERYTHROCYTE SEDIMENTATION RATE ELEVATION IN JUVENILE IDIOPATHIC ARTHRITIS

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Background: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disorder in paediatrics.¹ The erythrocyte sedimentation rate (ESR) is one of the key measures of the JIA activity.² However, in some patients, even in the active disease period, the ESR is not elevated.³

Objectives: The aim of the study was to assess the relationship between the IL2-IL21 rs6822844 locus polymorphic variants and a predisposition to the ESR elevation in JIA patients.

Methods: The study included 255 JIA patients from the Republic of Bashkortostan, Russia. The ESR was considered elevated if its value exceeded the upper limit of the normal range two or more times. Genotyping was performed by real-time PCR, statistical analysis – using the two-tailed Fisher exact test (p) and the odds ratio (OR) with a 95% confidence interval (CI).

Results: The girls/boys ratio was 65.88%/34.12%. The ESR elevation in the active disease period was seen in 70.98% of patients. When studying the IL2-IL21 rs6822844 polymorphic locus, a marginal significance level was noted for the rarer occurrence of the GT genotype in patients with the elevated ESR (14.92%