(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 × 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 × 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.

REFERENCES:

[1] Nakamachi Y, et al. MicroRNA-124a is a key regulator of proliferation and monocyte chemoattractant protein 1 secretion in fibroblast-like synoviocytes from patients with rheumatoid arthritis, Arthritis Rheum 2009;60 (5):1294–1304.
[2] Zhou Q, et al. Research of the Methylation Status of miR-124a Gene Promoter among Rheumatoid Arthritis Patients. Clin Dev Immunol 2013 (2013):524204.

Acknowledgements: The study was supported by Grant 76/2016 funded by Medical University – Sofia, Bulgaria.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2018-eular.5851

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

S. Bang[1], Y. Park[2], K. Kim[3], Y.B. Joo[4], S.-K. Cho[2], C.-B. Choi[2], Y.-K. Sung[2], T.-H. Kim[2], J.-B. Jun[2], D.-H. Yoo[2], H.-S. Lee[1], S.-C. Bae[2]. *[1]Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Guri*; *[2]Rheumatology, Hanyang University Hospital for Rheumatic Diseases*; *[3]Biology, Kyung Hee University, Seoul*; *[4]Rheumatology, St. Vincent's Hospital, Catholic University, Suwon, Korea, Republic of Ireland*

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 ΔDAS28, ΔCDAI 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 ΔPrGA (h^2=0.76) and ΔTJC (h^2=0.73); lower heritability was found for ΔDAS28 (h^2=0.32) with estimates for ΔESR (h^2=0.66), ΔSJC (h^2=0.62), ΔCDAI (h^2=0.60) and ΔVAS-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.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2018-eular.5286

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

S. Bang[1], Y. Park[2], H.-H. Kwon[1], H. Yoo[1], H.-S. Lee[1], S.-C. Bae[2]. *[1]Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Guri*; *[2]Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Korea, Republic of Ireland*

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 ≥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
DOI: 10.1136/annrheumdis-2018-eular.6862

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

S. Andres[1], K.M. Andersson[2], A. Damdimopoulos[3], G. Katona[1], M.I. Bokarewa[2,4]. *[1]Department of Chemistry and Molecular Biology*; *[2]Department of Rheumatology and Inflammation Research, University of Gothenburg, Gothenburg*; *[3]Department of Biosciences and Nutrition, Karolinska Institutet, Solna*; *[4]Sahlgrenska University Hospital, Gothenburg, Sweden*

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 sequencies. 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