<50%, *MAML2* (P=8x10^{-19}) and *EBF1* (P=1x10^{-12}). Interestingly, the expression of *IL23R* remained unaltered. Other genes that were significantly upregulated (1.5 – 2.0 fold) were *IL12RB2*, *TTC1* and *PSMD6*. Genes that were also significantly repressed (0.5 - 0.8 fold) were *SERBP1*, *ATXN7*, *PSIP1*, *ZNF385D*, *SIPA1L1*.
Conclusion: This combined genetic and functional meta-analysis elucidated novel genes, functional networks and pathways for psoriasis. These results will lead to important insights into the immunopathogenesis and treatment of psoriasis.

REFERENCES

[1] Tsoi LC, Stuart PE, Tian C, et al. Large scale meta-analysis characterizes genetic architecture for common psoriasis associated variants. Nat Commun. 2017 May 24;8:15382. PMID: 28537254.
[2] Luo L, Peng G, Zhu Y, et al. Genome-wide gene and pathway analysis. Eur J Hum Genet. 2010 Sep;18(9):1045-53. PMID: 20442747.
[3] Saeed M. Novel linkage disequilibrium clustering algorithm identifies new lupus genes on meta-analysis of GWAS datasets. Immunogenetics. 2017 May;69(5):295-302. PMID: 28246883.
[4] Nair RP, Duffin KC, Helms C, et al. Genome-wide scan reveals association of psoriasis with IL-23 and NF-kappaB pathways. Nat Genet. 2009 Feb;41 (2):199-204. PMID: 19169254.

Disclosure of Interests: Mohammad Saeed Shareholder of: Partner at Immuno-Cure - laboratory, which performs Autoimmune antibody testing, Grant/research support from: Participation in EULAR 2019 Meeting is sponsored by High-Q Pharma Pak
DOI: 10.1136/annrheumdis-2019-eular.306

AB0017 COMPARISON BETWEEN THE ALTERED PERIPHERAL BLOOD MIRNA EXPRESSION IN PATIENTS WITH RHEUMATOID ARTHRITIS AND SYSTEMIC LUPUS ERYTEMATOSUS

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Background: MicroRNAs (miRNAs) are a class of small, non-coding RNAs that negatively regulate gene expression at posttranscriptional level. Altered miRNA expression in the circulation has been described in inflammatory joint diseases such as rheumatoid arthritis (RA) as well as in systemic rheumatic diseases, such as systemic lupus erythematosus (SLE). miR-146a and miR-155 have been found to regulate key signaling pathways involved in the pathogenesis of RA and SLE [1-2].
Objectives: To compare the expression levels of miR-146a and miR-155 in peripheral blood (PB) from RA and SLE patients in regard to their use as disease biomarkers.
Methods: 63 RA patients and 40 SLE were included in the study. The expression levels of miR-146a and miR-155 in whole PB were determined by qPCR (Sybr-Green technology) and compared to healthy controls (HCs). Relative changes of gene expression levels of the studied miRNAs were calculated by $2^{-\Delta\Delta Ct}$ method. SPSS was used for statistical analysis.
Results: 29 (46.03%) of the RA patients showed overexpression of miR-146a in the PB when compared to HCs, but the levels were not statistically significant to differentiate patients from HCs (p=0.365). 34 (53.97%) of the RA patients didn't show a statistically significant expression of miR-155 in the PB when compared to HCs and PB expression of miR-155 couldn't be used for differentiating RA from HCs (p=0.074). In the group of SLE patients the PB levels of miR-146a were over-expressed in 25 (62.5%) and levels of miR-155 were increased in 20 (50.0%) of the patients (p<0.05).
Conclusion: Although miR-146a and miR-155 are involved in key signaling pathways in the pathogenesis of RA their whole PB expression could not fully reflect the local pathological process and thus to differentiate patients from HCs. The expression of both miRNAs in whole PB of SLE samples showed a possibility for discriminating patients from HCs. Further analysis with larger sets is needed to confirm if altered systemic miRNA expression levels could be used in the clinical practice as disease biomarkers.

REFERENCES

[1] Honarpisheh M, Köhler P, von Rauchhaupt E, Lech M. The Involvement of MicroRNAs in Modulation of Innate and Adaptive Immunity in Systemic Lupus Erythematosus and Lupus Nephritis. J Immunol Res. 2018; 2018:4126106.
[2] Zhou Q, Haupt S, Kreuzer JT, et al. Decreased expression of miR-146a and miR-155 contributes to an abnormal Treg phenotype in patients with rheumatoid arthritis. Anna Rheum Dis. 2015; 74:1265-1274.

Acknowledgement: The study was supported by Grant 60/2013 and Grant 51/2014 and funded by Medical University-Sofia.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.8016

AB0018 TRANSCRIPTOMIC CHARACTERIZATION OF SINGLE PATHOGENIC MEMORY B CELLS IN RHEUMATOID ARTHRITIS

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Background: Autoantigen-specific B lymphocytes are crucial players in the development of rheumatoid arthritis (RA). Despite the fact that ACPA+ autoreactive memory B cells have been observed in the majority of RA patients for a long time, their properties still remain enigmatic.
Objectives: In this study, we aimed to reveal transcriptomic nature of single pathogenic memory B cells from RA patients.
Methods: Single-cell full-length RNAseq data was generated from ACPA+ and control memory B cells from 7 human donors with established rheumatoid arthritis and subjected to transcriptome analyses as well as B cell receptor (BCR) assembly.
Results: Both transcriptome and BCR data was successfully generated from the majority of the sequenced cells. The success rate depended on chosen sequencing parameters as well as on a BCR assembling algorithm that was used. We observed expression of genes defining memory B cell population in our data as well as pathways crucial for their function.
Conclusion: Taken together, gene expression and BCR sequence data obtained from the same single cell can give novel insights into the biology and role of B cells in the development of the disease.
Acknowledgement: This work has received support from the EU/EFPIA Innovative Medicines Initiative 2 Joint Undertaking RTCure grant n° 777357.
Disclosure of Interests: Deimante Simaite Employee of: Sanofi, Linda Slot Grant/research support from: Sanofi, Veeranagouda Yaligara Employee of: Sanofi, Virginia Savova Employee of: Sanofi, Claus Reimertz Employee of: Sanofi, Carsten Struebing Employee of: Sanofi, Axel Dietrich Employee of: Sanofi, Emanuele de Rinaldis Employee of: Sanofi, Michel Didier Employee of: Sanofi, Matthias Herrmann Employee of: Sanofi, Frank Nestle Employee of: Sanofi, Hans Ulrich Scherer Grant/research support from: Sanofi, BMS, Rene Toes Grant/research support from: Sanofi
DOI: 10.1136/annrheumdis-2019-eular.1947

AB0019 REPLICATIVE STUDY OF GWAS-ASSOCIATED CANDIDATE GENE LOCI IN PATIENTS WITH OSTEOARTHRITIS FROM THE BASHKORTOSTAN REPUBLIC

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Background: Osteoarthritis (OA) is one of the most common joint diseases and a global socially significant problem. Currently, new methods of early diagnosis of the disease are being developed, before the development of destructive processes in various tissues of the joint. The leading role in determining the pathophysiology of OA is given to the identification of genetic and epigenetic mechanisms.
Objectives: The main goal of the study was replicative analysis of the associations of loci associated with OA according to the data of genome-wide analysis of associations (GWAS) located near the DOT1L, ALDH1A, GNL3, GLT8D1, ASTN2, FILIP1, SENP6, NCOA3, DVWA, CHA11 genes with various localization OA.
Methods: DNA samples from 410 women were used (mean age 45.45 ± 2.35). Patients with OA was carried out in accordance with the criteria of the American Association of Rheumatology (1995), the debut of the disease before the age of 55 years and radiographic confirmation. For genotyping, PCR-RFLP analysis using KASP@ technology was used. As a calculation tool, MS Office Excel 2007 (Microsoft), Statistica v.6.2 (StatSoft), SPSS v.13 (SPSS Inc) software packages are used.
Results: We conducted replicative analysis of the 12 loci that were the most significantly associated with OA in the results of GWAS study, among which rs12982744 and rs2302061 (DOT1L), rs4836732 (ASTN2), rs9350591 (FILIP1 &

SENP6), rs6976 (GLT8D1), rs6094710 (NCOA3), rs11177 (GNL3), rs7639618 (DVWA/COL6A4P1), rs3204689 (ALDH1A2), rs11842874 (MCF2L), s6539153 and rs835487 (CHST11).
The rs4836732 locus of the ASTN2 gene showed an association of the *C*C genotype with OA in general ($\chi2 = 5.064$, p = 0.024, OR = 2.78; 95% CI (1.11-6.97), with early manifestation of OA (up to 50 years) ($\chi2 = 5.357$, p = 0.004, OR = 5.35; 95% CI 1.53-18.68) and with generalized osteoarthritis ($\chi2 = 8.071$, p = 0.004, OR = 5; 95% CI 1.52-16.35), which is consistent with the results of GWAS.
The *T allele of the rs7639618 locus of DVWA gene showed an association with late onset OA ($\chi2 = 5.21$, p = 0.022, OR = 1.88; 95% CI 1.09-3.24).
The *T*T genotype (0.676) of the rs835487 locus (CHST11) was associated with OA of the hip ($\chi2 = 6.284$, p = 0.012, OR = 2.57; 95% CI 1.21-5.48), which contradicts the results GWAS, where the allele *G was significantly associated with OA of the hip in European populations.
An association of the allele *C ($\chi2 = 4.558$, p = 0.032, OR = 2.04; 95% CI 1.05-3.95) and its homozygous genotype *C*C (0.115) ($\chi2 = 6.398$, p = 0.01, OR = 22.3; 95% CI 1.22-408.21) in rs2302061 locus of the DOT1L gene with knee OA was find.
The *T*T genotype of the rs6976 (GLT8D1) was associated with early manifestation of OA ($\chi2 = 5.213$, p = 0.022, OR = 2.58; 95% CI 1.14-4.26).
The study of the rs3204689 locus (ALDH1A) revealed an association of the genotype *C*G with the generalized osteoarthritis ($\chi2 = 6.071$, p = 0.013, OR = 2.52; 95% CI 1.19-5.33) and the genotype *C*C turned out to be protective ($\chi2 = 5.226$, p = 0.022, OR = 0.39; 95% CI 0.17-0.89).
Conclusion: Thus, the replication of GWAS results does not always confirm the associations identified earlier, which may be due to a number of reasons.
Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.5870

Adaptive immunity (T cells and B cells) in rheumatic diseases

AB0020 INTERACTION MTHFR 677C/T AND PON1 -108C/T POLYMORPHISMS IS ASSOCIATED TO ATHEROGENIC RISK IN RHEUMATOID ARTHRITIS PATIENTS FROM SOUTHERN MEXICO

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Background: The risk of cardiovascular disease in rheumatoid arthritis (RA) patients is 1.5 times higher compared to the general population. Some factors relationships to cardiovascular disease in RA are high clinic activity of the disease, the autoantibodies-positive, the disease duration and pharmacological treatment[1], as well as single nucleotide polymorphisms. Methylenetetrahydrofolate reductase (MTHFR) is a key enzyme in folate metabolism and is considered a drug-metabolizing enzyme; MTHFR 677C/T polymorphism was described leading to reduced enzyme activity, increasing serum concentration of homocysteine, an intermediate product of methotrexate metabolism. Paraoxonase 1 (PON1) is a multifunctional enzyme that can detoxify through its homocysteine thiolactonase activity, the polymorphism identified in the position PON1 -108C/T exerts effects on serum activity and expression levels.
Objectives: We evaluate the association between the interaction MTHFR 677C/T and PON1 -108C/T polymorphisms and cardiovascular risk (CVR) in RA patients.
Methods: A cross-sectional study was performed including 250 RA patients diagnosed according to ACR/EULAR 2010 criteria, attended in a public hospital from southern Mexico. MTHFR 677C/T and PON1 -108C/T genotypes were determined by PCR-RFLP method. The clinic and metabolic parameters were evaluated. CVR was defined using different diagnostic tools. Logistic regression models were used to evaluate the association between interaction polymorphisms and CVR.
Results: We show high CVR in a variable prevalence according to diagnostics tools: TGs/HDL-c (64.8%), Castelli (50%) and Kannel (43%). Alleles frequency of 667C/T were 33% for C and 67% for T allele; PON1-108C/T 52% for C and 43% for T allele. In a multiple regression model adjusting by duration of disease, pharmacological therapy and DAS28-hsCRP score, carriers of the 667TT and -108CC genotypes had higher CVR according to TGs/HDL-c (>3%) (OR=4.68, p=0.019), Castelli (>3%) (OR=2.99, p=0.03) and Kannel index (>4.5% in woman and >5% in men) (OR=2.03, p=0.13).
Conclusion: Our results demonstrate an interaction between MTHFR 677C/T and PON1 -108C/T polymorphisms on the CVR, associated to atherogenic indexes in RA patients from southern Mexico.

REFERENCES
[1] Mackey RH, Kuller LH, Moreland LW. Cardiovascular disease risk in patients with rheumatic diseases. Clin Geriatr Med. 2017;33(1):105-117. doi: 10.1016/j.cger.2016.08.008.

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2019-eular.8009

AB0020B QUANTIFYING DIFFERENCES IN HERITABILITY AMONG PSORIATIC ARTHRITIS (PSA), CUTANEOUS PSORIASIS (PSC) AND PSORIASIS VULGARIS (PSV)

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Background: Epidemiological studies have established a large recurrence risk ratio among siblings suggesting a strong genetic component for psoriasis and psoriatic arthritis (1). Better understanding of the heritability of PsC, PsV and PsA will lead to more efficient genetic profiling for psoriatic disease.
Objectives: We set out to assess the heritability of cutaneous psoriasis without known arthritis (PsC); psoriasis vulgaris (psoriasis irrespective of arthritis, PsV) and psoriatic arthritis (PsA) by interrogating SNPs from a large scale genotyping array.
Methods: The heritability of PsC, PsV and PsA were estimated by interrogating 715 PsA, 1155 PsC, 2938 PsV patients and 3117 unaffected controls of European ancestry. The samples were genotyped on a custom Axiom Biobank plus genotyping array and core GWAS chip with 461,092 autosomal SNPs. Further imputation led to 1.3M well-imputed SNPs based on the autosomal reference panel of the HapMap Phase 3 (HM3) CEU cohort. After strict filtering, 230k autosomal SNPs without imputation and 401k autosomal SNPs after imputation were retained for heritability estimation.
The following two methods were used to determine the heritability of PsC, PsV and PsA from SNP based data: Linkage Disequilibrium Adjusted Kinships (LDAK) and GCTA which relies on the restricted maximum likelihood algorithm (ReML). Sex and the top 5 principal components were used as covariates to control for gender effect and population stratification in each analysis. Parallel analyses were performed after removing SNPs from the MHC region. The prevalence also was used to adjust the heritability estimation.
Results: The heritability assessment for psoriatic disease for each method is presented in the table with and without imputation. Although the heritability estimates vary depending on the method, the heritability of PsC appears to be greater than PsA, for analysis that was done with and without imputation. Similar trends are noted when non-MHC SNPs were assessed.

Table 1. Heritability estimation before and after imputation, including and excluding MHC SNPs

Test	PsA		PsC		PsV	
	h2 (sd)	Imp'ed h2 (sd)	h2 (sd)	Imp'ed h2 (sd)	h2 (sd)	Imp'ed h2 (sd)
LDAK (all SNPs)	0.45 (0.10)	0.48 (0.08)	0.81 (0.09)	0.72 (0.07)	0.68 (0.06)	0.60 (0.05)
LDAK (non MHC SNPS)	0.28 (0.10)	0.32 (0.09)	0.48 (0.09)	0.41 (0.08)	0.40 (0.07)	0.35 (0.05)
GTCA (all SNPs)	0.39 (0.09)	0.27 (0.07)	0.42 (0.06)	0.34 (0.05)	0.26 (0.03)	0.20 (0.03)
GTCA (non MHC SNPs)	0.32 (0.09)	0.20 (0.07)	0.34 (0.06)	0.27 (0.05)	0.22 (0.03)	0.16 (0.03)

Conclusion: SNP based heritability estimates suggest greater heritability for PsC as compared to PsA. Common environmental factors may need to be considered to account the strong recurrence rate of PsA over psoriasis among first degree relatives reported in previous epidemiological studies, as this finding is not noted from large SNP based association studies.

REFERENCES
[1] Chandran V, Schentag CT, Brockbank JE, Pellett FJ, Shaumugrajah S, Toloza SM, Rahman P, Gladman DD. Familial aggregation of psoriatic arthritis. Ann Rheum Dis. 2009; 68(5):664-7.

Disclosure of Interests: Quan Li: None declared, Vinod Chandran: None declared, Lam Tsoi: None declared, Rajan Nair: None declared, Dafna D Gladman Grant/research support from: AbbVie, Amgen, Celgene, Lilly, Novartis, Pfizer, and UCB, Consultant for: AbbVie, Amgen, BMS, Celgene, Galapagos, Gilead, Janssen, Lilly, Novartis, Pfizer, and UCB, James T. Elder: None declared, Proton Rahman: None declared
DOI: 10.1136/annrheumdis-2019-eular.3317