dently (dcSSc: P=3.20E-2, OR=1.13; PAH: P=2.19E-02, OR=1.32). However, our data revealed a stronger effect size with the subset of SSc patients showing both clinical manifestations (dcSSc with PAH: P=6.91E-3, OR=2.05).
Conclusions: We revisited the association of the MIF rs755622*C allele with SSc and described a phenotype-specific association of this variant with the susceptibility to develop PAH in dSSc patients.
Disclosure of Interest: None declared
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AB0004 PSORIATIC ARTHRITIS. GENES INVOLVED IN THE MESTIZO POPULATION

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Background: Psoriatic Arthritis (PsA) is not a regular systemic autoimmune disease, many expert define it with autoinflammatory disease, resulting in chronic inflammation of the synovium and consequent cartilage and bone erosion in approximately 10% of patients with skin psoriasis. It is important to identify novel genomic biomarkers associated with disease susceptibility but also able to detect early those patients with negative prognostic factors who may benefit from a more aggressive therapeutic approach. The over-expression of tumor necrosis factor (TNF)-a is a central element in the pathogenesis of psoriasis and psoriatic arthritis (2). The levels of TNF-alpha are under genetic control. An "A" at position *-308* in the *TNFA* promoter has been shown to be associated with increased level of TNF-alpha expression and "A" at position *-238* with a diminished level of TNF-α expression (3,4). Many authors consider that it is a disease only of Europeans descendants or Caucasians, however never be studied in mestizo population
Objectives: We investigate the potential association between the *TNFA*-238 G/A, *TNFA*-308 G/A, *IL10 -1082 G/A,-819C/T, -592C/A* polymorphisms and the Psoriatic Arthritis susceptibility.
Methods: The study included 52 PsA patients diagnosed by CASPAR criteria and 52 controls. The polymorphism of TNFA-308 G/A (rs1800629), TNFA-238 G/A (rs361525), IL10 -1082 G/A (rs1800896), -819C/T (rs1800871) and -592C/A (rs1800872) were genotyped by single specific primers -polymerase chain reaction (SSP-PCR). All subjects were from an unrelated Venezuelan-Mestizo population with a history of ancestors, at least back to the third generation
Results: When comparing allele and genotype frequencies between the groups studied, no significant differences were observed for the TNFA-308 G/A (rs1800629) and IL10 -1082 G/A (rs1800896), -819C/T (rs1800871) and -592C/A (rs1800872). However, our results showed a significant decrease in the frequency of the TNF-*238A* allele among PsA patients compared to healthy individuals (3.8% vs. 10.57%, respectively, OR: 0.31, 95% CI: 0.92 -1.05, p: 0.02), suggesting that *TNFA-238A* allele may have a protective effect (Table 1).

Table 1. Genotypic and allelic frequencies of the 308 G / AG (rs1800629) and -238 G / A (rs36152! variants of the TNFA gene in patients with psoriatic arthritis and healthy controls

TNFA-308 G/A (rs1800629)	PsA n=73	Controls n= 52	OR (IC95%)	*P*
Genotype				
GG	80,7%	84,6% (44)	0,76(0,27-2,12)	0,302
GA	19,3%	15,4% (8)	1,30(0,47-3,63)	0.302
AA	0%	0 % (0)		
Allele				
G	92,3%	90,4% (94)	1,27(0,48-3,37)	0,311
A	7,3 %	9,6% (10)	0,78(0,29-2,07)	0,311
TNFA-238 G/A (rs361525)	PsA n=73	Controls n= 52	OR (IC95%)	*P*
Genotype				
GG	92,3%	78,8% (41)	3,22(0,95-10,8)	*0,025
GA	7,7 %	21,2% (11)	0,31(0,09-1,05)	*0,025
AA	0	0		
Allele				
G	96,2%	89,4%(93)	2,95(0,91-9,61)	*0,0306
A	3,8%	10,6 %(11)	0,39(0,10-1,09)	*0,0306

NOTE: The values shown in parentheses represent the number of individuals carrying the genotype for the polymorphic site studied. The frequency is expressed as a percentage (p> 0.05: not significant, p <0.05: significant) psoriatic arthritis and healthy controls

Conclusions: This is the first genetic study carried out in Venezuelan mestizo patients with Psoriatic Arthritis to establish associations between genetic markers such as the polymorphisms of the promoter region of the TNFA and IL10 genes and the disease. In conclusion the *TNFA*-238 G/A polymorphism might play an important role in the development of Psoriatic Arthritis in Venezuelan mestizos and this association could not only clarify the different factors involved in a multifactorial disease, such as Psoriatic Arthritis, but also establish the relationship of these molecular markers with some clinical manifestations of the disease, which would allow in the future to determine the suitability or not to use some types of treatments, such as the use of anti-TNF therapy, for example.
References:
[1] Morales-Zambrano, et al. Int J Clin Exp Med. 2014; 7(9): 2605–2614.
[2] Bowes J, Barton A. Discov Med. 2010;10 (52):177–83.
[3] Liu Y, Helms C, et al. PLoS Genet, 2008;4(3): 1000041.
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AB0005 CYTOKINE MRNA GENE EXPRESSION ASSOCIATED WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Systemic lupus erythematosus (SLE) is a complex polygenic autoimmune disease, characterized by autoantibody production, inflammatory manifestation and imbalanced cytokine production. In accordance with the pivotal role of Th17 cell in autoimmunity and the altered Th17/Tregs balance in response to changes in the cytokine milieu we analyzed mRNA expression of several cytokines in peripheral blood of SLE patients. Quantification of mRNA expression in peripheral blood could be useful to assess the disease activity of SLE patients.
Objectives: The aim of the present study was to investigate the gene expressions at mRNA level of proinflammatory (TNFA, IL18, IL12B); Th17-related (IL23A); immunosuppressive (TGFB1 and IL10) cytokines and Treg-specific transcription factor Foxp3 in peripheral blood of women with SLE.
Methods: Total RNA from peripheral blood was isolated from 28 female patients with SLE and 17 healthy women. Quantitative real-time polymerase chain reaction was performed for 7 genes of interests, using the TaqMan detection system. Relative quantitative evaluation of mRNAs was performed by the comparative ΔΔCt method and results are presented as n-fold mean difference (RQ-relative quantity) of target genes relative to calibrator (healthy controls) after normalization to the reference gene-GAPDH. Disease activity in SLE was determined by SLEDAI and divided into three categories: mild (0–5), moderate (6–10) and high (>10).
Results: The results reveal considerable overexpression of IL23A in SLE patients compared to healthy controls (RQ=5.347; $p<0.001$). According to the level of disease activity we found the highest elevation of IL23A in patients with SLEDAI>10 (RQ=8.54; $p<0.001$) compared to the controls. In inactive to mild (SLEDAI 0–5) and moderate SLE (SLEDAI 6–10), IL23A was also upregulated in approximately equal rate (RQ=4.976; $p<0.001$ and RQ=4.64; $p<0.001$). In addition, immunosuppressive cytokines IL10 and TGFB1 mRNA were elevated significantly in SLE patients than in controls (RQ=1.79; p=0.0077 and RQ=1.78; p=0.02, respectively). We also found that the expression of proinflammatory TNFA and IL12B were significantly downregulated approximately 2-fold. The mRNA level of Foxp3 was downregulated only for patients with SLEDAI>10. A significant good correlation between IL18 and the SLEDAI score was found (r=0.5548; p=0.002). Higher IL18 expression was observed among patients with worsened SLE compared to those with mild (RQ=1.656; p=0.008) and moderate (RQ=1.474; p=0.034) disease activity. We further demonstrated positively correlation between the expression levels of IL23A and TGFB1 (r=0.7276; $p<0.001$) among SLE patients.
Conclusions: These results suggest that upregulation of IL23 and TGFB1 in addition to downregulated Foxp3 expression may contribute to skewing towards Th17 profile in SLE pathogenesis and this was the most markedly manifested at the highest level of disease activity. Our results support indirectly the idea for restoring Th17/Treg balance as a therapeutic target in SLE.
Disclosure of Interest: None declared
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AB0006 MICRORNA-499 IN BEHCET DISEASE AND POSSIBLE ASSOCIATION WITH DISEASE ACTIVITY

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Background: Behçet Disease (BD) is a relapsing inflammatory autoimmune disease. Although the etiology of BD is not yet known, genetic predisposition and immune dysregulation are thought to be critical factors in the pathogenesis of the disease. MicroRNAs (miRNAs) are small RNA fragments that can regulate the gene expression. miRNAs play a critical role in the pathogenesis of autoimmune or auto inflammatory diseases. Sinngle nucleotide polymorphisms (SNPs) may change the property of miRNAs through altering miRNA expression and/or maturation.
Objectives: The aim of this work was to detect miRNA-499 (rs3746444) genotyping and relative expression in BD patients in order to find out the possible association between them and disease activity and severity.
Methods: Relative expression of miRNA-499 was measured by Real-Time PCR and miRNA-499 gene (rs 3746444) genotyping was performed by TaqMan SNP

Genotyping Assay in blood samples obtained from 47 patients BD diagnosed according to 1990 international criteria for behcet disease and 50 matched healthy controls. Disease activity was done using BD current activity form (BDCAF).
Results: Study of miRNA-499 polymorphism, showed that the genotype frequencies of TT, CT, and CC were 21.3%, 63.8%, and 14.9% in BD patients and 18.0%, 52.0%, and 30.0% in the control group respectively. A significant increase in the relative expression of miRNA-499 was found in BD patients compared to control ($P<0.05$). There was no significant relation between relative expression of miRNA-499 and activity of BD patients assessed by BDCAF ($P>0.05$). In addition there was association between genotypes of miRNA-499 and posterior uveitis ($P<0.05$). There was association of the relative expression of miRNA-499 with miRNA-499 (rs3746444) polymorphism and vascular manifestations ($P<0.05$).
Conclusions: Genotyping of miRNA-499 showed higher percentage of TT genotype in BD patients than control and also miRNA relative expession, they may be implicated in pathogenesis of the disease. Genotype TT for miRNA-499 is associated with posterior uveitis. miRNA relative expression is associated with vascular manifestations and aneurysm.
Disclosure of Interest: None declared
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AB0007 SHARED GENETIC PREDISPOSITION IN RHEUMATOID ARTHRITIS–INTERSTITIAL LUNG DISEASE AND FAMILIAL PULMONARY FIBROSIS

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Background: Despite its high prevalence and mortality, little is known about the pathogenesis of RA–associated interstitial lung disease (RA-ILD). Given that familial pulmonary fibrosis (FPF) and RA–ILD frequently share the usual interstitial pneumonia pattern and common environmental risk factors, we hypothesized that the two diseases may share additional risk factors including FPF-linked genes.
Objectives: Our aim was to identify coding mutations of FPF-risk genes associated with RA-ILD.
Methods: We used whole-exome sequencing (WES) followed by restricted analysis of a discrete number of FPF-linked genes and performed a Burden test to assess the excess number of mutations in RA–ILD patients compared to controls.
Results: Among the 101 RA–ILD patients included, 12 (11.9%) had 13 WES-identified heterozygous mutations in the *TERT*, *RTEL1*, *PARN* or *SFTPC* coding regions. The burden test, based on 81 RA–ILD patients and 1010 controls of European ancestry, revealed an excess of *TERT*, *RTEL1*, *PARN* or *SFTPC* mutations for RA–ILD patients ($p=9.45'10^{-4}$, odds ratio [OR] 3.17 95% CI 1.53–6.12). Telomeres were shorter for RA-ILD patients with a *TERT*, *RTEL1* or *PARN* mutation than controls ($p=2.87x10^{-2}$).
Conclusions: Our results support the contribution of FPF-linked genes to RA–ILD susceptibility.
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AB0008 THE ASSOCIATION OF THE PTPN22 RS2476601 GENE POLYMORPHISM WITH JUVENILE IDIOPATHIC ARTHRITIS IN CHILDREN FROM RUSSIA

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Background: Juvenile idiopathic arthritis (JIA) is the most common chronic rheumatic disease in children. The exact cause of the disease is still unknown, but seems to be related to both genetic and environmental factors [1]. The protein tyrosine phosphatase non-receptor type 22 (*PTPN22*) gene single-nucleotide polymorphism (SNP) rs2476601 was shown to be associated with JIA in different populations, but according to resent reports this association is restricted only to females [2,3].
Objectives: The aim of the study was to determine whether the *PTPN22* rs2476601 SNP is associated with the development of JIA and its subtypes in children from Russia.
Methods: The study included 330 patients with JIA and 346 healthy controls from Russia. Genotyping was performed using real-time PCR method and statistical analysis - using two-tailed Fisher's exact test (p), odds ratio (OR), 95% confidence interval (95% CI).
Results: The frequencies of the genotype AG and the allele A were significantly higher and the frequencies of the genotype GG and the allele G were significantly lower in patients with JIA than in controls (p=0.016, OR=1.65, 95% CI 1.10–2.48; p=0.028, OR=1.48, 95% CI 1.05–2.08; p=0.016, OR=0.62, 95% CI 0.43–0.91; p=0.028, OR=0.68, 95% CI 0.48–0.95, correspondingly). The same analysis was then performed separately for patients with two the most frequent ILAR subtypes: persistent oligoarthritis (n=106) and RF-negative polyarthritis (n=85). Significant associations similar to those in the whole JIA group were found only for persistent oligoarthritis (p=0.018 for the genotype AG; p=0.037 for the allele A; p=0.022 for the genotype GG; p=0.037 for the allele G). No significant differences were found for patients with RF-negative polyarthritis ($p>0.6$). Sex-stratified analysis showed that for the whole JIA group and for persistent oligoarthritis the association with the *PTPN22* rs2476601 SNP is restricted only for girls (for girls with the genotype AG: p=0.024 and p=0.0098; with the allele A: p=0.016 and p=0.0061; with the genotype GG: p=0.015 and p=0.0047; with the allele G: p=0.016 and p=0.0061, correspondingly; for boys: $p>0.2$ for all comparisons).
Conclusions: In this study we revealed the association of the *PTPN22* rs2476601 SNP with the development of JIA and its persistent oligoarticular subtype in girls from Russia.
References:
[1] Ravelli A, Martini A. Juvenile idiopathic arthritis. Lancet. 2007;369:767–778.
[2] Chiaroni-Clarke RC, Li YR, Munro JE, Chavez RA, Scurrah KJ, Pezic A, et al. The association of PTPN22 rs2476601 with juvenile idiopathic arthritis is specific to females. Genes Immun. 2015;16:495–498.
[3] Goulielmos GN, Chiaroni-Clarke RC, Dimopoulou DG, Zervou MI, Trachana M, Pratsidou-Gertsi P, Garyfallos A, Ellis JA. Association of juvenile idiopathic arthritis with PTPN22 rs2476601 is specific to females in a Greek population. Pediatr Rheumatol Online J. 2016 Apr 23;14(1):25.
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AB0009 GENOMIC SIGNATURES MAY BE ASSOCIATED WITH VASCULAR PATHOLOGY ASSOCIATED WITH RHEUMATOID ARTHRITIS

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Background: Accelerated atherosclerosis and cardiovascular (CV) disease have been associated with rheumatoid arthritis (RA). Many genes have been implicated in atherosclerosis, RA or both. However, most of these studies described SNPs in *CD40, SMAD3, HLADR, CTLA4* and other alleles. Very few studies on genetic signatures have been performed that would link RA and CV pathology. We have previously associated some genomic profiles with pathological carotid atherosclerosis (ccIMT), arterial stiffness (PWV) and brachial artery flow-mediated vasodilation (FMD). In other studies we have also found 165 genes that separated anti-TNF responder patients from non-responders.
Objectives: Here we looked for associations between clinical and "vascular" response to biologics and vascular pathology in RA patients.
Methods: In this study, 19 RA patients were treated with either etanercept (ETN) or certolizumab pegol (CZP) for one year. We separated responders (R) and non-responders (NR) according to EULAR response criteria. Microarray gene expression study was performed (Affymetrix) followed by analysis using the GeneSpring software, hierarchy clustering and principal component analysis (PCA). "Vascular response" (VR) to biologics was defined as an at least 20% improvement in FMD, ccIMT or PWV. Good Vascular Response (GVR) was defined as an at least 20% improvement in two or three of these variables.
Results: Among the 19 patients, 13 were R and 6 were NR. With respect to VR, FMD, ccIMT and PWV responded to anti-TNF treatment in 10, 9 and 8 patients, respectively. GVR was observed in 8 patients and 5 patients had VR in all 3 parameters. When comparing clinical response and VR, 7 out of 8 patients showing GVR also had good clinical response to biologics. Up-regulation of 99 and down-regulation of 67 genes separated clinical R and NR patients. Significant correlation was found between ccIMT improvement upon biological therapy and clinical response (R=0.418, p=0.04).
Conclusions: Genomic signature analysis may be able to separate clinical responders and non-responders to biologics, as well as patients that show or do not show imporvement of vascular pathology.
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