disease. High monozygotic twin discordance implies a role for non-genetic effects in disease pathogenesis. Previous epigenome-wide association studies (EWAS) have demonstrated a role for DNA methylation in SLE, but different immune cell subsets have so far been insufficiently characterised. The disease discordant twin model is a powerful design for detecting SLE-associated DNA methylation variation.

Objectives: To investigate genome-wide DNA methylation changes in sorted CD4+ T-cells, monocytes, granulocytes and B-cells from twin pairs with at least one SLE-affected twin.

Methods: Altogether 15 SLE twin pairs participated in the study, of which 6 pairs were monozygotic (MZ) and 9 were dizygotic (DZ), including 2 concordant pairs (1 MZ, 1 DZ). Disease activity was evaluated using the SLE disease activity index (SLEDAI). Peripheral blood was processed using gradient density centrifugation for the granulocyte fraction and the mononuclear cell fraction was sorted serially for CD14+ monocytes, CD4+ T-cells and B-cell enrichment using a RoboSep device (Stemcell Technologies). DNA was extracted using the DNA/RNA/miRNA Universal kit (Qiagen). Genome-wide DNA methylation was evaluated using the Infinium HumanMethylation450K BeadChip (Illumina). Paired analyses were performed using a Wilcoxon test with $p<0.01$ and median differential methylation $>7\%$ considered as statistically significant. Top differentially methylated genes were validated using pyrosequencing.

Results: In paired analyses of discordant SLE twins without restriction to probe category, we found 176, 510, 393 and 2882 differentially methylated CpGs in CD4+ T-cells, monocytes, granulocytes and B-cells, respectively. Restricted to the promoter and transcription start sites, there were 55, 327, 247 and 1628 genes in CD4+ T-cells, monocytes, granulocytes and B-cells with differentially methylated CpGs, respectively. In all cell types, there was a profound hypomethylation of interferon-regulated genes, including *IFI44L, DTX3L, PARP9* and *IFITM1*, which was more pronounced in twins with recent flare within the past 2 years. In contrast to the other cell types, hypermethylation was predominantly observed in B-cells. Using Ingenuity Pathway Analysis, the top upstream regulators of hypermethylated genes in B-cells were *TNF, miR-146a-5p* and *EP300*. Hypomethylation of CpGs was validated in all cell types at the genes *IFI44L, PARP9, IFITM1, LGALS3BP, LOXL1, MIR10A, PLSCR1* and *RSAD1*, in B-cells and granulocytes at *TACSTD2* and at *MIR146B* in B-cells. Hypermethylation of CpGs was validated in B-cells alone for *CXCR5, DDR1* and *TRAF5*.

Conclusions: Robust hypomethylation of interferon-regulated genes is common to all major cellular compartments in SLE twins. The finding of hypermethylated CpGs in B-cells is novel and might be of interest to SLE pathogenesis.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.6090

THU0218 CIRCULATING MICRORNAS AS BIOMARKERS FOR DIAGNOSIS AND TYPIFYING THE ATHEROTHROMBOTIC STATUS IN ANTIPHOSPHOLIPID SYNDROME

C. Perez-Sanchez[1], I. Arias-de la Rosa[1], M.A. Aguirre[1], P. Ruiz-Limon[1], N. Barbarroja[1], Y. Jimenez-Gomez[1], M.C. Abalos-aguilera[1], E. Collantes-Estevez[1], M. Teresa-Herranz[2], J. Lozano-Herrero[2], C. Martinez[2], R. Gonzalez-Conejero[2], M.J. Cuadrado[3], C. Lopez-Pedrera[1]. *[1]IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba; [2]IMIB-Arrixaca /University of Murcia/ Internal Medicine Service, Morales Meseguer Hospital, Murcia, Spain; [3]Lupus Research Unit and St. Thomas Hospital, London, United Kingdom*

Background: The course of antiphospholipid syndrome (APS) may rapidly progress from asymptomatic to severe manifestations. Thus, timely diagnosis is essential to improve accuracy of therapy. The role of circulating microRNAs (miRNAs) as potential biomarkers of disease has not yet been analysed in APS.

Objectives: To investigate the contribution of circulating miRNAs to the pathogenesis of APS and their potential role as non-invasive biomarkers of the disease.

Methods: Ninety APS patients and 42 healthy donors (HD) were included in the study. Clinical and inflammatory parameters were analysed. As a complement to standard clinical follow-up, the ankle-brachial index (ABI) and carotid intima-media thickness (CIMT) were determined. miRNA expression profiling was performed in plasma by PCR-Array, and the Ingenuity Pathways analysis software (IPA) was used to identify specific miRNAs and target proteins associated to the pathogenesis of APS. RT-PCR and ELISA/Bioplex of selected genes and proteins were used to validate microarray data. The diagnostic value of specific miRNAs signatures (ratios) as disease biomarkers was evaluated by ROC curves analysis. To assess the specificity of these signatures in APS, the expression of the selected miRNAs was analysed in plasma from 23 thrombotic patients without associated autoimmune disease. Monocytes isolated from HD and endothelial cells (ECs) were treated in vitro with antiphospholipid antibodies (aPL-IgGs) purified from the serum of APS patients, and the changes promoted on the levels of selected miRNAs and their potential targets were analysed.

Results: The PCR-Array identified 39 circulating miRNAs differentially expressed, including 19 up-regulated and 20 down-regulated in APS. IPA analysis recognized 11 miRNAs as potential modulators of target genes involved in the physiopathology of APS. Logistic Regression and ROC curve analyses identified a signature of 10 miRNA ratios as biomarkers for diagnosis of APS with great accuracy (AUC:0.81), along with 2 miRNA ratios as biomarkers for typifying the atherothrombotic status (pathologic CIMT) of APS (AUC:0.76). Patients with thrombosis but without associated autoimmune disease displayed a specific miRNA profile, distinct from that of APS patients. The miRNA signature was related to clinical features of APS such as the occurrence of foetal loss and the type of thrombosis suffered, and correlated with parameters linked to autoimmunity (aPL-IgG titers), inflammation, and thrombosis (ABI, ESR, TF, PAI-1, MCP-1, VEGF-A and VEGF-R1). In vitro treatment of monocytes and endothelial cells with aPL-IgG antibodies promoted a significant deregulation in the secreted levels of the selected miRNAs and atherothrombotic target proteins.

Conclusions: miRNA levels in the serum of APS patients -modulated by aPL-IgG antibodies- are potential novel biomarkers for diagnosis and typifying of their atherothrombotic status, thus constituting a useful tool in the prevention and management of the disease.

Acknowledgements: Supported by CTS794 and ISCIII (FIS15/1333 and RIER RD16/0012/0015).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.4699

THU0219 AUTOANTIBODY PROFILE OF CHILDREN WITH JUVENILE DERMATOMYOSITIS FROM A TERTIARY CARE CENTRE IN NORTH INDIA

S. Guleria[1,1], A. Sharma, A. Gupta, A. Rawat, D. Suri, S. Singh. *Pediatric allergy and immunology, Pgimer Chandigarh, Chandigarh, India*

Background: Juvenile dermatomyositis (JDM) is a rare childhood autoimmune inflammatory muscle disorder that can result in severe disability or death. Children with JDM can have autoantibodies in their sera like other autoimmune diseases [1]. Over the last few years, few novel Myositis Specific Antibodies (MSA) have been identified. Some phenotypical associations have been described with these autoantibodies like anti p-140 (anti NXP2) has been shown to have correlation with calcinosis in children with JDM [1–2].

Objectives: To study autoantibody profile and to look for phenotypical associations of autoantibodies in JDMS.

Methods: Cross-sectional retrospective study. All children diagnosed to have JDM, registered from 1995 to 2015 in Pediatric Rheumatology Clinic at Post Graduate Institute of Medical Education and Research Chandigarh, India and who were tested for autoantibodies were included in the study. Clinical findings, antinuclear antibodies (ANA), autoantibody for MSA and myositis associated autoantibodies (MAA) were noted from the careful scrutiny of case records. Immunoglobulin G (IgG) antibodies against Jo1, threonyl-tRNA synthetase (PL7), alanyl-tRNA synthetase (PL12), glycyl-tRNA synthetase (EJ), Signal Recognition Particle (SRP), Mi-2, MDA-5, Transcriptional intermediary factor 1-γ (TIF-1γ), Ku, PMScl 100, Scl 70 and SSA/Ro 52 have been done by Immunodot. Evaluation for anti p-140 or Nuclear Matrix Protein (NXP2) and anti 200/100 or 3-Hydroxy-3-Methyglutaryl-Coenzyme (HMG CoA reductase) was done using ELISA.

Results: Antinuclear antibody (ANA) testing was done in 97 patients. Forty six (47.4%) tested positive. In addition, MSA and MAA were assessed. Anti-SRP antibodies were present in 4 (11.4%) children, anti-MDA5 in 3 (8.6%), anti-Mi2 in 1 (2.9%) and 1 patient tested positive for anti-SSA/Ro52 antibodies. All 4 children with anti-SRP were girls, had polycyclic course and 2 of them developed calcinosis. Patients with anti-MDA5 had predominant skin involvement, less severe muscle disease and followed a monocyclic course. Two of them had arthritis/arthralgia at the time of presentation. The only patient with anti-Mi2 had normal muscle strength/endurance at the time of follow up. None of the patients had anti synthetase antibodies (anti-Jo1, anti-PL-7, anti-PL-12, anti-EJ), anti-ku or anti-Scl-70. None of the subjects tested positive for anti-NXP2 or anti- HMG CoA.

Conclusions: Prevalence of autoantibodies in children with JDM in our study is similar to what has been described previously. Type of autoantibodies, though, is not similar. This may be due to ethnic differences of the population. Autoantibodies were tested in children while they were on treatment. This may have resulted in lower positivity. Evaluation of autoantibody profile at the time of diagnosis may assist in predicting the course of disease and response to treatment.

References:

[1] Targoff IN, Mamyrova G, Trieu EP, Perurena O, Koneru B, O'Hanlon TP, et al. A novel autoantibody to a 155-kd protein is associated with dermatomyositis. Arthritis Rheum 2006; 54: 3682–9.

[2] Gunawardena H, Wedderburn LR, Chinoy H, Betteridge ZE, North J, Ollier WER, et al. Autoantibodies to a 140-kd protein in juvenile dermatomyositis are associated with calcinosis. Arthritis Rheum 2009;60: 1807–14.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.2954

THU0220 SELETALISIB, A NOVEL SELECTIVE PI3KΔ INHIBITOR WITH THERAPEUTIC POTENTIAL IN INFLAMMATION AND AUTOIMMUNITY

A. Payne, M. Juarez, G.I. Johnston, E. Helmer, M. Thomson. *UCB Pharma, Slough, United Kingdom*

Background: PI3Kδ is predominantly expressed in lymphocytes; the role it plays in immune disease has encouraged the development of inhibitors targeting