monitored by laser-doppler, and pro-inflammatory and oxidative stress markers were quantified by flow cytometry and RT-PCR. In a parallel cohort of SLE patients (n=12), the effects of in vivo treatment with ubiquinol on spliceosome components was evaluated.

Results: As a general feature, a significant reduction in splicing factors and spliceosome components was found in all the leukocytes of SLE patients. Interestingly, we found a specific altered profile of splicing factors and spliceosome components when compared monocytes (U2AF1, FBP11, SRSF9), lymphocytes (RBM22, PRP8, SRSF5) and neutrophils (RNU4, CA150). The reduced levels of some components of spliceosome in both monocytes and neutrophils were linked to the occurrence of thrombotic events, foetal loss and arterial hypertension. In lymphocytes, those reduced levels were strongly related to the positivity for anti-dsDNA antibodies in SLE patients, thus suggesting that reduced spliceosome machinery would contribute to increase in altered autoantigen assembly, inducing increased autoantibody production. Correlation studies demonstrated an inverse relationship among reduced levels of spliceosome components/splicing factors and high activity of the disease (measured as SLEDAI), endothelial dysfunction, and increased expression levels of peroxides and peroxynitrites, as well as of altered mitochondrial membrane potential in monocytes and neutrophils. In vitro treatment of leukocytes from HDs with anti-dsDNA promoted a reduction in spliceosome components associated with the expression of proinflammatory and oxidative mediators. Finally, in vivo treatment with ubiquinol reversed reduced expression in SLE of spliceosome components related to their proaterothrombotic profile.

Conclusions: These results reveal the existence of SLE- associated spliceosome alterations -promoted by anti-dsDNA antibodies-which could be related to the development and activity of this autoimmune condition and have influence on the induction of mechanisms that drive atherothrombosis as well as the therapeutic response.

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AB0129 HMGB1+ MICROPARTICLES IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS WITH LUPUS NEPHRITIS

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Background: High mobility group box protein 1 (HMGB1) is a nuclear DNA-binding protein that can function as an alarmin when is released from activated and dying cells. In association with nucleosomes, HMGB1 may contribute to the pathogenesis of systemic lupus erythematosus (SLE). Some previous reports have associated HMGB1 with the pathogenesis of cutaneous lupus and lupus nephritis (LN). HMGB1 may also be contained in microparticles (MPs). These vesicles have a wide spectrum of biological activities in intercellular communication, and they compete with apoptotic cells to bind mononuclear phagocytes.

Objectives: To evaluate the association of MP-HMGB1+ circulating with LN and to correlate them with LN activity.

Methods: Blood samples from 60 SLE patients were used to isolated MPs from platelet-poor plasma by centrifugation and their count, cell source and phenotype were characterized by flow cytometry. Renal pathology was reported using the standardized International Society of Nephrology/Renal Pathological Society classification. Inactive lupus nephritis (LN) was defined by the presence of one or more of the following criteria: 24 hrs proteinuria 500 mg/dl or inactive urine sediments (<5 red cells/HPF) and no red cell casts and no leucocyturia (<5 white cells/HPF) and stable serum creatinine.

Results: Mean age of SLE patients was 31.9±10.8 years, and mean disease duration was 7.8±6.2 years. 73% patients had LN and 89% were female. Patients with LN had significantly higher frequency of MP-HMGB1+, no significant differences were found among patients with active versus inactive LN or among patients with proliferative vs non-proliferative LN; MP-HMGB1+ had a moderate positive correlation with disease activity (SLEDAI, r=0.367, p=0.020), anti-C1q antibodies titers (r=0.42, p=001) and 24 hours proteinuria (r=0,33, p=,032), but no correlation was found with activity or chronicity indexes on renal biopsies. A ROC curve for MP-HMGB1+ and renal involvement showed a good discriminative ability (AUC 0.706). A cutoff of 15.7% of MP-HMGB1+ showed the best discrimination threshold with a sensitivity of 63.3% and specificity of 83.3%.

Conclusions: In our cohort of patients with SLE, MP-HMGB1+ was significantly higher in patients with LN and in patients with active disease. Given the multiple implication of HMGB1 in SLE, including the active kidney recruitment of mononuclear phagocytes, we consider that MP-HMGB1+ could be considered as a potential biomarker for LN in SLE patients.

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AB0130 MESENCHYMAL STEM CELLS ALLEVIATE SLE THROUGH PROMOTING TREG CELLS BY HLA-G

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Background: Soluble human leukocyte antigen-G (sHLA-G) is a non-classical HLA class I molecule, exhibiting strong immunosuppressive properties by inducing the differentiation of T regulatory cells (Treg). Mesenchymal stem cells (MSCs) transplantation alleviates disease progression in systemic lupus erythematosus (SLE) patients. However, the underlying mechanisms are largely unknown.

Objectives: The aim of the present study is to explore whether sHLA-G is involved in upregulating Treg cells by MSCs, which contributes to therapeutic effects of MSCs transplantation in SLE.

Methods: The serum sHLA-G levels of SLE patients and healthy controls were detected by ELISA. The percentages of peripheral blood CD4 + ILT2 +, CD8 + ILT2 +, CD19 + ILT2 + cells and Treg cells were determined by flow cytometry. Ten patients with active SLE, refractory to conventional therapies, were infused with MSCs and serum sHLA-G was measured 24 h after infusion. Peripheral blood mononuclear cells (PBMCs) were isolated from SLE patients and co-cultured with UC-MSCs for 3 days at different ratios (50:1, 10:1, and 2:1) with or without anti-HLA-G antibodies, and the frequencies of CD4 + CD25 + Foxp3 + T cells were then determined by flow cytometry.

Results: The concentrations of serum sHLA-G were comparable between SLE patients and healthy controls. However, there was a negative correlation between sHLA-G levels and SLE disease activity index (SLEDAI) scores in active SLE patients (SLEDAI >4). We found that serum sHLA-G levels were negatively correlated with blood urea nitrogen, serum creatinine and 24-hour urine protein in SLE patients. The sHLA-G levels were significantly lower in SLE patients with renal involvement than those without renal involvement. The expression of ILT2 on CD4 + T cells from SLE patients decreased significantly compared to that of healthy controls. A positive correlation between the frequencies of Treg and CD4 + ILT2 + T cells was found in SLE patients. The levels of sHLA-G increased 24 h after UC-MSC transplantation. The frequencies of Treg cells and the expressions of ILT2 on CD4 + Tcells were significantly increased 24 h after transplantations. *In vitro* studies showed that MSCs increased the frequency of Treg cells in SLE patients in a dose-dependent manner, which was partly abrogated by the anti-HLA-G antibody.

Conclusions: Our results suggested that MSCs might alleviate SLE through upregulating Treg cells, which was partly dependent on sHLA-G.

Disclosure of Interest: None declared

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AB0131 PLATELET MICROPARTICLES (PMPS) ARE HIGHER IN PATIENTS WITH SLE COMPARED TO HEALTHY CONTROLS

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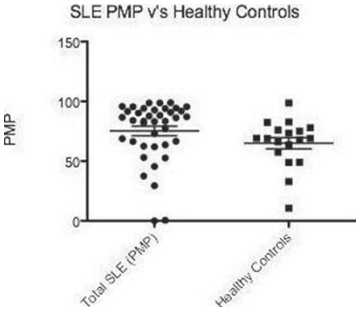
Background: Patients with SLE have an increased risk of cardiovascular disease (CVD) and reasons for this are unknown. Microparticles (MPs) are membrane-bound particles released by many cells, 70–90% are derived from platelets. MPs are a rich source of autoantigens, including DNA and have many functions including thrombosis and inflammation. PMPs can induce foam cell formation and promote adherence of platelets to endothelial lesions. MPs are potentially important in the pathogenesis of autoimmune rheumatic disease and in cardiovascular disease.

Objectives: To determine if EMPs and PMPs are increased in patients with SLE. Our secondary aim was to determine if there was a difference between those with/without subclinical cardiovascular disease and healthy controls.

Methods: Atherosclerotic plaque was previously determined in patients with SLE who had no known history of CVD by carotid and femoral ultrasound scans. Plaque and thickened intima media thickness (IMT) >0.1cm were defined according to the Mannheim Carotid Consensus. Data regarding plaque area, IMT and echolucency were collected. Plasma was stored at -80° at the time of scan. Plasma from n=57; plaque (n=16), no plaque (n=23) and healthy controls (HC) (n=18) were analysed for presence of endothelial and platelet microparticles (EMPs and PMPs), as per protocol. Samples were stained with Annexin V and platelet and endothelial antibodies, CD42a, CD31, CD105 and CD144. MPs were measured using flow cytometry. Statistical analysis was carried out using PRISM.

Results: A total of 57 plasma samples were tested. The average age of those with SLE was 45±12 years. 96% were female. 56% were Caucasian, 18% Asian, 21% Afrocaribbean, 5% other ethnicity. 18% of the SLE patients were smokers. Of the 18 HC, the average age was 37±7 years, 83% were female. 88% were Caucasian and 12% other ethnicity. 11% of the HCs were smokers. PMPs were significantly higher in patients with SLE compared to healthy controls (p=0.025). Patients with SLE without plaque had more PMPs compared to healthy controls

(p=0.037). There was no correlation between age and PMPs. There was no statistical significance between those with SLE with plaque and healthy controls or in EMP levels between the three groups. There was no correlation between EMPs or PMPs with disease activity as measured by BILAG.



Conclusions: PMPs were raised in patients with SLE compared to the healthy controls regardless of whether there was atherosclerotic plaque evident on imaging. Therefore, raised PMPs were associated with SLE itself and did not stratify a subset of patients with subclinical CVD. Further research is required to define whether PMP are important in the pathogenesis of SLE and to clarify the relationship of subclinical CVD in larger cohorts.

Disclosure of Interest: None declared

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AB0132 ANTIPHOSPHOLIPID SYNDROME PATIENTS SHOW AN ALTERED PROFILE OF ENDOTHELIAL PROGENITOR CELLS AND ENDOTHELIAL MICROPARTICLES

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Background: Antiphospholipid Syndrome (APS) is an autoimmune disease characterized by recurrent thromboembolic events and pregnancy morbidity associated to the presence of specific serum antibodies directed against membrane phospholipids and proteic co-factors (1). Endothelial dysfunction represents the earlier and reversible stage of subclinical atherosclerosis that characterizes these patients. An altered profile of endothelial progenitor cells (EPCs) and endothelial microparticles (EMPs) could promote endothelial damage (2). Few studies suggested that EMP release is stimulated by circulating anti-phospholipids (aPL). A previous study on EPC reservoir in 7 APS patients showed no difference compared to healthy subjects.

Objectives: Our aim was to evaluate circulating EPCs and EMPs in primary APS patients (PAPS).

Methods: We studied primary APS patients with previous thromboembolic events and sex and age-matched healthy controls (HC). Circulating EPCs was identified by flow cytometry analysis as CD34+/KDR+ positive cells isolated from peripheral blood mononuclear cells (PBMCs); EMPs was obtained by centrifugation of whole blood and quantified by flow cytometry (CD31+/CD41a-). Data were expressed a s mean±standard deviation or median (interquartile range) when appropriate; correlations between EPC and EMP levels with aPL were investigated by Spearman test. P values <0.05 were considered statistically significant.

Results: We enrolled 12 PAPS patients (mean age 44±12 years) and 12 HC. Compared to HC, PAPS patients showed a lower EPC percentage (0.01±0.006% *vs* 0.04±0.003%, p=0.0008) and a higher EMP number (104±80 MPs/microliter *vs* 20±8, $p<0.0001$). EMPs number positively correlated with *anticardiolipin* and *antibeta2 glicoprotein* I, both IgM and IgG ($p<0.05$ and $r>0.7$ for all correlations).

Conclusions: The results of this study suggest that endothelial cells, activated by circulating aPL, release EMPs that can perpetuate the endothelial damage. Moreover, our cohort of APS patients has a reduced number of circulating EPC that could contribute to the impairment of endothelial repair. Both the chronic endothelial damage and the lack of an efficient repair could contribute to the progression of atherosclerosis in PAPS patients.

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AB0133 BLOOD CONCENTRATION OF IMMUNOGLOBULIN BINDING PROTEIN 1 AS A BIOMARKER TO PREDICT LUPUS NEPHRITIS

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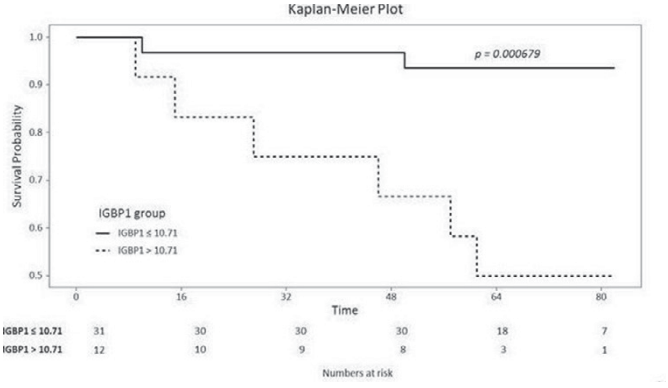
Background: Systemic lupus erythematosus (SLE) is a chronic systemic autoimmune disease of unknown etiology, and renal involvement is an important factor associated with a high morbidity and mortality. Immunoglobulin binding protein 1 (IGBP1) is a phosphoprotein associated with Ig-α of the B cell receptor complex. Intracellular IGBP1 interacts with the catalytic subunit of protein phosphatase (PP2A) and regulates differentiation, proliferation, and apoptosis of B cells. Functional studies reported that high PP2A levels alter the phenotype and function of T cells in SLE patients. Recently, we reported that urinary IGBP1 levels were associated with the pathologic activity in lupus nephritis (LN). However, the role of plasma IGBP1 (pIGBP1) in the clinical features including the development of nephritis has not been identified in SLE.

Objectives: To determine the role of pIGBP1 as a biomarker related with LN.

Methods: Blood samples of SLE patients were collected between Jan 2009 and Dec 2010 in a tertiary hospital. The levels of pIGBP1 were measured in SLE patients with (n=44) or without (n=39) nephritis, and healthy subjects (n=14). Clinical parameters including baseline characteristics, laboratory data, medications and SLE Disease Activity Index (SLEDAI) were collected from electronic medical record. Activity and chronicity index in renal pathology of LN were scored blindly by a renal pathologist. To identify factors related to the development of LN, Cox proportional hazard regression model and Kaplan-Meier curves were used.

Results: The concentrations of pIGBP1 in SLE patient were higher than those in healthy individual (9.6±8.4 ng/mL vs 4.5±2.4 ng/ml) and positively correlated with SLEDAI score. However, the concentrations were not different between LN and non-nephritis SLE and were not associated with activity index score in renal pathology. During follow-up more than 5 years, nephritis was developed in 8 patients (20.5%) among 39 SLE patients who did not have renal involvement at baseline. Interestingly, levels of pIGBP1 (p=0.002), CRP (p=0.009), or anti-dsDNA antibody (p=0.03) were significantly elevated in 8 patients who developed LN compared to who did not. Kaplan-Meier survival curve showed that initial pIGBP1 (>10.71 ng/mL) as well as anti-dsDNA (>30.7 IU/mL) were associated with high probability of LN development in the future.



Conclusions: Based on our results, high concentration of pIGBP1 could be a valuable marker to represent high SLE activity and a predictor for developing nephritis in SLE patients.

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