activation lead to multisystem tissue damage. Plasmacytoid dendritic cells (pDCs) play a central role in the pathogenesis of SLE through dysregulated type I IFN production, together with activated myeloid DCs (mDCs), amplifying vicious spiral of autoimmune disorders(1). Therefore, control of the aberrant DC activation may provide an alternative treatment strategy against SLE.

Objectives: Mycophenolate mofetil (MMF), which has been used to treat lupus nephritis, specifically blocks proliferation of B and T lymphocytes by inhibition of inosine-5-monophosphate dehydrogenase (IMPDH). In addition, although there is evidence indicating the immunosuppressive effects of MMF on human monocyte-derived dendritic cells(2,3), there are no reports showing its effects on human blood DC subsets. Here we focused on the effects of MMF on the functions of the blood pDCs and mDCs.

Methods: We isolated human blood DCs from healthy donors using cell sorting(4) and examined the function of mycophenolic acid (MPA), which is metabolic products of MMF, on DC subsets in response to TLR-ligands and serum from patients with active SLE. Written informed consent was obtained from all healthy adult donors and SLE patients.

Results: We found that therapeutic plasma concentration range of MPA down-regulated expression of CD40, CD80 and CD86 dose-dependently on mDCs and pDCs without inducing apoptosis, in response to R848(TLR7/8 agonist) and CpG2216(TLR9 agonist), respectively. Of note, MPA profoundly suppressed IL-12 production and STAT4 expression in the mDCs and IFN- α production and IRF7 expression in the pDCs(Fig 1). We also observed inhibition of nuclear translocation of IRF-7 in pDCs treated with MPA by confocal microscopy(Fig 2). Furthermore, we identified that MPA had an inhibitory effect on SLE serum-induced IFN- α production by human PBMCs.

Conclusion: Our data suggest that MMF can drive a wedge into the vicious spiral of autoimmune disorders through regulating the function of not only lymphocyte but also DC subsets. Thus, we unveiled a part mechanism of the therapeutic ability of MMF against SLE.

References:

- [1] A Plasmacytoid Dendritic Cells-Type I Interferon Axis is Critically Implicated in the Pathogenesis of Systemic Lupus Erythematosus. *Int. J. Mol. Sci.* 2015; 16, 14158-14170.

- [2] Mycophenolate mofetil inhibits differentiation, maturation and allostimulatory function of human monocyte-derived dendritic cells. *Clin Exp Immunol.* 2003;134:63-69.
 - [3] Mycophenolic acid inhibits maturation and function of human dendritic cells and B cells. *Human Immunol.* 2009;70: 692-700.
 - [4] Miyamoto et al. *Arthritis Research & Therapy* 2010, 12:R87.
- Disclosure of Interests:** None declared
DOI: 10.1136/annrheumdis-2020-eular.3199

AB0142

ANTIPHOSPHOLIPID SYNDROME AND ATHEROSCLEROSIS

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Background: Antiphospholipid syndrome (APS) is a systemic autoimmune disease with unknown etiology and complex pathogenesis. Recent studies have shown that the pathogenesis of the atherosclerotic process is related to the inflammatory component of the immune response, as well as to elements of autoimmunity. A number of autoimmune rheumatic diseases, including rheumatoid arthritis (RA), SLE and APS, are characterized by accelerated atherosclerosis and therefore at increased risk of cardiovascular disease and mortality. The risk of early atherosclerosis in patients with autoimmune disease is determined by traditional risk factors, chronic generalized inflammation, and target-specific autoimmune processes. These processes are complemented by the chronic use of drugs, such as KS, which worsen BMI, lead to hyperglycemia and hyperlipidemia.

Objectives: The aim of this study is to investigate the incidence of atherosclerosis at selected typical sites in patients with APS.

Methods: We examined 139 patients divided in to three groups: APS, SLE and healthy controls. We performed US examination of carotid arteries with IMT measurement and Calcium score of coronary arteries and aorta. All the patients were tested for: CBC, lipid panel, liver probes, ESR, anti-CL, anti-b2GPI anti-Prothrombin antibodies and ANA screen and ANA-profile as well.

Results: With the Kruskal-Wallis analysis, we found a statistically significant difference in IMT between the study groups for left ($p = 0.005$) and right ($p = 0.014$) carotid arteries. Comparative analysis between the groups showed that pathological levels of IMT ($> 900 \mu\text{m}$) in the right carotid artery were the highest in patients with antiphospholipid syndrome 15 (26.3%). In healthy controls, 3 (7.3%) were identified and no cases were reported for patients with SLE. The data for the left carotid artery (LCCA) are similar. 15 (26.3%) were registered for AFS, 4 for healthy controls (9.2%), and no patients with pathological values for IMT were registered in the SLE group. We compared the results for intima-media thickening between groups with the Chi-square test, finding a statistically significant correlation for the two carotid arteries - IMT-RCCA $p = <0.001$ for IMT-LCCA $p = 0.002$. Descriptive statistics show that the highest frequency of positive calcium score is characterized by the APS group 12 (31.6%), in patients with SLE they are 3 (15%), in healthy controls the case is 3%.

In our study, the AFS group had the highest incidence of positive CaScore, and its maximum values were significantly higher than the other two groups. The maximum agatston score for patients with antiphospholipid syndrome is 908 HU (Hounsfield Units), for SLE it is 2.1 HU, for healthy controls it is 233HU.

With the Kruskal-Wallis statistical analysis we examined the relationship of calcium score with the individual groups. Aortic aortic valve score was negative in all subjects. We find statistically significant differences between the calcium score groups.

Conclusion: The APS group is statistically significant in both pathological IMT and higher plaque incidence compared to healthy controls and patients with SLE without the presence of antiphospholipid antibodies.

Based on the data obtained we can conclude that the antiphospholipid antibodies tested and their serum levels did not directly influence the values of the coronary artery and aortic Agatston score.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2020-eular.6063

AB0143

EXPRESSION OF HERV-E CLONE 4.1 GAG TRANSCRIPTS IN PERIPHERAL BLOOD MONONUCLEAR CELLS OF SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS

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Background: Human endogenous retrovirus (HERV)-E clone 4.1 gag transcripts have been detected in peripheral blood mononuclear cells (PBMCs) of systemic lupus erythematosus (SLE) patients and seem to be associated to autoantibody production. To date, no study aimed to investigate whether their expression in

cytokine-stimulated vs. unstimulated PBMCs of SLE patients could be related with clinical manifestations.

Objectives: We aimed to correlate the expression of HERV-E clone 4.1 *gag* transcripts of unstimulated and phyto-haemoagglutinin (PHA) and interleukin-2 (IL-2)-stimulated PBMCs of SLE patients and healthy controls (HCs) and to evaluate the association between their expression and the demographic and clinical data of the SLE cohort.

Methods: PBMCs were isolated from 18 SLE patients and 22 age- and gender-matched controls. Cells from 10 SLE patients and 15 HCs were harvested for RNA isolation, HERV-E clone 4.1 *gag*- and RPL-13-selective cDNA synthesis and SYBR Green RT-PCR analysis. The expression of *gag* transcripts was normalized to that of the housekeeping gene RPL-13, using the Pfaffl method. PBMCs of the remaining patients and HCs were stimulated with PHA/IL-2 and HERV-E clone 4.1 *gag* expression assessed as described before. Statistical analysis was carried using a SPSS software, version n.23.

Results: Table 1 presents the demographic data of patients. The normalized mean $\pm$ SD *gag* expression was 1.6 ± 2.2 and 0.80 ± 0.79 in unstimulated PBMCs of SLE patients and HCs, respectively; and 1.1 ± 0.7 and 1.1 ± 0.4 in stimulated SLE and HC PBMCs, respectively. No significant difference emerged between patients and controls and between stimulated and unstimulated PBMCs (fig. 1). *Gag* transcripts expressed in PHA/IL-2-stimulated PBMCs of SLE patients significantly correlated with oronasal ulcers and high titers of anti-dsDNA antibodies ($p=0.01$ and $p=0.004$, respectively), while *gag* transcripts of unstimulated SLE PBMCs were significantly associated to the number of ACR criteria fulfilled ($p=0.02$).

Table 1 Demographic and clinical characteristics of SLE patients

Overall cohort of SLE patients (n.18)	Unstimulated conditions	Stimulated conditions	P
Number of patients	10	9	>0.05
Gender	Female	Female	>0.05
Mean age $\pm$ SD at diagnosis (years)	40.6 $\pm$ 14.6	26.4 $\pm$ 6.5	0.001
Mean disease duration $\pm$ SD (years)	12.9 $\pm$ 6.3	11.8 $\pm$ 7.6	>0.05
Mean SLEDAI $\pm$ SD	8.0 $\pm$ 5.8	5.7 $\pm$ 4.6	0.004
Mean SLICC $\pm$ SD	2.3 $\pm$ 2.3	1.6 $\pm$ 1.4	>0.05
Central nervous system involvement (n.,%)	1, 10%	1, 11.1%	>0.05
Renal involvement (n.,%)	0, 0%	1, 11.1%	>0.05
Cutaneous involvement and photosensitivity (n.,%)	9, 90%	8, 88.8%	>0.05
Oronasal ulcers (n., %)	3, 30%	3, 33.3%	>0.05
Joint involvement (n.,%)	8, 80%	6, 66.6%	>0.05
Hematologic involvement (n., %)	4, 40%	6, 66.6%	0.003
Serositis (n., %)	1, 10%	4, 44.4%	0.046
Anti-nuclear antibodies (n., %)	10, 100%	9, 100%	>0.05
Anti-double stranded DNA antibodies ($\times 10^3$ IU/L), mean $\pm$ SD	15.4 $\pm$ 16.7	26.8 $\pm$ 74.3	>0.05
Mean C3 $\pm$ SD levels (g/L)	0.88 $\pm$ 0.12	1.2 $\pm$ 1.1	0.001
Mean C4 $\pm$ SD levels (g/L)	0.11 $\pm$ 0.03	0.16 $\pm$ 0.08	>0.05
Chloroquine (n., %)	5, 50%	8, 88.8%	>0.05

Figure 1. HERV-E clone 4.1 *gag* transcript normalized expression in unstimulated (a) and PHA/IL-2- stimulated (b) PBMCs of SLE patients and controls

Conclusion: According to these preliminary findings, the expression of HERV-E clone 4.1 *gag* transcripts in unstimulated and stimulated PBMCs does not significantly differ between SLE patients and controls. The significant association with some clinical variables in SLE patients needs to be confirmed on wider cohorts.

References:

- [1] Ogasawara H, et al. Quantitative analyses of messenger RNA of human endogenous retrovirus in patients with systemic lupus erythematosus. *J Rheumatol.* 2001;28(3):533-8.
- [2] Piotrowski PC, et al. Expression of human endogenous retrovirus clone 4-1 may correlate with blood plasma concentration of anti-U1 RNP and anti-Sm nuclear antibodies. *Clin Rheumatol.* 2005;24(6):620-4.

Acknowledgments: None

Disclosure of Interests: None declared
DOI: 10.1136/annrheumdis-2020-eular.1947

AB0144 **STRATIFICATION OF PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME BY MEASURING B-CELL HEALTH**

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Background: Primary Sjögren's syndrome (pSS) is a heterogeneous immune disorder with broad clinical phenotypes that can arise from a large number of genetic, hormonal, and environmental causes. B-cell hyperactivity is considered to be a pathogenic hallmark of pSS. However, whether B-cell hyperactivity in pSS patients is a result of polygenic, B cell-intrinsic factors, extrinsic factors, or both, is unclear. Despite controversies about the efficacy of rituximab, new B-cell targeting therapies are under investigation with promising early results. However, for such therapies to be successful, the etiology of B-cell hyperactivity in pSS needs to be clarified at the individual patient level.

Objectives: To measure naïve B-cell function in pSS patients and healthy donors using quantitative immunology.

Methods: We have developed standardised, quantitative functional assays of B-cell responses that measure division, death, differentiation and isotype switching, to reveal the innate programming of B cells in response to T-independent and dependent stimuli. This novel pipeline to measure B-cell health was developed to reveal the sum total of polygenic defects and underlying B-cell dysfunction at an individual level. For the current study, 25 pSS patients, fulfilling 2016 ACR-EULAR criteria, and 15 age- and gender-matched healthy donors were recruited. Standardized quantitative assays were used to directly measure B cell division, death and differentiation in response to T cell-independent (anti-Ig + CpG) and T-cell dependent (CD40L + IL-21) stimuli. Naïve B cells (IgD⁺CD27⁻) were sorted from peripheral blood mononuclear cells and were labeled with Cell Trace Violet at day 0 to track cell division until day 6. B cell differentiation was measured at day 5.

Results: Application of our standardized assays, and accompanying parametric models, allowed us to study B cell-intrinsic defects in pSS patients to a range of stimuli. Strikingly, we demonstrated a hyperresponse of naïve B cells to combined B cell receptor (BCR) and Toll-like receptor (TLR)-9 stimulation in pSS patients. This hyperresponse was revealed by an increased mean division number (MDN) at day 5 in pSS patients compared with healthy donors ($p=0.021$). A higher MDN in pSS patients was observed at the cohort level and was likely attributed to an increased division burst (division destiny) time. The MDN upon BCR/TLR-9 stimulation correlated with serum IgG levels ($r_s=0.52$; $p=0.011$). No difference in MDN of naïve B cells after T cell-dependent stimulation was observed between pSS patients and healthy donors. B cell differentiation capacity (e.g., plasmablast formation and isotype switching) after T cell-dependent stimulation was also assessed. At the cohort level, no difference in differentiation capacity between groups was observed, although some pSS patients showed higher plasmablast frequencies than healthy donors.

Conclusion: Here, we demonstrate defects in B-cell responses both at the cohort level, as well as individual signatures of defective responses. Personalized profiles of B cell health in pSS patients reveal a group of hyperresponsive patients, specifically to combined BCR/TLR stimulation. These patients may benefit most from B-cell targeted therapies. Future studies will address whether profiles of B cell health might serve additional roles, such as prediction of disease trajectories, and thus accelerate early intervention and access to precision therapies.

Disclosure of Interests: Gwenny M. Verstappen: None declared, Jessica Catherine Tempamy: None declared, HoChan Cheon: None declared, Anthony Farchione: None declared, Sarah Downie-Doyle: None declared, Maureen Rischmueller Consultant of: Abbvie, Bristol-Meyers-Squibb, Celgene, Glaxo Smith Kline, Hospira, Janssen Cilag, MSD, Novartis, Pfizer, Roche, Sanofi, UCB, Ken R. Duffy: None declared, Frans G.M. Kroese Grant/research support from: Unrestricted grant from Bristol-Myers Squibb, Consultant of: Consultant for Bristol-Myers Squibb, Speakers bureau: Speaker for Bristol-Myers Squibb, Roche and Janssen-Cilag, Hendrika Bootsma Grant/research support from: Unrestricted grants from Bristol-Myers Squibb and Roche, Consultant of: Consultant for Bristol-Myers Squibb, Roche, Novartis, Medimmune, Union Chimique Belge, Speakers bureau: Speaker for Bristol-Myers Squibb and Novartis., Philip D. Hodgkin