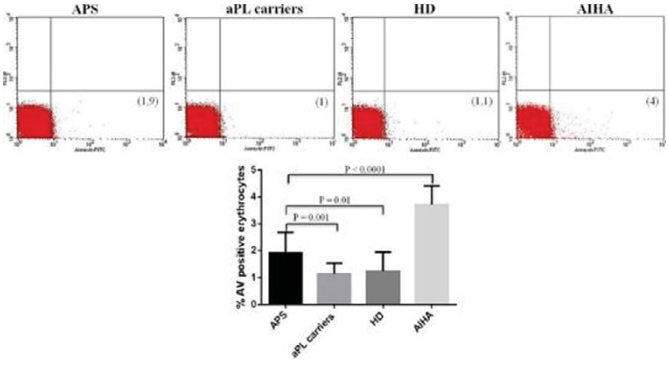
Methods: The expression of PRL-R on B cells CD19$^+$, and autophagy-related key regulator protein ATG14$^+$, on T regulatory cells CD25$^+$, were measured by flow cytometry, and expressed in percentages of SLE patients (1997, ACR criteria), and healthy controls. Active SLE was considered by SLEDAI ($\geq$4). The organs affected and treatments were evaluated.
Results: A total of 40 SLE patients and 20 healthy controls were included. Mean age of patients and controls was 30.67±4.16. Mean duration of disease was 6±4.6 years. Twenty patients were active (SLEDAI 8.45±1.9) and of these, lupus glomerulonephritis was observed in 13 patients (65%). The expression of PRL-R on B cells of active SLE was higher than in inactive SLE (50.5% vs 26.5%). In active SLE especially in patients with glomerulonephritis, the mean amount of PRL-R on B cells/ml was 6,645/ml (range 3167–6957). In contrast, patients with inactive SLE, had a low amount of PRL-R, 522.5/ml (range 15–895). In the relation of autophagy, the mean expression of ATG14$^+$ in 20 active SLE patients was 11.19% in comparison with inactive SLE patients, 7.13%, (p=0.04), and in healthy donors, 7.445% (p=0.0281).
Conclusions: Our study suggest: In active SLE patients the expression of PRL-R and autophagy-related key regulator protein ATG14+ are very high in B cells and T regulators respectively, in comparison with inactive SLE and healthy donors.
These novel findings suggest the interaction between PRL-R and autophagy in order to promote clinical/immune activation with overproduction of autoantibodies. PRL-R and ATG14$^+$ may be a new target of SLE treatment.
References:
[1] Lech M, Anders HJ, The pathogenesis of lupus nephritis. J Am Soc Nephrol, 2013, 24, 1357–1366.
[2] Jara LJ, Medina G, Saavedra MA, et al. Prolactic has a patogenyc role in systemic lupus erythematosus, Inmmunol Res, 2017, Jan 28.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6887

AB0150 INCREASED ERYPTOSIS LEVELS IN PRIMARY ANTIPHOSPHOLIPID SYNDROME PATIENTS

M. Vomero[1], F. Ceccarelli[1], A. Finucci[1], C. Pensa[1], C. Barbati[1], T. Colasanti[1], F.R. Spinelli[1], L. Massaro[1], S. Truglia[1], C. Perricone[1], F. Miranda[1], F.R. Mauro[2], R. Foà[2], F. Conti[1], G. Valesini[1], C. Alessandri[1]. *[1]Department of Internal Medicine and Medical Specialties, Lupus Clinic, Sapienza University of Rome; [2]Department of Cellular Biotechnologies and Hematology, Hematology, Sapienza University of Rome, Rome, Italy*

Background: Erythrocytes (RBCs) hold a crucial role in hemostasis and their integrity is influenced by different stimuli including circulating inflammatory mediators. Even though RBCs do not have nuclei and mitochondria, they have developed a process allowing them to undergo a rapid self-destruction named eryptosis. The exact mechanism of erythrocytes cell death is not fully clarified yet but it seems to involve Ca^{2+} and ceramide formation, leading to cell shrinkage and externalization of phosphatidylserine (PS) (1). Interaction between platelets and erythrocytes could participate in an increasing risk of thrombotic episodes typical of several diseases including antiphospholipid syndrome (APS). In fact, not only signals triggering eryptosis are involved in thrombosis activation, but also recent studies have demonstrated how PS-exposing erythrocytes are able to adhere to the vascular wall causing an impairment of circulation (2,3).
Objectives: Enhanced eryptosis is known to contribute to several pathological conditions (1) but the involvement of this process in APS has not been investigated yet. For this reason the aim of the study was to evaluate eryptosis levels in APS, healthy subjects positive for antiphospolipid antibodies without clinical manifestations (aPL carriers), autoimmune haemolytic anaemia (AIHA) and healthy donors (HD).
Methods: 27 patients with primary APS (M/F 5/22, mean age 51.1±7.6 years), 14 aPL carriers (M/F 3/11, mean age 48.9±8.4 years) were recruited after written informed consent. Moreover 10 AIHA patients and 12 HD were also enrolled as positive and negative control group respectively. RBCs were isolated from whole blood after centrifugation and eryptosis levels were analysed by flow cytometry, evaluating the percentage of annexin V-positive cells (PS-exposing cells). Flow cytometry was also use to estimated cellular volume from forward scatter (FSC).
Results: APS patients showed higher levels of eryptosis compared to HD (p=0.01). Interestingly, the percentage of annexin V-positive RBCs was lower in aPL carriers respect to APS patients (p=0.001). Moreover, an inverse correlation between RBCs volume and eryptosis was found in APS patients (r=-0.4, p=0.03). No clinical correlation between eryptosis and clinical manifestations were noticed. As expected, eryptosis was upregulated in AIHA patients compared to all populations studied ($p<0.0001$).
Conclusions: Our study provides for the first time evidence of eryptosis enhancement in APS patients suggesting a possible contribution of RBCs apoptosis in the pathogenesis of the disease.
References:
[1] Lang E, Lang F. Triggers, inhibitors, mechanisms, and significance of eryptosis: the suicidal erythrocyte death. Biomed Res Int. 2015;2015:513518.
[2] Borst O, Abed M, Alesutan I, Towhid ST, Qadri SM, Foller M, Gawaz M, Lang F. Dynamic adhesion of eryptotic erythrocytes to endothelial cells via CXCL16/SR-PSOX. Am J Physiol Cell Physiol. 2012;302:C644-C651.
[3] Pretorius E, du Plooy JN, Bester J. A Comprehensive Review on Eryptosis. Cell Physiol Biochem. 2016;39:1977–2000.

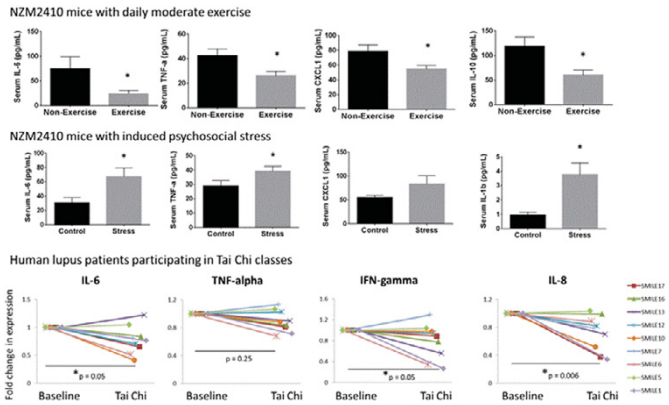


Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.4734

AB0151 STRESS MODERATION IMPACTING LUPUS WITH EXERCISE (S.M.I.L.E.): INFLUENCE OF DAILY MODERATE EXERCISE AND STRESS MODIFICATION ON AUTOIMMUNE-MEDIATED INFLAMMATION IN MICE AND HUMANS WITH LUPUS

N.A. Young[1], E. Thomas[1], B. Snoad[1], J. Sharma[1], M. Mobeen[1], J. Yedimenko[1], H. Steigelman[1], A. Meara[1], G. Valiente[2], S. Ardoin[1], N. Powell[3], J. Sheridan[3], W. Jarjour[1]. *[1]Rheumatology and Immunology; [2]Medical Oncology; [3]Institute for Behavioral Medicine Research, The Ohio State University Wexner Medical Center, Columbus, United States*

Background: Despite numerous studies indicating the positive effects of exercise and psychological stress reduction in patients with autoimmune disease, these therapeutic modalities are currently underemphasized due to the absence of comprehensive immunological characterization and regimen standardization.
Objectives: In order to examine the influence on the immune system at the cellular and tissue level, disease pathology was analyzed in the NZM2410 mouse model of lupus nephritis. To translate these results and begin to characterize a consensus treatment regimen, a pilot cohort of systemic lupus erythematosus (SLE) patients with active disease was enrolled into a daily Tai Chi program, which emphasized moderate exercise levels with meditative breathing to provide daily physical activity and stress reduction.
Methods: Mice were exercised daily by treadmill walking at moderate intensity. Social disruption stress was induced in mice by disturbing the social order within an established hierarchy. All mice were removed from the study when experimental removal criteria was reached [blood urea nitrogen (BUN)>50 mg/dL; weight loss>20%]. Kidney tissue and serum were collected from mice at experimental endpoint. SLE patients completed daily Tai Chi exercises and data was collected at baseline and throughout the study via questionnaires to access physical activity and stress levels, activity trackers (Fitbit), and serum sample analysis.
Results: Histopathological analysis of NZM2410 mice demonstrated that psychosocial stress induction significantly exacerbated and daily moderate exercise significantly reduced lupus nephritis disease pathology, as measured by BUN levels, complement component 3 and IgG complex deposition in glomeruli, pathological grading of H&E-stained kidney sections, and renal macrophage infiltration. Furthermore, stressors induced levels of IL-6, TNF-α, and IL-1β, while exercise suppressed IL-6, TNF-α, IL-10, and CXCL1 in mice. Compared to baseline data, questionnaires confirmed a significant reduction in perceived social stress and an increase in combined metabolic equivalent of task (MET) and overall physical activity in SLE patients. Moreover, fitness activity tracker data showed a significant increase in steps, distance, and activity calories with no changes in body mass index or vigorous activity levels. Interestingly, this correlated with an increased average time in bed each night. Analysis of pro-inflammatory serum cytokine



expression revealed suppression in the relative fold change of IL-6 by 23%, IL-8 by 30%, TNF-α by 11%, and IFN-γ by 21% with Tai Chi.
Conclusions: These data suggest that moderate exercise and stress management can have potent immunoregulatory effects on the chronic, systemic inflammation associated with SLE and identify daily Tai Chi exercise as a viable adjunct therapy to compliment current pharmacological interventions.
References:
[1] Wang C, et al. A randomized trial of tai chi for fibromyalgia. The New England journal of medicine 2010, 363(8): 743–754.
Acknowledgements: Funding: Center for Integrative Health and Wellness and Wexner Medical Center.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.5455

AB0152 DISEASE ACTIVITY AND DAMAGE SCORES CORRELATED DIFFERENTLY WITH THE PATIENT REPORTED OUTCOMES IN PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME COMPARED TO LUPUS ASSOCIATED WITH SECONDARY SJÖGREN'S SYNDROME

N. Thompson, V. Gupta, A. Gandhi, R. Radmore, S. Cho, D.A. Isenberg, E.C. Jury, C. Ciurtin. *Rheumatology, University College London, London, United Kingdom*

Background: Previous studies showed a poor correlation between EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) and EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) in patients with Sjögren's syndrome (SS) (1). There are no previous studies correlating these scores with the SS Disease Damage Index (SSDDI) or assessing comparatively patients with primary (pSS) and secondary SS associated with lupus (SLE/SS).
Objectives: We aimed to assess how well scores assessing disease activity, damage and patient reported outcomes correlate with each other in patients with pSS compared to SLE/SS.
Methods: We conducted a cross-sectional study of 55 patients with pSS and 15 SLE/SS. Detailed clinical and laboratory data, along with patient reported outcomes (ESSPRI) and disease activity and damage scores (ESSDAI, BILAG and SSDDI) were collected. We compared the clinical and laboratory parameters of the two patient groups (pSS and SLE/SS) and assessed the correlations between maximum ESSDAI score since diagnosis and ESSDAI, ESSPRI, SSDDI and BILAG scores at the time of assessment.
Results: The table below shows comparatively the differences between the pSS and SLE/SS patient groups.

Table 1

Demographic	pSS (n=55)	SLE/SS (n=15)	Significance
Sex n (female/male %)	55 (100/0)	15 (100/0)	
Ethnicity n (C/A/MN/O)	43/6/3/3	9/1/5/0	P=0.4571
Age mean (range)	58 (28–84)	56 (25–78)	P=0.5923
Disease duration mean (range)	12 (2–34)	23 (3–40)	P=**0.005
Anti-Ro+ % (n)	76 (42)	73 (11)	P=0.7273
Anti-La+ % (n)	49 (27)	27 (4)	P=0.0565
ESSPRI median [IQR]	5 [3–7]	4 [2– 6]	P=0.3382
ESSDAI median [IQR]	2 [0– 4]	2 [1–4]	P=0.8884
Maximum ESSDAI [IQR]	4 [2–6]	3 [2–6]	P=0.9519
SSDDI median [IQR]	1 [1–2]	1 [0–2]	P=0.1992
Global BILAG median [IQR]		0 [0–2]	
Treatment			
Hydroxychloroquine (%)	65	40	P=0.0775
Methotrexate (%)	5	33	P=**0.0092

Unpaired T test performed; **p<0.01, n = total number, % percentage, IQR = interquartile range, ethnicity: C = Caucasian, A = Asian, MN = African Caribbean, O = Chinese, anti-Ro = anti-Sjögren's-syndrome-related antigen A, anti-La = anti-Sjögren's-syndrome-related antigen B.

We found significant correlations of SSDDI score with disease duration and maximum ESSDAI score in patients with pSS (r=0.27, p=0.05 and r=0.67, p=0.0001, respectively). In SLE/SS patients, ESSPRI scores correlated with both BILAG and maximum ESSDAI score (r=0.55, p=0.03 and r=0.7, p=0.02, respectively). The SSDDI score correlated with the disease duration only in pSS patients (r=0.27, p=0.05).
Conclusions: Our study showed that there was no similar correlation between various disease scores in patients with pSS compared to SLE/SS patients. If the patient reported outcomes correlated with the disease activity (ESSDAI and BILAG) in SLE/SS patients, this correlation was not seen in pSS patients, in which the significant correlations were found only between damage scores, highest disease activity score and disease duration.
References:
[1] Responsiveness of disease activity indices ESSPRI and ESSDAI in patients with primary Sjögren's syndrome treated with rituximab, Ann Rheum Dis 2012;71:.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.2470

AB0153 DELETION OF RECEPTOR FOR ADVANCED GLYCATION END PRODUCTS (RAGE) DOES NEITHER AFFECT AUTO-ANTIBODY PRODUCTION NOR DEVELOPMENT OF RENAL DISEASE IN PRISTANE-INDUCED LUPUS

N. Chevalier, R. Rzepka, R. Voll. *University Freiburg Medical Center, Freiburg, Germany*

Background: Systemic lupus erythematosus (SLE) is characterized by autoantibodies to diverse autoantigens, especially to nuclear components such as double-stranded DNA (dsDNA) or nucleosomes. Still, it remains unclear why poorly immunogenic molecules such as dsDNA and nucleosomes become targets of humoral autoimmunity in SLE. Increased signaling via pattern-recognition receptors (PRRs) through pathogen-associated molecular patterns (PAMPs) or endogenous damage-associated molecular patterns (DAMPs) released from damaged or stressed host cells and tissues, may be critically involved in the break of tolerance against such nuclear antigens. One important PRR in this context may be RAGE. Among many others, RAGE recognizes High mobility group box 1 (HMGB1). HMGB1 is a DNA-binding nuclear protein that has been found at elevated levels in patients with SLE and other autoimmune diseases; likewise perpetuation of RAGE signaling sustains inflammation and leads to the establishment of chronic inflammatory disorders.
Objectives: We therefore examined, using the Pristane-induced SLE model, if increased RAGE signaling may be involved in the break of tolerance against nuclear antigens and contributes to chronic inflammation.
Methods: To that end, WT and RAGE-/- animals were injected intra-peritoneally with a single dose of pristane. Disease manifestations were determined after 7 months and included the determination of proteinuria and renal pathology by evaluating the glomerular cellularity and matrix on H&E stained paraffin-embedded kidney sections and glomerular depositions of IgG and C3c. In addition to that we checked for auto-antibody production at several time points during disease development and immune cell distribution, differentiation and phenotype in inflamed kidneys and spleen.
Results: Apart from a slight decrease in $GL7^{hi}Fas^{hi}$ germinal center B cells and $B220^{+}CD21^{low}CD23^{hi}$ follicular B cells in RAGE-/- animals, we did not detect differences in auto-antibody secretion or disease manifestations between RAGE-/- and WT mice.
Conclusions: Our data contrast with recently published data showing that a deletion of RAGE exacerbated lupus nephritis and lymphoproliferation in a different SLE model (B6-MRL Fas lpr/j). Therefore, we are currently looking into the effects of RAGE deletion in additional models of auto-antibody-mediated immune disease.
Disclosure of Interest: None declared
DOI: 10.1136/annrheumdis-2017-eular.6419

AB0154 CIRCULATING CPG DNA PROMOTER FRAGMENTS IN SLE ACTIVATE INTRARENAL TLR9 SIGNALING AND ACCELERATE RENAL INFLAMMATION AND FIBROGENESIS

P. Korsten, B. Tampe. *Department of Nephrology and Rheumatology, Universitätsmedizin Göttingen, Göttingen, Germany*

Background: In systemic lupus erythematosus (SLE), lupus nephritis (LN) is associated with chronic inflammation and perpetuated fibroblast activation, both determined by epigenetic mechanisms involving aberrant CpG DNA promoter methylation. During SLE progression, global methylation patterns are commonly lost. These CpG DNA promoter methylation patterns are not limited to the kidney, circulating CpG-rich DNA is also detectable in the blood allowing for biomonitoring ("liquid biopsy"). However, little is known about its specific contribution to determining disease progression. In the kidney, CpG-rich DNA activates TLR9 signaling mechanisms involved in inflammation and fibrogenesis. Based on these observations, we hypothesized that CpG-rich DNA promoter fragments potentially accelerate renal inflammation and fibrogenesis in SLE-associated LN.
Objectives: To analyze the role of circulating CpG-rich DNA on endothelial TLR9 signalling and the effect of experimental modification of oligodinucleotides on kidney inflammation in the Pristane-induced murine model of SLE.
Methods: We isolated circulating CpG-rich DNA from blood samples in a cohort of SLE patients. Then, we tested how these DNA promoter fragments influenced the LN phenotype in a TMPD ("pristane")-induced mouse model. Further, we investigated how this renal response could be influenced by the administration of either human or synthetic methylated/unmethylated CpG-rich DNA oligodinucleotides. Additionally, the effects of the administration of cicruclating CpG-rich DNA fragments on TLR9-signalling was analyzed in endothelial cell cultures.
Results: We show that circulating CpG-rich DNA promoter fragments are detectable in SLE patients' blood. Furthermore, SLE-associated LN is associated with accumulation of unmethylated CpG-rich DNA promoter fragments, implicating a mechanistic connection. These observations were further corroborated in a rodent model of TMPD-induced SLE where administration of CpG-rich DNA (isolated from LN patients or synthetic unmethylated CpG-rich DNA oligonucleotides) worsened the renal phenotype in terms of inflammation and fibrogenesis.
Causal contribution of TLR9 was further confirmed in *Tlr9*$^{+/-}$-knockout mice with protection from renal inflammation and kidney fibrosis after administration of unmethylated CpG-rich DNA promoter oligonucleotides. TLR9-mediated intrarenal