variant genotype for Apal and TaqI was associated with a higher risk of fibromyalgia in SLE patients.

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Acknowledgements: The Faculty of Medicine and Surgery, University of Malta provided funding for this research.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.770

AB0078

LIPID IMMOBILIZATION AS A METHOD TO OBTAIN ANTIGENIC NANO-OBJECTS

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Objectives: Objective of the study is to research the effect of emulsion polymerization on active sites of cardiolipin antigen determinant in antiphospholipid syndrome (APS) in patients with systemic lupus erythematosus (SLE).

Methods: Having integrated antigen nanoobjects we developed immobilized magnetocontrollable antigen nanosystems and put them to an evaluation test. The nanosystems are polyacrylamide granules with a built in antigen. To obtain stable immobilized multi-use biopharmaceuticals with targeted properties (shape, particle diameter, pore size, density) we used a modified version of emulsion polymerization method using polyacrylamide carrier gel. This method permitted a greater sorptive capacity, preserving the antigen in maximum native state, and opened up the possibility of controllable modification of nanoobjects. Cardiolipin was used as the antigen in question.

Results: Following the method described above we performed sorption of anti-cardiolipin antibodies from blood plasma of SLE patients who showed clinical presentations of antiphospholipid syndrome. Blood serum from 10 apparently healthy individuals served as control. The level of cardiolipin antibodies was determined before and after sorption by indirect solid phase immunoenzyme method. In the eluate we estimated total protein by Lowry method. In vitro testing showed that the obtained antigen nanosystems based on immobilized cardiolipin could effectively remove cardiolipin antibodies from whole blood of SLE patients with clinical presentations of APS to achieve the values of healthy individuals (before sorption cardiolipin antibodies 0.328 ± 0.028 ; after sorption 0.059 ± 0.017 ; $p < 0.001$; sorption capacity 8.00 ± 0.390 mg/ml).

Conclusion: The method of emulsion polymerization with consideration to hydrophobic and hydrophilic properties of lipid molecules permits obtaining and modifying biomolecules with certain properties, in a controlled fashion.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1075

AB0079

ENDOTHELIAL FUNCTION IN SYSTEMIC LUPUS ERYTHEMATOSUS PATIENTS: IMPACT OF CAFFEINE CONSUMPTION ON ENDOTHELIAL PROGENITOR CELLS

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Background: As widely demonstrated, circulating endothelial progenitor cells (EPCs) could be considered biomarkers of endothelial dysfunction. Their frequency and function varied in systemic lupus erythematosus (SLE) patients, with a significant association with subclinical atherosclerosis¹. Caffeine, one of the most widely consumed products in the world, seems to interact with multiple components of the immune system by acting as a non-specific phosphodiesterase inhibitor². In terms of cardiovascular disease (CVD), data from the literature showed a U-shaped association between habitual coffee intake and CVD³. In this view, Spyridopoulos et al. demonstrated a significant improvement in mature endothelial cells and EPCs migration in relation to coffee consumption in coronary artery disease both in mouse models and in patients⁴. Finally, caffeine seems to play a positive effect on SLE disease activity status, as demonstrated by the inverse association between its intake and SLE Disease Activity Index 2000 (SLEDAI-2K) and the serum levels of inflammatory cytokines⁵. At the best of our knowledge, there are no data about the effect of caffeine on cardiovascular risk in SLE patients.

Objectives: The aim of this study was to evaluate the possible role of caffeine intake on endothelial function in SLE patients, by evaluating its effect on circulating EPCs.

Methods: We performed a cross-sectional study enrolling SLE patients, fulfilling the revised 1997 ACR criteria. According with the protocol study, we excluded patients with history of smoking, CVD, chronic kidney failure, dyslipidaemia, and/or diabetes. At recruitment, the clinical and laboratory data were collected and disease activity was assessed using the SLEDAI-2k. Caffeine intake was evaluated using a 7-day food frequency questionnaire, previously employed in SLE cohort⁵. At the end of questionnaire filling, blood samples were collected. EPCs were isolated from peripheral blood mononuclear cells (PBMC) by a flow cytometry analysis and they were defined as early EPCs CD34+KDR+CD133+ cells and late EPCs CD34+KDR+CD133-, expressed as a percentage within the lymphocyte gate.

Results: We enrolled 19 patients (F:M 18:1, median age 45 years, IQR 15; median disease duration 240 months, IQR 168). In this cohort, we observed a mean±SD SLEDAI-2k value of 1.3 ± 3.3 and the most frequent disease-related feature was joint involvement (73.7%). Concerning treatment at the time of enrolment, the majority of patients were receiving treatment with hydroxychloroquine (78.9%) and seven with glucocorticoids (36.8%). The median intake of caffeine was 163 mg/day (IQR 138) and we used this value as cut-off to categorize SLE patients in 2 groups: group 1 (N=10, caffeine intake ≤ 163 mg/day) and group 2 (N=9, caffeine intake > 163 mg/day). Patients with less intake of caffeine showed a significantly more frequent history of lupus nephritis ($p=0.03$), haematological manifestations ($p=0.0003$) and anti-dsDNA positivity ($p=0.0003$). Moving on EPCs, a positive correlation between caffeine intake and EPCs percentage was observed ($p=0.04$, $r=0.4$) (Figure 1A). Moreover, patients with more caffeine intake showed higher levels of early EPCs ($p=0.02$) (Figure 1B).

Conclusion: This is the first report analysing the impact of caffeine on EPCs frequency in SLE patients. We found a positive correlation between its intake and both early and late EPCs percentage, suggesting a caffeine influence on endothelial function in SLE patients. Nonetheless, these results support the possible impact of dietary habits on autoimmune diseases.

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Figure 1. A. Correlation between KDR+CD34+ cells and daily caffeine intake
B. KDR+CD34+CD133+ cells percentage in group 1 (N=10, caffeine intake ≤ 163 mg/day) and group 2 (N=9, caffeine intake > 163 mg/day)

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.1224

AB0080

ALTERED CONCENTRATIONS OF DIFFERENT SMALL EXTRACELLULAR VESICLE POPULATIONS IN PLASMA OF PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME

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Background: Antiphospholipid syndrome (APS) is a systemic autoimmune disorder characterized by thrombosis, obstetric complications, and the presence of antiphospholipid antibodies (aPL) that cause endothelial injury and thrombophilia [1]. Extracellular vesicles (EVs) are involved in various thrombotic disorders [2], including APS [3, 4], and therefore may influence the prothrombotic status of APS patients. One of the hallmarks of activated endothelium is the expression of adhesion molecules, such as ICAM-1 (CD54) and E-selectin (CD62E), that play a key function in the interactions with leukocytes and platelets.

Objectives: To determine the level of total tetraspanin (CD81/CD63/CD9)-positive vesicles and specific EV populations (CD54- and CD62E-positive EVs) in plasma from APS patients.

Methods: Whole blood was collected from 4 APS patients and 3 healthy blood donors (HBDs) and processed to obtain platelet-depleted plasma. The size and concentration of EVs were determined using ExoView platform (NanoView

Biosciences, MA, USA). In brief, EVs were captured and immobilized on ExoView Tetraspanin chips using the capture antibodies CD81, CD63, and CD9. Size was determined using SP-IRIS technology. Concentration measurements were performed with fluorescently labeled detection antibodies, specifically tetraspanins (CD81/CD63/CD9) for total EVs and CD54 and CD62E for specific EV populations.

Results: Analysis of EVs size confirmed the presence of small EVs (sEVs, < 70 nm) in both study groups. The size of EVs did not vary significantly between study groups (mean size $\pm$ SD in APS vs. HBD; CD81 (63.1 $\pm$ 1.5 nm vs. 66.6 $\pm$ 10.6 nm), CD63 (63.3 $\pm$ 1.64 nm vs. 69.2 $\pm$ 13.2 nm), and CD9 capture spot (61.8 $\pm$ 1.18 nm vs. 64.1 $\pm$ 7.64 nm)). The levels of total EVs (tetraspanin-positive) were increased 1.7-fold, 1.4-fold, and 2.2-fold for CD81, CD63, and CD9 capture spots, respectively, in APS patients compared to HBDs (Figure 1A). In addition, CD54- and CD62E-positive EVs represented a small population (< 2 %) of the total EVs (Figure 1B). The levels of CD54 were increased 2.9-fold, 3.0-fold, and 2.5-fold on CD81, CD63, and CD9 capture spots, respectively, and similarly, the levels of CD62E were increased 2.2-fold, 2.7-fold, and 2.0-fold on CD81, CD63, and CD9 capture spots, respectively, in APS patients compared to HBDs (Figure 1A).

Figure 1. Concentration of tetraspanin- (CD81/CD63/CD9), CD54- and CD62E- positive sEVs in APS patients and HBDs.

Conclusion: Higher levels of sEVs and increased percentage of CD54- and CD62E-positive sEVs in plasma of APS patients could indicate an altered and activated endothelium in those patients.

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Disclosure of Interests: Ula Stok: None declared, Alex Shephard Employee of: NanoView Biosciences., Sasa Cucnik: None declared, Snežna Sodin-Šemrl: None declared, Polona Zigon: None declared

DOI: 10.1136/annrheumdis-2021-eular.1371

AB0081

ENDOTHELIAL MARKERS WITH DYSREGULATION IN SYSTEMIC LUPUS ERYTHEMATOSUS: A SYSTEMATIC LITERATURE REVIEW

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Background: Systemic lupus erythematosus (SLE) is a severe, lifelong autoimmune disease known for its multisystem organ involvement. SLE patients are known to be at risk for premature atherosclerosis at a relatively young age (1). Endothelial dysregulation is one of the pathophysiologic mechanisms that can lead to the higher risk for cardiovascular disease in SLE (2). Multiple endothelial markers with dysregulation in SLE have been described so far, of which some are associated with disease activity.

Objectives: To report a systematic literature review regarding endothelial markers that are dysregulated in SLE and search for associations with disease activity.

Methods: The search was performed according to the Preferred Reporting Items for Systematic review and Meta-analysis Protocols (PRISMA-P) 2015 (3). In

July 2020, the search terms were used in Embase, MEDLINE, Web of Science, Google Scholar and Cochrane. Inclusion criteria were 1) published studies after the year 2000 that reported measurements of endothelial cell markers in serum and/or plasma of SLE patients (diagnosed according to ACR/SLICC criteria), 2) English language peer reviewed articles and 3) disease activity measurement (i.e. SLEDAI, BILAG, SLAM, ECLAM or PGA). Exclusion criteria were 1) case reports or editorials, 2) studies performed in animals and 3) studies with microRNA/cytokine biomarkers. There was no minimum count for study population. The screening process is shown in figure 1.

Results: From 1892 hits, we identified 110 eligible articles. Table 1 shows an overview of the most frequently studied endothelial markers. These identified endothelial markers are involved in endothelial cell (EC) activation, EC apoptosis, disturbed angiogenesis, defective vascular tone control, immune dysregulation and coagulopathy. In most studies, dysregulation of the endothelial marker was associated with disease activity. The majority of the studies had a cross-sectional design, longitudinal data on endothelial markers in SLE are scarce.

Conclusion: We identified multiple endothelial markers that are dysregulated in SLE and this dysregulation was often associated with disease activity in cross-sectional studies. Our future plan is to test the identified endothelial markers in (longitudinally collected) samples of (childhood onset) SLE patients, disease- and healthy controls. This will be a next step in unravelling the pathophysiology of premature atherosclerosis and cardiovascular events in SLE-patients in young adulthood.

Table 1.

Endothelial marker	Articles (no. of studies)	Significant correlation with SLEDAI (no. of studies)			Studies with control groups (no. of studies)	Longitudinal data (no. of studies)
		Yes	No	Unknown		
VCAM-1	26	20	1	5	23	3
VEGF	22	13	5	4	20	2
ICAM-1	18	11	5	2	17	3
Thrombomodulin	17	10	5	2	13	2
E-Selectin	13	6	5	2	10	2
MCP-1	8	6	2	0	7	1
P-Selectin	6	3	2	1	6	1
IP-10	6	5	1	0	5	0
Pentraxin-3	5	5	0	0	5	1
vWF	5	4	1	0	5	0
Neopterin	3	2	1	0	2	0
Fas	3	0	2	1	2	0
Angiopoeitin-2	3	3	0	0	2	1
Endothelin-1	3	1	2	0	3	0
PAI-1	3	1	1	1	2	0
Adrenomedullin	3	2	0	1	2	0
TWEAK	3	1	1	1	1	2
PECAM-1	3	1	1	1	3	0

Figure 1.

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