shown to enhance their inhibitory effect of CD4⁺ T cell pro-inflammatory function and replication. We have reported a decreased serum levels of sema3A in systemic lupus erythematosus (SLE) compared to healthy controls and in correlation with SLE disease activity [1]. Sema3A was found to be over expressed in podocytes and epithelial cells in animal models with diabetic nephropathy. Increased urinary sema3A was also detected in diabetic patients with proteinuria and in contrast-induced acute renal injury [2-3].

Objectives: To assess urine sema3A secretion in SLE patients with and without renal involvement compared to rheumatoid arthritis patients as disease control and healthy controls.

Methods: 50 ml of fresh urine samples were collected, centrifuged and the supernatant was then concentrated up to 50 times the initial concentration and subjected to specific human Sema3A ELISA kit (MBS732622, San Diego, CA, USA).

Results: Thirty-eight lupus patients fulfilling the 2012 SLICC criteria were recruited, 33 (87%) of whom were women, at a mean age of 35±12 years. Eight patients had active nephritis (21%) and additional 5 had a history of nephritis but were in remission. APLA was diagnosed in 13 (34%) of patients. Disease activity was evaluated by the Systemic lupus erythematosus disease activity index 2000 (SLEDAI 2K) and was 8.2±7.7.

Sema3A was lower in lupus patients compared to rheumatoid arthritis and healthy controls, 4.9±3.9 ng/mL, 8.5±2.7 ng/mL, 9.855±1.7 ng/mL, p=0.0006. Lupus nephritis patients demonstrated lower urine sema3A concentration compared to lupus patients without renal involvement 4±3.4 ng/ml, 6.5±3.8 ng/ml, p=0.03. Sema 3A reversely correlated with proteinuria r=-0.43 p=0.006 and SLEDAI 2K -0.3, p=0.04, but not with creatinine concentration, disease duration and complement concentration. There was no difference in urinary sema3A between SLE patients with or without APLA syndrome.

Conclusion: Urinary excretion of Sema 3A was found to be decreased in the SLE patients with renal disease, reversely correlating with disease activity and proteinuria. These findings are in line with previous reports of decreased serum level of Sema3A in SLE, that may result in reduced efficacy of regulatory T cells, driving autoimmunity and kidney damage. The discrepancy between low sema3A urinary excretion in SLE nephropathy and increased urinary secretion in other "non- auto immune" conditions with renal damage, suggests that sema3A in the kidneys is protective in autoimmune diseases and detrimental in "non-auto immune" conditions. This differential effect of sema3A may have to do with different populations of effector cells and different expression of sema3A receptors (neuropilin1). Further studies should evaluate semaphorin 3A role in lupus nephritis and its potential as a treatment option.

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AB0190

CROSSTALK BETWEEN SALIVARY GLAND EPITHELIAL CELLS AND B LYMPHOCYTES IN PRIMARY SJÖGREN'S SYNDROME

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Background: Primary Sjögren's syndrome (pSS) is an auto-immune disorder characterized by lymphocytic infiltrates and destruction of the salivary glands. Mechanisms leading to B lymphocytes chronic activation remain partially understood and we assumed that salivary gland epithelial cells (SGECs) might play a key role in B lymphocytes activation and differentiation.

Objectives: We aimed to study the interactions between SGECs from pSS patients or controls and B lymphocytes.

Methods: Patients with pSS according to 2016 EULAR/ACR criteria and controls with sicca symptoms were studied. RNASeq analysis was performed on SGECs and B lymphocytes sorted from salivary gland and blood using a FACS ARIA. Enrichment analysis was performed using Ingenuity Pathway Analysis software. Validation of the results was performed by qPCR (Biomark technology). Primary

cultured SGECs from pSS patients (n=6) and controls (n=6) were co-cultured with B lymphocytes sorted from healthy donors blood and stimulated with or without Poly(I:C), INFα or IFNγ for 5 days. Transwell assays were performed. Survival, activation (CD38 positivity) and differentiation of B lymphocytes were assessed at day 5 by flow cytometry.

Results: The RNASeq analysis of B lymphocytes sorted from salivary gland showed an up-regulation of CD40 and CD48 which are involved in their activation. The analysis of sorted SGECs highlighted IL-7, interferon (IFN) signaling pathways and genes potentially involved in immune responses, including HLA-DRA, BST2 (bone marrow stromal cell antigen 2) and BAFF-R.

Co-culture experiments showed an increase of B lymphocytes viability when co-cultured with SGECs compared to B lymphocytes cultured alone (p<0.05). Co-culture with SGECs from pSS compared to controls lead to an increased survival of B lymphocytes (calculated as the percentage of alive co-cultured B lymphocytes – percentage of alive cultured alone B lymphocytes) without stimulation or stimulated with Poly(I:C) (p<0.01) (Figure 1A). Similarly, SGECs from pSS were more likely to induce higher activation of B lymphocytes compared to SGECs from controls, assessed by the percentage of CD38+ B lymphocytes (significant after stimulation with Poly(I:C)) (Figure 1B). To determine whether the activation of B lymphocytes and SGECs required a direct cell contact, we used transwell experiments. Preliminary results suggested that the increase of B lymphocytes viability could depend mostly on soluble factors that are currently being identified and will be communicated at the congress.

Figure 1. A: Difference between the percentage of alive B lymphocytes co-cultured with SGECs and the percentage of alive B lymphocytes cultured alone at day 5. B: Difference between the percentage of CD38+ B lymphocytes co-cultured with SGECs and the percentage of CD38+ B lymphocytes cultured alone at day 5. In green for SGECs from controls, in orange for SGECs from pSS patients. One asterisk indicates p-value <0.05, two asterisks indicate p value < 0.01.

Conclusion: Epithelial cells from patients with pSS have better ability than controls to stimulate survival and activation of B cells. According to preliminary results, this effect could be mediated at least partially by soluble factors. The pathways responsible for this stimulation are being determined by RNASeq analysis of purified epithelial cells and B lymphocytes and inhibitory experiments that can represent new therapeutic perspectives are ongoing.

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AB0191

ENDOTHELIN-1 LEVEL IN PATIENTS WITH ANTIPHOSPHOLIPID SYNDROME, ITS ASSOCIATION WITH ENDOTHELIAL DYSFUNCTION AND ATHEROSCLEROSIS

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Background: It is known that endothelin-1 is one of the leading factors in the development of coronary artery disease, acute myocardial infarction, atherosclerosis of cerebral and peripheral vessels, pulmonary hypertension, ischemic lesion

of the brain vessels etc. Patients with rheumatic diseases also have an elevation of endothelin-1 in serum. But it remains unclear whether the endothelin-1 level may reflect endothelium dysfunction in patients with antiphospholipid syndrome (APS) and serve as an early marker of atherosclerosis.

Objectives: The aim of the study was to evaluate the endothelin-1 concentration, its association with antiphospholipid antibodies and atherosclerotic vascular lesions in patients with APS.

Methods: According to our observation, there were 82 patients, among which 34 (41.6%) with primary antiphospholipid syndrome (PAPS) and 48 (58.4%) with secondary antiphospholipid syndrome (SAPS). The control group consisted of 37 practically healthy persons. The groups of patients were comparable by age, sex, and duration of the disease. The APS diagnosis was established according to the international classification criteria (2006). The content of the anticardiolipin antibodies IgG, anti-beta2-glycoprotein-1 antibodies IgG, IgA, IgM and endothelin-1 were determined by the immune enzyme method using commercial sets of Trinity Biotech Captia USA - Ireland, ORGenTec GmbH Germany and «Endothelin-1» (Cormay, England). All patients were assessed for the level of endothelium-dependent vasodilation (EDVD), the thickness of the intima-media complex of the common carotid artery (IMT), the presence of atherosclerotic plaque (AP) and clinical manifestations of vascular involvement.

Results: The analysis of endothelin-1 levels has showed that its content was in 2.3 times higher in patients with APS than in the control group. The proportion of people with optimal endothelin-1 content was twice lower, and the proportion of people with extremely high and high rates was 1.6 and 5.3 times higher, respectively, among patients with APS, than in the control group. Also differences in the endothelin-1 level have been established depending on the type of APS. The content of endothelin-1 was significantly higher (1.3 times) in patients with SAPS, than in PAPS. Among the patients with SAPS, the proportion of patients with an optimal level of endothelin-1 was 1.7 times lower, and the proportion of patients with high levels was 1.6 times higher than in patients with PAPS. The significantly lower endothelin-1 level was recorded in patients with highly positive antibodies to cardiolipin and beta-2 glycoprotein-1. Correlation analysis has shown direct correlation between anticardiolipin antibodies of the IgG class and anti-beta2-glycoprotein-1 antibodies and endothelin-1 concentration ($r=0.35$ and 0.34). High endothelin-1 level was an adverse factor of structural and functional atherosclerotic changes of the heart and blood vessels in patients with APS. IMT increasing and EDVD decreasing were from 1.7 to 6.6 times more frequent among patients with high endothelin-1 level (>10 pg/ml), than patients with optimal endothelin-1 level (≤ 5.0 pg/ml).

Conclusion: Thus, the obtained data has showed that the excess concentration of endothelin-1 is a circulating marker of early atherosclerosis, since it is closely associated with subclinical manifestations of atherosclerotic vascular damage

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AB0192 ASYMPTOMATIC VERTEBRAL FRACTURES WORSEN ORGAN DAMAGE IN WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background:

Objectives: To investigate the influence of asymptomatic vertebral fractures on organ damage and to identify risk factors associated with critical organ damage in women with systemic lupus erythematosus (SLE).

Methods: 207 women with SLE were included in this study. Bone mineral density (BMD) measurements of the hip and spine were performed using the dual energy X-ray absorptiometry (DXA). Vertebral fracture assessment (VFA) was done for detection vertebral fractures using a method described by Genant. Accumulated damage was scored using the SLICC/ACR damage index (SDI). Critical organ damage was defined as SDI >3 .

Results: Vertebral fractures were developed in 55 (26.5%) women with SLE. Half of all women with SLE ($n=31$, 15.0%) had asymptomatic vertebral fractures which were diagnosed for the first time in this study. 131 (63.3%) women with SLE had critical organ damage (SDI >3). Average SDI before and after morphometry was 4.5 ± 2.1 and 5.4 ± 2.5 respectively. Multivariate analysis showed age ($p=0.01$) and cumulative dose of glucocorticoids ($p=0.00005$) were significantly associated with critical damage in women with SLE.

Conclusion: Detection of vertebral fractures helps in counting accumulated organ damage correctly. VFA in the combination with DXA in women with SLE is an effective method for diagnostic asymptomatic vertebral fractures.

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AB0193

THE EFFECTS OF NON-INVASIVE VAGUS NERVE STIMULATION ON FATIGUE AND NEUROCOGNITION IN PARTICIPANTS WITH PRIMARY SJÖGREN'S SYNDROME

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Background: Primary Sjögren's syndrome (pSS) sufferers have rated physical and mental fatigue ('brain fog') as the most important symptoms needing improvement. Previous data from our group suggest that stimulation of the vagus nerve can invoke immunological responses and concurrently an improvement of patient reported symptoms of fatigue¹.

Objectives: This follow up study uses the gammaCore device (electroCore) and a sham device to assess the effects of non-invasive vagus nerve stimulation (nVNS) on patient reported symptoms of fatigue in pSS. In addition, neurocognitive tests were used to assess the effect of nVNS on short term memory, executive function and attention.

Figure 1

Methods: 40 pSS participants were assigned to use active ($n=20$) or sham ($n=20$) nVNS devices. Participants and research staff were blinded to the active/sham device assignment. The participants were instructed to use the device twice daily for a study period of 56 days. The following patient reported measures of fatigue and neuropsychological tests were collected at baseline and day 56; Profile of Fatigue (PRO-F, Physical and Mental), visual analogue scale (VAS) of abnormal fatigue, trail making, Digit Symbol Substitution Test (DSST), Stroop test and digit span. 7 subjects were excluded from the analysis due to withdrawal from the study. Changes in fatigue and test scores from baseline to day 56 were compared between devices using t-tests.

Results: Physical fatigue was significantly reduced between baseline and day 56 in the active group but not the placebo group ($p=0.047$). The mean reduction in physical fatigue was 30% and 6% for the active and sham arms respectively (Figure 1). In both the active and sham subject groups there were no significant changes in the patient reported mental fatigue or neuropsychological test scores.

Conclusion: This sham controlled scientific study of vagus nerve stimulation in pSS suggests nVNS may improve patient reported symptoms of physical fatigue, which is consistent with our published data. There were no improvements in the neuropsychological test scores which is consistent with no improvements in patient reported mental fatigue. nVNS has been shown to activate the anti-inflammatory reflex, therefore assessment of peripheral inflammatory markers may help our understanding of nVNS, inflammation and fatigue.

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