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.

REFERENCES

- Vadasz Z, Haj T, Halasz K, Rosner I, et al. Semaphorin 3A is a marker for disease activity and a potential immunoregulator in systemic lupus erythematosus. *Arthritis Res Ther*;14(3):R146.
- Mohamed R, Ranganathan P, Jayakumar C, et al. Urinary semaphorin 3A correlates with diabetic proteinuria and mediates diabetic nephropathy and associated inflammation in mice. *J Mol Med (Berl)* 2014;92:1245-1256.
- Ning L, Li Z, Wei D, et al. Urinary semaphorin 3A as an early biomarker to predict contrast-induced acute kidney injury in patients undergoing percutaneous coronary intervention. *Braz J Med Biol Res*. 2018;51(4)

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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