Conclusion: Our data revealed that adrenergic receptors are differentially expressed by salivary epithelium of SS patients compared to control tissues. This finding was further substantiated by the increased levels of cAMP, indicating a profound sympathetic stimulation of this secretory tissue. The dilated ER lumen of the salivary gland epithelial cells from SS patients confirmed the occurrence of ER stress. Moreover, the finding that catecholamines induce severe ER stress *in vitro* in SGEc under conditions resembling chronic stress suggests a causal relationship between sympathetic tone and ER stress. Deciphering the role of chronic stress in ER machinery will provide important insights that may lead to novel therapeutic targets for SS.

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Acknowledgement: The research has been funded in part by the European Union's Horizon 2020 multicentric protocol HARMONICSS; H2020-SC1-2016; grant agreement no: 731944.

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.1438

THU0224 THE HEPATITIS VIRUS PRE S1 PROTEIN RETARDS THE ONSET OF LUPUS-LIKE GLOMERULONEPHRITIS IN NZB/W F1 MICE

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Background: Infection can trigger autoimmunity but the nature of the pathogen could enhance or inhibit the onset of the disease. In this study we tested the tolerogenic effect of the surface Hepatitis B Virus capsid protein preS1 in a lupus mouse model.

Objectives: To evaluate the effect of administration of Hepatitis B virus preS1 subunit to NZB/WF1 mice

Methods: Mice (10 each group) were injected with a total volume of 200µl of 32.5 µg PreS1 in 200µl PBS (group 1), 200µl PBS (group 2), 3 times at 11th, 14th and 17th weeks of age. Urine samples were collected weekly to evaluate proteinuria by reactive strips. Blood samples were collected before every injection, at 22th and 28th weeks, and at death to evaluate levels of anti-C1q and anti-dsDNA by home-made ELISA tests. Tissues were harvested for histological analyses. Proteinuria free and survival rates were analyzed by Kaplan-Meier method using Mantel-Cox test for comparisons. Neurocognitive functions were evaluated with Staircase, Y-Maze and Forced Swim Test.

Abstract THU0224 – Figure 1

Results: Anti-dsDNA and Anti-C1q levels (OD±SD) were significantly higher in PBS than in preS1 treated mice (Figure 1). Mean proteinuria levels (mg/dl±SD) were higher in PBS than in preS1 treated mice. Proteinuria free survival rate (<300 mg/dl) was lower in group 2 than group 1 (p=0.016; Figure 2). Also survival rate was significantly lower in PBS than in preS1 injected mice (p=0.033). Memory deficits (p<0.01) and anxiety-like behavior was pronounced in PBS treated mice. Severe segmental and focal glomerulonephritis in both groups with large proliferation of mesangial and endothelial cells and Russell bodies were found by histological analysis. Mice treated with preS1 had more chronic inflammation in the kidneys and extramedullary hematopoiesis in the spleen and liver. Notably, in salivary glands, severe acute inflammation was observed in group 1 and chronic inflammation in group 2.

Conclusion: HBV capsid protein preS1 causes a delay in the onset of lupus-like glomerulonephritis and ameliorates behavioral disorders in NZB/BF1 mice. This peptide seems to induce a tolerizing rather than a pathogenic effect in these autoimmune prone mice models.

Abstract THU0224 – Figure 2

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Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2019-eular.5397

THU0225 THE MOLECULAR PROFILING OF MONOCYTES FROM PATIENTS WITH PRIMARY ANTIPHOSPHOLIPID SYNDROME IDENTIFIES SEVERAL NETWORKS RELATED TO THEIR ATHEROTHROMBOTIC STATUS. ROLE OF ANTIPHOSPHOLIPID ANTIBODIES ON MONOCYTE MIRNA SECRETION

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Objectives: 1. To characterize the mRNAs and microRNAs transcriptomes of monocytes, key immune cells in the atherothrombotic pathology of Antiphospholipid Syndrome patients (APS). 2. To evaluate the role of antiphospholipid antibodies (aPL) in the regulation of these processes. 3. To identify and characterize circulating microRNAs secreted by activated monocytes.

Methods: Monocytes from peripheral blood of 40 APS patients and 40 healthy donors were purified by negative immunomagnetic selection. Gene expression microarray (Agilent G4112F platform) and nCounter microRNA expression array (Nanostring) were performed on purified RNA. Functional categorization of altered genes and miRNAs was made using IPA software, and miRNA-mRNA interaction networks showing inverse correlation expression were identified. Genes and miRNAs integrating the networks were validated in the whole APS cohort by RT-PCR, as well as on a set of thrombotic non-autoimmune patients. Predicted miRNA-mRNA interactions were tested by microRNA transfection experiments.

In parallel, a miRNA array in the plasma of those patients was performed, and common deregulated miRNAs between monocytes and plasma were identified. Monocytes isolated from HD were treated *in vitro* with purified aPLs and the altered gene/miRNA expression induced in monocytes was evaluated. Moreover, the effects of aPLs on the secretion of common deregulated microRNAs in the supernatant of cultured cells were assessed.

Results: Microarray identified 518 altered genes in APS monocytes. Relevant biofunctions on which these genes were involved included hematological and cardiovascular system development and function, inflammatory response, and embryonic development, among others. Gene alterations were validated in the whole cohort, demonstrated to be stable along the time, divergent of the gene profile in monocytes from non-autoimmune thrombotic patients, and associated to thrombotic recurrences and early atherosclerosis. Analysis of miRNA profiles showed altered expression of 22 miRNAs in APS monocytes. Fifty-four genes were inversely correlated and predicted as CVD-related target genes of 19 differentially expressed miRNAs in monocytes. Association of these genes and miRNAs with the