depression.³ Previous studies have suggested microglia, as critical mediators of depression in SLE.

Objectives: To date, the pathophysiology of most depression symptoms in SLE has not been well determined. We focused our attention on the potential role of microglia in neuroinflammation in SLE patients.

Methods: Cerebrospinal fluid was collected from 3 healthy people and 3 SLE patients. According to the hospital anxiety and depression scale (HADS), we investigate the depression of SLE patients. The cytokines were screened using a RayBio Human Cytokine Antibody Array in cerebrospinal fluid samples by analysing a variety of inflammatory cytokines such as IL-6, Leptin and TNF- α . Cerebrospinal fluid of SLE patients and normal people were tested by ELISA for TNF- α . The depression status of MRL/lpr (C3MRL-Faslpr/J) mice and Balb/c mice was determined by tail suspension test, open-field test and sucrose preference test. Immunofluorescence and Western blot was utilised to detect the activation of microglial cells in brain tissue. Microglia cells were stimulated by TNF- α , Western blot showed the expression of CD68 and activated NF- κ B. The concentrations of IL-6 and IL-1 β in the cell supernatants were measured by ELISA. After using of NF- κ B signalling pathway inhibitor PDTC, the activation of microglia stimulated by TNF- α was determined by immunofluorescence, quantitative PCR, Western blot analysis and ELISA.

Results: The results showed that the level of TNF- α in cerebrospinal fluid of patients with lupus was higher than normal people. At 14 weeks, MRL/lpr mice appear depression by tail suspension test, open-field test and sucrose preference test, MRL/lpr mice had more reactive microglia in the cortex when compared to Balb/c. After microglial cell were stimulated by TNF- α , microglia were active and effectively release IL-6, IL-1 β and iNOS. Moreover, the expression of CD68 and activated NF- κ B signalling pathway were also higher significantly. However, the use of NF- κ B signalling pathway inhibitor PDTC reverse the TNF- α induced microglial activation.

Abstract AB0174 – Table 1. Disease characteristics in SLE patients and control.

patient	Sex	Age, years	disease	depression	cerebrospinal fluid test results	course of disease, years
1.	female	25.	normal	no	negative	0.
2.	female	31.	normal	no	negative	0.
3.	female	25.	normal	no	negative	0.
4.	male	33.	SLE	yes	Low chloride, protein content increased	6.
5.	female	40.	SLE	yes	negative	5.
6.	female	40.	SLE	yes	Low chloride	2.

Abstract AB0174 – Figure 1. The level of TNF- α in cerebrospinal fluid of patient with lupus was higher than normal people.

Abstract AB0174 – Figure 2. MRL/lpr mice appear depression by tail suspension test, open-field test and sucrose preference test, MRL/lpr mice had more reactive microglia in the cortex when compared to Balb/c at 14 weeks.

Abstract AB0174 – Figure 3. After microglial cell were stimulated by TNF- α (25 pg/ml), microglia were active and effectively release IL-6, IL-1 β and iNOS.

Abstract AB0174 – Figure 4. the use of NF- κ B signalling pathway inhibitor PDTC reverse the TNF- α induced microglial activation.

Conclusions: The study showed that the different level of inflammatory cytokines of cerebrospinal fluid of SLE patients. Our results highlight the potential role of microglia in neuroinflammation in SLE patients with depression.

REFERENCES:

- [1] Bialas AR, et al. Microglia-dependent synapse loss in type I interferon-mediated lupus. *Nature* 2017.
- [2] McHugh J. Systemic lupus erythematosus: IFN drives synapse loss via microglia. *Nat Rev Rheumatol* 2017;13(8):449.
- [3] Zhang L, et al. Prevalence of depression and anxiety in systemic lupus erythematosus: a systematic review and meta-analysis. *BMC Psychiatry* 2017;17(1):70.

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AB0175 DYSREGULATION OF NF- κ B IN GLANDULAR EPITHELIAL CELLS RESULTS IN SJÖGREN'S-LIKE FEATURES

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Background: Hyposalivation and lymphocytic infiltration in salivary glands are common manifestations of primary Sjögren's syndrome^[1]. NF-kappa B (NF- κ B) signalling is one of the most important proinflammatory pathways, and is inhibited by A20 (also known as TNFAIP3)^[2]. Although mounting studies are pointing to the central role of epithelial cells in pSS^[3-5], whether pSS-like features can be initiated by immune activation of epithelium remains to be explored.

Objectives: We sought to investigate the hypothesis that epithelial cells are capable of initiating the major pathological salivary gland hallmarks of primary Sjögren's syndrome. In order to achieve this we employ a keratin 14 (KRT14) promoter-driven knockout of the A20 NF- κ B signalling inhibitor.

Methods: A20 gene expression was knocked out in KRT14⁺ cells, namely ductal and myoepithelial cells. Whole pilocarpine-stimulated saliva was collected from A20^{-/-} mice and wildtype (WT) littermate controls at 10, 20 and 30 weeks of age. Submandibular SGs were harvested at all time points for histological examination and qPCR.

Results: In submandibular SGs of A20^{-/-} mice at 30 weeks of age, 10% of all cells were CD45⁺ leukocytes and 3% were CD3⁺ T cells, both significantly more than controls. B cell proportion increased over time in A20^{-/-} mice, but was not significantly different to controls. CD45⁺ cells formed immune foci (>50 CD45⁺ cells together) localised to striated ducts, present at significantly greater frequencies than control mice. CD45⁺ cells, T cells and occasional B cells in A20^{-/-} mice also invaded striated ducts. Expression of the pro-inflammatory cyto/chemo-kines IFN γ , TNF α , IL-6, CXCL10 and CXCL13 was also significantly greater in A20^{-/-} mice. Functionally, both volume and mucin 10 content of whole stimulated saliva from A20^{-/-} mice was significantly reduced compared to controls.

Conclusions: We present a model for epithelial cell involvement in pSS SG pathology development. We confirm that saliva production defects, foci formation and striated duct invasion can be triggered solely by immune activated epithelial cells.

REFERENCES:

- [1] Brito-Zerón P, et al. Early diagnosis of primary Sjögren's syndrome: EULAR-SS task force clinical recommendations. *Expert Rev. Clin. Immunol.* 2016;12:137–156.
- [2] Shembade N, Ma A, Harhaj EW. Inhibition of NF-kappaB signaling by A20 through disruption of ubiquitin enzyme complexes. *Science* 2010;327:1135–9.
- [3] Spachidou MP, et al. Expression of functional Toll-like receptors by salivary gland epithelial cells: increased mRNA expression in cells derived from patients with primary Sjögren's syndrome. doi:10.1111/j.1365-2249.2006.03311.x
- [4] Ittah M, et al. B cell-activating factor of the tumor necrosis factor family (BAFF) is expressed under stimulation by interferon in salivary gland epithelial cells in primary Sjögren's syndrome. *Arthritis Res. Ther.* 2006;8: R51.
- [5] Fox RI, Kang HI, Ando D, Abrams J, Pisa E. Cytokine mRNA expression in salivary gland biopsies of Sjögren's syndrome. *J. Immunol* 1994;152:5532–9.

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AB0176 MORPHOLOGICAL HEART CHANGES IN ANIMALS WITH EXPERIMENTAL SYSTEMIC LUPUS ERYTHEMATOSUS

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Background: Heart pathology in systemic lupus erythematosus (SLE) refers to the most common manifestations of the disease and largely determines its prognosis.^{1,2} The pathogenetic constructions of myocardium, endocardium and coronary vessel lesions remain insufficiently studied.^{3,4} Histological evaluation of separate cardiac structures is performed on native models of SLE in linear mice.

Objectives: to study in the experiment on animals (rats) with SLE model the degree of cardiomyocytes, myocardium, endocardium, valves and cardiac vessel damage, comparing the results with thymus and spleen tissues histological data.

Methods: The SLE modelling was performed in 53 white non-breeding rats (34 females and 19 males) using full Freund's adjuvant, splenic deoxyribonucleic acid of cattle, cyclophosphamide, azid and sodium deoxyribonucleate. Cadmium sulfate, lithium oxybutyrate and ammonium molybdate were added for feeding animals. Histological heart specimen were stained with hematoxylin and eosin, altsyon blue (pH=2.6), van Gieson. PAS-reaction was applied.

Results: Experimental SLE is accompanied by the development of cardiopathy in all animals with cardiomyocytes hypertrophy, dystrophy and necrosis, morphological signs of coronary vessel, myocardial stroma, endocardium and heart valves sclerosis, proliferation of vascular endothelium, which has dispersion and direct correlation relationships with the degree of lymphoma-macrophage infiltration, interstitial tissue, perivascular and valvular histiocytic cell infiltration, and the vessels endothelium damage nature is closely linked to the presence of mast cells in myocardial stroma, it is defined by endocardium necrosis and valves collagenolysis, decrease in spleen lymphoid tissue, and also in the brain layer cells and Gassal cells in the thymus.

Conclusions: In the case of experimental lupus cardiopathy, there is determine heart structures lesion, what is more, the immune disorders are involved in their pathogenetic constructions, as indicated by the damage of the immunocompetent organs' (thymus and spleen) corresponding structures.

REFERENCES:

- [1] Falasinnu T, Chaichian Y, Simard JF. Impact of sex on systemic lupus erythematosus-related causes of premature mortality in the United States. *J. Womens Health* 2017;26(11):1214–1221.
- [2] Hasham MG, Baxan N, Stuckey DJ, et al. Systemic autoimmunity induced by the TLR7/8 agonist Resiquimod causes myocarditis and dilated cardiomyopathy in a new mouse model of autoimmune heart disease. *Dis. Model Mech* 2017;10(3):259–270.
- [3] Mavrogeni S, Koutsogeorgopoulou L, Markousis-Mavrogenis G, et al. Cardiovascular magnetic resonance detects silent heart disease missed by echocardiography in systemic lupus erythematosus. *Lupus* 2013;1(1):961203317731533.
- [4] Myung G, Forbess LJ, Ishimori ML, et al. Prevalence of resting-ECG abnormalities in systemic lupus erythematosus: a single-center experience. *Clin. Rheumatol* 2017;36(6):1311–1316.

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AB0177 TOLL-LIKE RECEPTOR 7(TLR7) IS UPREGULATED ON PERIPHERAL B CELLS AND ASSOCIATED WITH DISEASE ACTIVITY AND DAMAGE IN PRIMARY SJOGREN SYNDROME

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Objectives: Primary Sjogren Syndrome (pSS) is characterised by activation of B cells, increased production of RNA-associated antibodies and elevated proportion of transitional B cell. Toll-like receptors 7 (TLR7) have been reported promoting the effects above in some murine models of SS. We took up this study to identify if TLR7 expression is associated with disease activity and the role of TLR7 in pSS.

Methods: 21 pSS patients and 12 healthy controls (HCs) were selected. The mRNA expression of TLR7 was determined by real-time PCR on peripheral B cells of both pSS patients and HCs. We measured BAFF serum concentrations by ELISA, and the BAFF-R, TACI and BCMA expression was analysed on each B cell subset (CD27⁺CD24^{hi}CD38^{hi}/transitional B cell; CD27⁺CD24^{lo}CD38^{lo}/naive B cell); by flow cytometry. The results were compared among patients with diverse degree of disease activity and damage to HCs.

Results: The expression level of TLR7 mRNA were elevated in pSS patients compared with HCs (p=0.004), and correlated with the SSDAI (SS disease activity index) (r=0.803; p=0.009) and the SSDI (SS damage index) (r=0.881; p=0.002). Serum BAFF concentrations increased in pSS patients compared with HCs (p=0.041), but not correlated with TLR7 expression. TACI expression in pSS patients in total B cells and traditional B cells compared to HCs were elevated and are both associated with TLR7 expression (r=0.763, p=0.048, r=0.820, p=0.004, respectively). A lower BAFFR expression was seen in transitional B cell compared with HCs (p=0.018). BCMA expression was of no significance.

Conclusions: Increased TLR7 expression on peripheral B cells were associated with disease activity and damage, suggesting that TLR7 may play a role in the development in pSS. Increased serum BAFF concentration and TACI expression were associated with TLR7 expression, indicating that BAFF may regulate TLR7 expression through TACI according to previous studies. TLR7 may be a potential treatment target of pSS and worth of further study.

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AB0178 SUPPRESSION OF ENDOPLASMIC RETICULUM STRESS BY 4-PBA IMPROVES THE MANIFESTATIONS OF MURINE LUPUS THROUGH MODULATING REGULATORY T CELLS

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Background: Impaired function of regulatory T cells (Treg) contributes to the pathogenesis of systemic lupus erythematosus (SLE). It has been reported that the aberrant responses of T lymphocytes to endoplasmic reticulum (ER) stress in patients with SLE.

Objectives: In the present study, we investigated whether ER stress inhibition through 4-phenylbutyric acid (4-PBA) ameliorates lupus manifestation on