Conclusions: The alteration of B cells subsets is an early event in LN without differences regardless the period of renal involvement (nephritic onset or later LN development). The association between persistent proteinuria and a lower percentage of plasmablasts at the baseline could be a negative prognostic factor considering the correlation between persistent proteinuria and worse renal outcome.

Disclosure of Interest: None declared

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AB0172 THE RELATIONSHIP BETWEEN THE DIFFERENT TYPES OF CELL DEATH IN SYSTEMIC CONNECTIVE TISSUE DISEASES

V. Shishkin, G.V. Kudriavtseva, Y.A. Malenkov, V.V. Shishkin. *Saint Petersburg State University, Saint Petersburg, Russian Federation*

Objectives: To study the basic mechanism of cell death (autophagy, apoptosis and necrosis) typical of patients with rheumatoid arthritis (RA), systemic lupus erythematosus (SLE) and systemic scleroderma (SSD). During systemic connective tissue diseases and especially in SLE, a close relationship between various types of cellular death is observed.

Methods: 7 SLE-, 10 RA-, 10 SSD patients' and 5 donors' sera were studied. The level of Ca ions was registered by the method of **atomic absorption spectrometry.** Adenosine monophosphate-activated protein kinase (AMPK) was estimated by the Western blotting method. The activity of ATP-ase was measured spectrophotometrically. In order to find out the level of p53 protein, the immune-enzyme "Human p53 Platinum ELISA" method was employed. The quantity of hemoprotein (Cyt c) and the level of 8-hydroxy-2'-deoxyguanosine (8-OH-dG) was measured by employing the immune-enzyme method.

Results: Assessing the functional activity of AMPK is an specific marker and a strategic biopower regulator of autophagy, as well as a specific indicator of red-ox cellular potential. In systemic connective tissue diseases, the oxidative stress is matched by urinary calcium and a decrease in the level of calcium in the blood. It reflects the level of seriousness of osteoporosis especially in case of RA. Molecular chaperones (HSP) play a key role in the changing of the way of cellular death. The family of chaperones HSP60 – HSP 100 shows ATPase activity which is most distinct during SLE and RA. The de-energisation of cells during systemic connective tissue diseases and the disappearing of the link between respiration and oxidative phosphorylation lead to proapoptotic protein – Cyt c is being released from mitochondria. High levels of Cyt c reflect cellular mitochondrial apoptosis and show the growing of hypoxia in SLE and RA. The level of protein p53 – a biological marker of apoptosis – is expressed when the DNA is destroyed. It reflects a higher level of the oxidative damage done to the DNA and the extent of the oxidative stress in SLE. This is also evidenced by the data collected by finding out the level of 8-OH-dG which is a biological marker of the free-radical damage of the DNA.

Comparison of markers of autophagy, apoptosis and necrosis in sera in SLE, RA and SSD: AMPK activity (units·mg of protein), the total level of ATP-ase active of HSP-60 – HSP-100 (nmol Pi/min·mg protein), (mM/l), quantity of (ng/ml): Cyt c, p53-protein, 8-OH-dG

Abstract AB0172 – Table 1

Groups	AMPK	ATP-ase		Cyt c	p53 protein	8-OH-dG
SLE	8,7 ±0,3	8,4±0,3	1,99 ±0,12	39,7 ±1,4	1,45±0,03	27,9±3,2
RA	5,7 ±0,2	7,9±0,2	1,87 ±0,24	26,8 ±2,3	1,27±0,04	24,2±2,3
SSD	2,8 ±0,4	5,1±0,2	2,12 ±0,09	14,9 ±2.6	0,98±0,03	18,6±3.4
Donor	1,4 ±0,3	4,0±0,7	2,57 ±0,32	11.7 ±0,3	0,73±0,07	12,56 ±2,4

Conclusions: Chaperone-mediated induction of the immune response by autophagy, an evolutionary enshrined only in mammals, perhaps, is the central link in the pathogenesis of systemic connective tissue diseases.

REFERENCE:

[1] Shishkin VI, et al. Ann Rheum Dis 2017;76:6–507.

Disclosure of Interest: None declared

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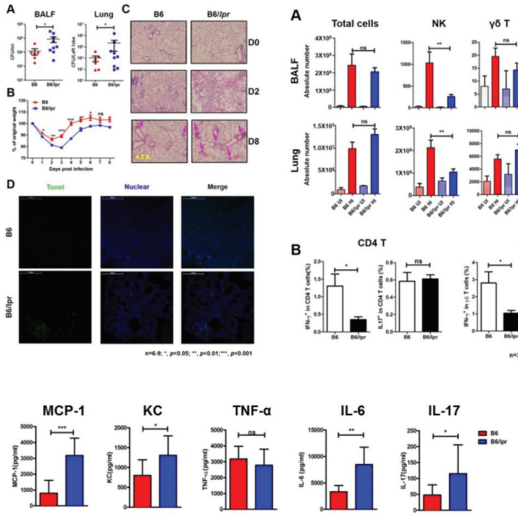
AB0173 OVERWHELMING INFLAMMATION INCREASED SUSCEPTIBILITY OF SLE-PRONE MICE TO PULMONARY BACTREIAL INFECTION

W. Li[1], X. Tang[2], S. Huang[2], L. Sun[2]. *[1]The Affiliated Drum Tower Hospital of Nanjing University Medical School, nanjing, China; [2]Department of Rheumatology and Immunology, The Affiliated Drum Tower Hospital of Nanjing University Medical School, nanjing, China*

Background: Aside from the disease itself, infections represent the major cause of morbidity and mortality in systemic lupus erythematosus (SLE) patients. Inherent defects in immune system play an important role in increasing rates of infection. However, the underlying mechanism of this dificiency remains largely unknown.

Methods: Lupus-prone mice B6/*lpr* were anaesthetized and infected with 1×108 CFU of *Haemophilus influenzae* (Hi) intranasally. Then bacterial clearance, body weight change and lung pathology were monitored. Apoptosis of lung cells was analysed by TUNEL assay. Both innate and adaptive immune response in the lung cells determined by flow cytometry. Cytokines in the bronchoalveolar lavage fluid (BALF) were measured by ELISA.

Results: Although both wild-type (WT) and B6/*lpr* mice survived after pulmonary Hi infection, a delay of bacterial clearance and inflammatory resolution was observed in B6/*lpr* mice. Tissue damage was more severe in the lungs of B6/*lpr* mice, as more apoptotic cells were detected on Day2 after infection. Cells from lupus-prone lungs produced more pro-inflammatory cytokines IL-6, MCP-1 and KC. TNF-α is comparable between the two groups. NK, γδ T and CD4 T cells are required for control bacterial infection. We that compared with WT controls, in response to infection fewer NK cells were detected in B6/*lpr* lungs. The numbers of γδ and CD4 T cells were not different, but their ability to secrete IFN-γ was significant lower in B6/*lpr* mice.



Abstract AB0173 – Figure 1

Conclusions: The increased susceptibility of SLE-prone mice to pulmonary *Haemophilus influenzae* infection may due to the elevated inflammatory responses and the deficient production of IFN-γ by immune cells.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.3393

AB0174 TNF-A MODULATES MICROGLIA ACTIVATION VIA NF-KB ACTIVITY IN SYSTEMIC LUPUS ERYTHEMATOSUS WITH DEPRESSION

X. Kong[1], K. Shen[2], J. Ji[1], T. Fu[3], J. Yang[3], Z. Gu[1]. *[1]Department of Rheumatology, Affiliated Hospital of Nantong University; [2]Department of Pharmacy, Affiliated Hospital of Nantong University; [3]Research Center of Clinical Medicine, Affiliated Hospital of Nantong University, Nantong, China*

Background: Systemic lupus erythematosus (SLE) is a complex autoimmune disease accompanied by damage to a variety of tissue injuries, such as joints, kidney, and the peripheral and central nervous systems (CNS).[1] The diffuse CNS lupus manifests with a diverse array of neuropsychiatric symptoms that range from headaches, anxiety, depression, to cognitive impairment and, in rare cases, psychosis.[2] Additionally, up to 24% of SLE patients will display

depression.[3] Previus studies have suggested microglia, as critical mediators of depression in SLE.

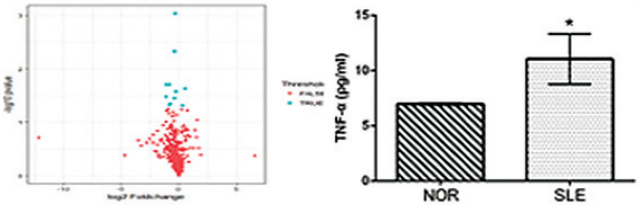
Objectives: To date, the pathophysiology of most depression symptoms in SLE has not been well determined. We focused our attention on the potential role of microglia in neuroinflammation in SLE patients.

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-κB. The concentrations of IL-6 and IL-1β in the cell supernatants were measured by ELISA. After using of NF-ΚB signalling pathway inhibitor PDTC, the activation of microglia stimulated by TNF-α was determined by immunofluorescence, quantitative PCR, Western blot analysis and ELISA.

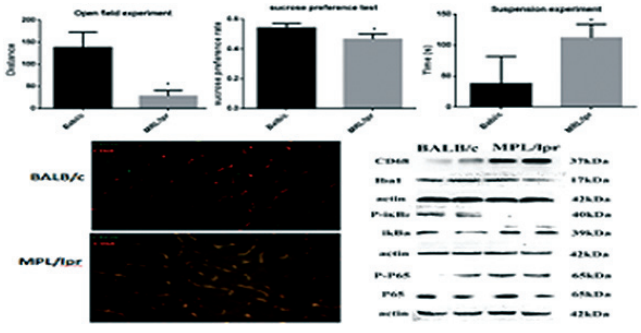
Results: The results showed that the level of TNF-α in cerebrospinal fluid of patients with lupus was higher than normal people. At 14 weeks, MRL/lpr mice appear depression by tail suspension test, open-field test and sucrose preference test, MRL/lpr mice had more reactive microglia in the cortex when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

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

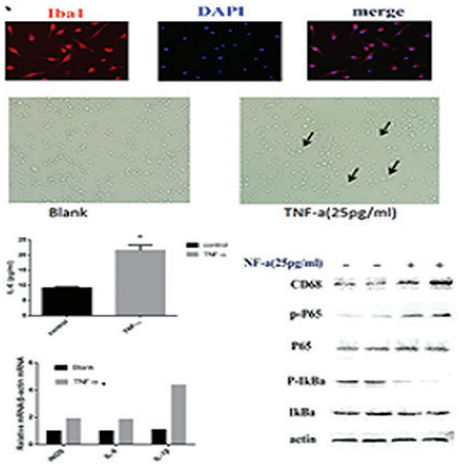
patient	Sex	Age, years	disease	depression	cerebrospinal fluid test results	course of disease, years
1	female	25	normal	no	negative	0
2	female	31	normal	no	negative	0
3	female	25	normal	no	negative	0
4	male	33	SLE	yes	Low chloride, protein content increased	6
5	female	40	SLE	yes	negative	5
6	female	40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



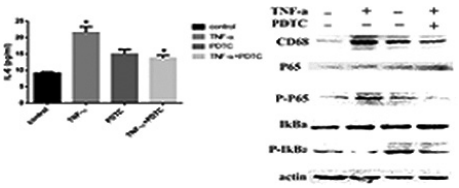
Abstract AB0174 – Figure 1. The level of TNF-α in cerebrospinal fluid of patient with lupus was higher than normal people.



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), microglias were active and effectively release IL-6, IL-1β and INOS.



Abstract AB0174 – Figure 4. the use of NF-κB 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-KB IN GLANDULAR EPITHELIAL CELLS RESULTS IN SJÖGREN'S-LIKE FEATURES

X. Wang[1], A. Shalaan[2], S. Liefers[1], G. Proctor[2], H. Bootsma[1], F. Kroese[1], S. Pringle[1]. *[1]Rheumatology and Clinical Immunology, UMCG, Groningen, Netherlands; [2]Division of Mucosal and Salivary Biology, King's College London Dental Institute, London, UK*

Background: Hyposalivation and lymphocytic infiltration in salivary glands are common manifestations of primary Sjögren's syndrome[1]. NF-kappa B (NFκB) 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 epitheliums 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 NFκB signalling inhibitor.