and KEGG biological pathway analysis were performed to predict the functions of differentially expressed lncRNAs and co-expressed potential targeting genes. Subsequently, a ceRNA (lncRNA-miRNA-mRNA) network including 2320 ceRNA pairs was constructed based on predicted miRNAs shared by lncRNAs and mRNAs.

Conclusion: The expression profile provided a systematic perspective on the potential functions of lncRNAs, miRNAs, mRNAs and circRNAs in the pathogenesis of pSS. Therefore, this study will aid in the development of new diagnostic biomarkers and drug therapies.

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POS0786

UNMET TREATMENT NEEDS IN SYSTEMIC LUPUS ERYTHEMATOSUS (SLE): A CROSS-SECTIONAL ASSESSMENT OF DISEASE ACTIVITY IN SLE PATIENTS DURING THEIR LAST VISIT

Q. Gioti¹, K. Chavatzas², G. Belevonis¹, S. Koutsovit¹, C. Katsimpari¹, I. Sofianos¹, A. Tatsi¹, P. Tzanis¹, A. Lazarini¹, K. Klavdianou¹, I. Giannakopoulou¹, E. Kalavri¹, E. Theotikos¹, A. Elezoglou¹, D. Boumpas², A. Fanouriakis^{1,2}, ¹"Asklepieio" General Hospital, Department of Rheumatology, Athens, Greece; ²"Attikon" University Hospital, Rheumatology and Clinical Immunology Unit, Athens, Greece

Background: The current goal of treatment in SLE is remission or low disease activity (LDA) and prevention of flares, achieved with the lowest possible dose of glucocorticoids. Nevertheless, in current clinical practice a significant number of patients still has active disease.^{1,2}

Objectives: To assess the current disease activity state of SLE patients during their most recent visit in two centers (Department of Rheumatology in "Asklepieio" Hospital and Rheumatology Unit in "Attikon" Hospital, both in Athens, Greece).

Methods: Cross-sectional study of patients with a diagnosis of SLE for at least one year. Patients were divided into four groups: 1) *Remission off-therapy*: SLE Disease Activity Index (SLEDAI)=0 without prednisone or immunosuppressive drugs (IS), 2) *Remission on-therapy*: SLEDAI=0, prednisone dose ≤5mg/day and/or IS (conventional and biologic, maintenance phase), 3) *LDA*: SLEDAI ≤4, prednisone dose ≤7.5mg/day and/or IS (maintenance phase), 4) *Active disease*: SLEDAI >4 and/or prednisone dose >7.5mg/day and/or IS (induction phase).² Hydroxychloroquine was allowed in all groups.

Results: 205 patients were included [95.1% female, mean (SD) age 48.4 (14.9) years and median disease duration (IQR) 6.2 (12.6) years]. A history of lupus nephritis and neuropsychiatric SLE was present in 16.6% and 17.1% of our patients, respectively, and 39% of patients had SLICC/ACR damage index (SDI) > 0. At last visit, remission off-therapy and remission on-therapy was present in 8.3% (n=17) and 15.1% (n=31) of our patients, respectively. Seventy-five patients (36.6%) had LDA, whereas 82 patients (40%) had active disease. More than 85% (86.3%) of patients were in treatment with hydroxychloroquine and 64.4% were receiving immunosuppressive drugs. Regarding glucocorticoids, 50.2% (n=103) were treated with prednisone dose ≤7.5mg/day and over 40% (42.4%, n=87) did not receive prednisone at all. A SLEDAI score 0 and 1-4 was achieved in 24.4% and 42.9% of patients, respectively, but only 3.9% had a SLEDAI > 8, indicative of high disease activity.

Conclusion: Although the majority of our patients were treated with hydroxychloroquine and glucocorticoids in acceptable levels of daily dose, four out of ten patients in our practice have active disease during their last visit. Achieving treatment goals in SLE patients remains a challenge for future novel therapies.

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POS0787

BERBERINE MODULATE LUPUS SYNDROME VIA THE REGULATION OF GUT MICROBIOTA IN MRL/LPR MICE

Y. Bao¹, J. Ji¹, Z. Xue², Z. Gu¹. ¹Affiliated Hospital of Nantong University, Department of Rheumatology, Nantong, China; ²Affiliated Hospital of Nantong University, Research Center of Clinical Medicine, Nantong, China

Background: Intestinal flora disorder and immune abnormalities have been reported in systemic lupus erythematosus (SLE) patients^{1,2}. Berberine (BBR) showed significant effects in regulating the intestinal flora, repairing gut barriers

and regulating immune cells^{3,4}. While few reports mentioned the abnormal gut microbiota and metabolites in Chinese SLE patients.

Objectives: Our investigation tried to illustrate the relationship between gut microbiota, intestinal metabolites and disease activity in Chinese SLE patients. And the effect of BBR to intestinal dysbacteriosis, multiple organ damages and over-activated immune system in MRL/Lpr mice.

Methods: 16S high-throughput (16S rRNA) sequence, qRT-PCR and gas chromatography technology were used to determine the gut microbiota and metabolites in 104 SLE patients from Affiliated Hospital of Nantong University, China. BBR was orally treated to the MRL/Lpr mice in low, medium and high doses. After 6 weeks treatment, mice were sacrificed. Serum, faeces and organs were collected for further studies.

Results: Chinese SLE patients showed higher abundance of *Bacteroidetes* and lower abundance of *Firmicutes*. The results of qRT-PCR showed high *Firmicutes/Bacteroidetes* (F/B) ratio of SLE patients. The F/B ratio was negative correlated with SLE disease activity index (SLEDA) score. Almost all the tested short-chain fatty acids (SCFAs) found statistically significant results in SLE and LN (lupus nephritis) patients, especially the propanoic acid and butyric. BBR altered the relative abundance of *Bacteroides* and *Verrucomicrobia* and the butyric acid content in colon of MRL/Lpr mice. The increase of tight junction protein also indicated the gut barrier was repaired by BBR. Treg and Th17 cells in spleen and mesenteric lymph node (MLN) were increased. These results revealed a positive therapeutic effect of berberine on SLE from gut microbiota to immune status.

Conclusion: Our study highlights current status of intestinal dysbacteriosis in Chinese patients with SLE and differences in intestinal metabolites among patients with different disease states. The regulation of intestinal flora and the repairment of gut barrier by intestinal metabolites in BBR treated mice seemed to be the factor that directed the immune responses and disease outcomes. The ultimate goal of our study was to determine the beneficial effects of regulating the gut microbiota on the treatment of SLE. The application of berberine is a relatively safe and convenient way. In the coming investigations, we plan to focus on the study of berberine and its metabolites on intestinal function and systemic immunity.

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Figure 1.

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POS0788

CIRCULATING EXOSOMES PROMOTE LUPUS NEPHRITIS IN MRL-LPR MICE

X. Sha¹, X. Ge¹, Y. Jin¹, T. Chen¹, X. Ni¹, W. Zheng², J. Ji¹, Z. Gu¹. ¹Affiliated Hospital of Nantong University, Department of Rheumatology, Nantong, China; ²Affiliated Hospital of Nantong University, Research Center of Clinical Medicine, Nantong, China

Background: Systemic Lupus Erythematosus (SLE) is a prototypic autoimmune disease that characterized by the loss of self-tolerance and the production of autoantibodies (autoAbs) [1, 2]. Lupus nephritis (LN), the severe organ-threatening manifestations of SLE, could cause massive damage to patients [3, 4]. Currently, some exosomal microRNAs (miRNAs) are considered as potential biomarkers in SLE. However, the role of exosomal miRNAs in Lupus Nephritis (LN) remains unclear.

Objectives: The purpose of this study was to investigate molecular mechanism of plasma exosomal miRNAs in the development of Lupus Nephritis.

Methods: Circulating exosomes were isolated from plasma of patients with LN, SLE without LN (NLN). Plasma exosomes were authenticated by Western Blot, Nanosight Tracking Analysis (NTA) and transmission electron microscopy (TEM). Fluorescence microscopy of co-cultured plasma exosomes and podocytes demonstrated that exosomes were uptaken into podocytes. Moreover, cell apoptosis and the inflammation factors was assessed using Western Blot. We analyzed the expression profiles of miRNAs in LN and NLN exosomes and the expression profiles of mRNAs of podocytes stimulated with LN and NLN exosomes with the help of next generation sequencing (NGS).

Results: We demonstrate that exosomes derived from LN plasma could be taken by neighboring podocytes and promote the apoptosis of podocytes and the expression of inflammation factors. In addition, the sequencing found that miRNAs were differentially expressed in LN and NLN exosomes and mRNAs were differentially expressed in podocytes stimulated with LN and NLN exosomes.

Conclusion: LN plasma exosomes have a potency to stimulate the apoptosis of podocytes and the expression of inflammation factors. Moreover, differentially expressed miRNAs in exosomes play a potential role in the development of LN.

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POS0789

APPLICATION OF THE NEW ACR/EULAR 2019 CLASSIFICATION CRITERIA OF SYSTEMIC LUPUS ERYTHEMATOSUS TO A INCEPTION, MONOCENTRIC COHORT OF UNDIFFERENTIATED CONNECTIVE TISSUE DISEASES POPULATION AT ONSET OF THE DISEASE

E. Elefante^{1,2}, A. Parma¹, V. Nannipieri¹, V. Signorini³, C. Stagnaro³, D. Zucchi³, L. Carli³, F. Ferro³, C. Tani³, M. Mosca³. ¹University of Pisa, Rheumatology Unit, Department of Clinical and Experimental Medicine, Pisa, Italy; ²University of Siena, Department of Medical Biotechnology, Siena, Italy; ³University of Pisa, Rheumatology Unit, Department of Clinical and Experimental Medicine, Pisa, Italy

Background: undifferentiated connective tissue diseases (UCTDs) are a group of systemic autoimmune diseases that share clinical and serological manifestations with definite connective tissue diseases (CTDs), but do not satisfy existing classification criteria¹. Within this group, it is possible to identify very heterogeneous conditions: transitory and self-limiting forms, stable conditions over time and forms that will evolve towards definite CTDs, in particular Systemic Lupus Erythematosus (SLE). The availability of new classification criteria for CTDs could be useful in identifying major CTDs from their onset and help in the differentiation from stable UCTDs, which will maintain their undifferentiated profile over time.

Objectives: the aim of this study was to apply the new ACR/EULAR 2019 classification criteria of SLE² to patients included, at the onset of UCTD, to evaluate how many patients could be re-classified as SLE.

Methods: this is a retrospective observational study that enrolls patients who received the diagnosis of UCTD at the Rheumatology Unit of Pisa, according to the classification criteria proposed by Mosca et al¹, and were then regularly followed in the same clinic (inception cohort). For each patient, demographics, comorbidities, treatment, clinical and serological data were collected, at baseline and during follow-up. The new ACR/EULAR 2019 classification criteria of SLE were applied to the inception cohort at the onset of the disease. The characteristics of patients re-classified as SLE according to the new classification criteria and those of patients who "remained" classified as UCTD were compared.

Results: we enrolled 202 patients with a diagnosis of UCTD, mainly female (F:M 193:9) and of Caucasian ethnicity (97.5%), mean age at the diagnosis 38,5 $\pm$ 13,2 years and a median follow-up of 5 years (IQR 2-10).

During the follow-up, 10 patients (4.9%) in our cohort developed clinical and serological characteristics that led to a diagnosis of a definite CTD, in particular: 7 SLE, 2 Mixed Connective Tissue Disease (MCTD) and 1 Sjogren's syndrome. Applying the ACR/EULAR 2019 classification criteria of SLE to patients enrolled at the onset of the disease, 38/202 (18.8%) would have been classified as SLE (with a median score of 12 (IQR 11-15)) on the basis of the presenting clinical and serological manifestations. Interestingly, 6/7 patients who received a diagnosis of SLE during the follow-up were among these 38 patients.

Among the items of the new classification criteria of SLE, the most frequently satisfied by patients "re-classified" were arthritis (63.2%), hematological (44.7%) and skin (23.7%) manifestations; as for the "immunological" items, hypocomplementemia (71%), SLE-specific (52.6%) and antiphospholipid (35.1%) autoantibodies. Comparing the subgroup of patients "re-classified" as SLE with that of patients who "remained" UCTD, we found that the first group presented more frequently hematological manifestations, hypocomplementemia and anti-dsDNA, anti-Sm, anti-RNP, anti-beta2GPI positivity at the onset of the disease ($p < 0.01$). Moreover, during the follow-up, the subgroup of patients "re-classified" as SLE developed more frequently malar ($p < 0.05$) and discoid rash and arthritis ($p < 0.01$) compared to patients who "remained" UCTD.

Conclusion: The development of increasingly sensible and specific classification criteria for definite CTDs may guide in the identification of stable UCTDs since their early stages and consequently in better definition of these conditions that can be considered as a distinct clinical entity.

The early identification of stable UCTD is of great importance not only for clinical management (follow-up schedules as well as therapeutic protocols) but also for scientific implications.

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POS0790

RELATIONSHIPS BETWEEN SALIVA IMMUNOGLOBULINS FREE LIGHT CHAINS CONCENTRATION AND CLINICAL, IMMUNOLOGICAL, HISTOLOGICAL PARAMETERS IN PATIENT WITH PRIMARY SJOGREN'S SYNDROME

E. Kuvardin¹, I. Kholopova², E. Belyakova³, I. Grigor'eva¹, I. Bekhtereva³, A. Maslyanskiy¹, Y. Krivolapov³, S. Lapin². ¹Almazov National Medical Research Centre, Rheumatology Department, Saint - Petersburg, Russian Federation; ²Pavlov First Saint - Petersburg State Medical University, Center for Molecular Medicine, Laboratory of Autoimmune Diagnostics, Saint - Petersburg, Russian Federation; ³North-Western State Medical University named after I.I. Mechnikov, Pathological Department of Clinical Molecular Morphology, Clinic named after E.E. Eichwald, Saint - Petersburg, Russian Federation

Background: Patients with primary Sjogren's syndrome (pSS) exhibit biological signs of B cell activation such as serum polyclonal hypergammaglobulinaemia, increased levels of free light chains (FLC) and positivity for autoantibodies. B-cells may comprise up to 50% of lymphocytic infiltrates in salivary glands of patients with the disease. For that reasons measuring saliva B-cells products might have diagnostic value in pSS.

Objectives: To evaluate relationships between saliva free light chains concentration and clinical, immunological, histological parameters in patient with pSS.

Methods: Saliva and blood FLC concentrations were measured in patient with pSS (n = 24) and healthy volunteers (n = 11). Patients fulfilled the ACR/EULAR 2016 criteria of pSS. Saliva collected during assessment unstimulated salivary flow was used for analysis. Quantitative assessment of CD3⁺, CD4⁺, CD8⁺, CD20⁺, CD21⁺, CD68⁺, CD138⁺ cells was performed in minor salivary glands of 9 patient by immunohistochemistry. Cells quantity was calculated in 4 mm² (area of section).

Results: FLC concentration in saliva of pSS patients was higher than in healthy volunteers ($p < 0.01$). Medians of saliva κ - and λ - free light chains concentrations in patients and healthy persons were 1,08 mg/L [25;-75- percentiles 0,58;1,91], 1,038 mg/L [0,55;2,03] and 0,36 mg/L [0,32; 0,54], 0,35 mg/L [0,21; 0,52] respectively. Median of saliva κ : λ chains ratio in pSS patient was 0,94 [0,6;1,5]. The ratio didn't differ from healthy persons ($p = 0,24$). Saliva κ - and λ - free light chain concentrations in patient with pSS correlated with patients age ($r_s = 0,51$, $p = 0,033$ and $r_s = 0,43$, $p = 0,011$, respectively) and unstimulated salivary flow ($r_s = -0,48$, $p = 0,02$ and $r_s = -0,49$, $p = 0,017$, respectively). Concentration of κ - free light chain correlated with number of CD138⁺ cells ($r_s = 0,733$, $p = 0,025$). Interesting that saliva λ - free light chain concentration didn't correlate with quantity of plasmatic cells.

Conclusion: Measuring saliva FLC concentration might be offered as diagnostic marker of pSS. Concentration κ - free light chain can directly mirror the glands quantity of plasmatic cells.

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