classification of the disease by pathological conditions.³ However, the association with MFG-E8 expression and clinical features of SLE patients is not fully understood.

Objectives: To clarify the clinical significance of MFG-E8 in SLE, we analysed the correlation between the expression level of MFG-E8 in circulating phagocytic leukocytes and clinical parameters of the patients.

Methods: A multi-centre, exploratory and prospective SLE cohort was established. Among SLE patients who visited our division from May 2015 to March 2017 and satisfied the 1997 revised criteria, patients with one or both of BILAG A or B, or with SLEDAI-2K $\geq$ 4 and clinical symptoms were defined as active SLE. These patients were then matched with randomly selected patients by age, gender, history of nephritis, and daily glucocorticoid dose as an inactive SLE group. Age and sex matched healthy controls (HC) were also recruited. The expression level of MFG-E8 in monocytes and its concentration in serum of the patients were measured by FACS and ELISA, respectively. The clinical parameters of the patients were collected from their clinical records.

Results: A total of 108 cases were enrolled, consisting of 36 active (mean age: 44.2 $\pm$ 18.6, female: 80.6%, nephritis: 69.7%), 38 inactive SLE and 24 HC cases. The absolute number and the proportion of MFG-E8 positive-monocytes to total monocytes were significantly higher in the active SLE group ($p<0.01$), whereas serum MFG-E8 level showed no significant difference among the group. Importantly, the proportion was also significantly correlated with SLEDAI-2K, serum levels of anti-ds-DNA antibody and complement and C1q (table 1). Notably, elevated proportion of MFG-E8-positive monocytes to total monocytes was observed in the patients with cutaneous or musculoskeletal involvement or leukocytopenia. In addition, the proportion of MFG-E8-positive monocytes to total monocytes significantly decreased from the baseline in active SLE patients after 6 months treatment and increased concordantly with disease activity in 6 refractory cases. Then we further analysed the accuracy to discriminate between active and inactive SLE patients and found that the proportion of MFG-E8 monocytes showed significant accuracy of disease activity, which is equivalent to serum levels of anti-ds-DNA antibody, complement and C1q, by receiver operating characteristic curve analysis (figure 1).

Abstract FRI0282 – Table 1. Correlation with SLEDAI and serological markers (Spearman's rho)

		n	Number of MFG-E8 positive monocyte	Proportion of MFG-E8 positive monocyte	Serum MFG-E8
a) Activity	SLEDAI-2K	74	0.570**	0.634**	-0.110
b) Serological markers	CH50	51	-0.503**	-0.591**	0.049
	Anti-ds-DNA antibody	74	0.425**	0.449**	-0.027
	C1q	69	0.526**	0.568**	0.001

* $p<0.05$, ** $p<0.01$ by Spearman's correlation coefficient

Abstract FRI0282 – Figure 1. Receiver operating characteristic curve analysis for discriminating active from inactive SLE

Conclusions: Our study indicate that the proportion of MFG-E8-positive monocytes to total monocyte in peripheral blood was positively associated with disease activity of SLE and may be a novel mechanistic biomarker to determine the disease activity.

REFERENCES:

- [1] Science 2004;304(5674):1147–50.
- [2] J Leuko Biol. 2008;83:1300–7.
- [3] Lupus 2014;23:386–94.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.3628

FRI0283

DYNAMIC CONTRAST ENHANCED MRI (DCE-MRI) DEMONSTRATES HIPPOCAMPUS PERMEABILITY IN SLE

M. Mackay, B. Diamond, D. Eidelberg, A. Hoang, P.C. Sanelli. The Feinstein Institute for Medical Research, Manhasset, USA

Background: Cross-reactive, anti-dsDNA/N-methyl d-aspartate receptor antibodies (DNRAb) have been implicated in the pathogenesis of cognitive impairment in SLE. The mouse model demonstrates selective effects of DNRAb on hippocampal neurons following blood brain barrier (BBB) breach. ¹ We previously identified abnormal hippocampal glucose hypermetabolism in SLE patients that correlated with serum DNRAb titers and poor performance on neuropsychological (NP) testing.² However, little is known about how antibodies access brain in humans.

Objectives: BBB permeability (BBBP) in SLE and healthy control (HC) subjects was evaluated with DCE-MRI. We hypothesised that brain areas with abnormal hypermetabolism² in SLE subjects would also demonstrate altered BBBP.

Methods: 6 SLE subjects with no history of NP symptoms and 6 HCs were recruited (all female). All subjects underwent NP testing and DCE-MRI on a 3.0 tesla magnet (Siemens Healthineers, GERMANY). MRI sequences were acquired according to standard protocols; permeability imaging used DCE technique with axial 3D-SPGR T1-WI sequences and 80 cine phases using TR=25 ms, TE=3.8 ms, FOV=24 mm, and matrix size of 128 $\times$ 256. Magnevist Gadolinium contrast (Bayer Healthcare, GERMANY) was dosed IV at 0.1 mmol/kg, at 5cc/sec following a 5 s delay. Post-processing of images into BBBP parameters of K-trans (mL/100 gm/min) and VE (mL/100 gm) was performed using Olea Sphere 2.2, 2.3 (Olea Medical, France) with the Tofts extended permeability model. This technique was standardised with the arterial input function centred in the cavernous ICA segment for all subjects.

Analyses: Regions-of-interest (ROI) from previously identified hypermetabolic regions (hippocampus, orbitofrontal cortex, posterior putamen/globus pallidus/thalamus) were selected. Mirror ROIs were placed in bilateral MRI cerebral hemispheres for sampling at same brain levels. Regional DCE curves were generated to compare permeability phases. T-tests were used to evaluate demographic and NP testing differences.

Results: SLE subjects performed significantly worse than HCs on cognitive testing (table 1). Mean DCE curves (figure 1) show perfusion (initial spike) and permeability phases of contrast in the sampled tissues. Compared to HCs, SLE subjects demonstrate significantly increased signal in the permeability phase in the hippocampus, indicating leakage of contrast into the extravascular space.

Abstract FRI0283 – Table 1. Subject characteristics and neuropsychological testing scores

	Healthy Control (n=6)	SLE (n=6)	p
Age	35.04 $\pm$ 9.6	38.0 $\pm$ 13.2	.669
NP Testing*			
Matching Grids	40.9 $\pm$ 9.7	25.8 $\pm$ 9.2	.023
Match to Sample	35.4 $\pm$ 13.5	16.4 $\pm$ 5.9	.01
Continuous Processing	86.3 $\pm$ 13.9	65.6 $\pm$ 5.5	.013

*Automated Neuropsychological Testing Metric: resulted as throughput scores that represent efficiency as a function of accuracy and time

Abstract FRI0283 – Figure 1. Dynamic Contrast Enhanced MRI Curves show increased hippocampus permeability in SLE

Conclusions: This is the first report of increased BBBP in SLE subjects that is specific to the hippocampus; a region that we have previously reported to have abnormal resting metabolism in SLE subjects. These data, including the abnormal NP testing, support the murine model of autoantibody-mediated cognitive impairment following disruption of the BBB. The results also suggest that DCE-MRI may be an effective, non-invasive tool to measure BBBP and its role in neuropsychiatric SLE pending confirmatory studies with increased sample size.

REFERENCES:

- [1] Kowal C, et al. *Immunity* 2004;21:179–88.
- [2] Mackay M, et al. *Lupus Sci Med* 2015;2:e000074.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.7427

FRI0284

ALTERED PATTERNS OF HISTONE ACETYLATION POINT TO MECHANISMS OF TRANSCRIPTIONAL DYSREGULATION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

B. Anić¹, A. Blažeković², D. Bosnić¹, M. Sentić¹, M. Mayer¹, M. Cerovec¹, K. Gotovac Jerčić², F. Borovečki². ¹Department of Internal Medicine, Division for Clinical Immunology and Rheumatology, University Hospital Centre Zagreb; ²Department for Functional Genomics, University of Zagreb School of Medicine, Zagreb, Croatia

Background: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease designated by a heterogeneous course and systemic nature. It arises as a result of complex pathways, as well as the interaction of genetic and environmental factors, leading to the altered reactivity of the immune system that culminates in autoantibody formation. Epidemiological studies have shown an important role of the genetic component in the emergence of SLE and genome-wide association studies have identified more than 50 SLE-associated risk loci, pointing to a complex genetic background.

Objectives: The aim of the study was to further elucidate the genetic mechanisms influencing the development of SLE.

Methods: We performed chromatin immunoprecipitation experiments to ascertain the levels of histone acetylation in peripheral blood mononuclear cells collected from 5 recent onset and treatment naive SLE patients compared to 5 age and gender matched controls.

Results: The analysis revealed 16 379 significantly enriched genomic regions in control patients compared to 39 204 significantly enriched genomic regions in SLE patients. Among the SLE specific regions several pathways were significantly enriched including the adaptive immune system pathway, cytokine signaling in immune system, disease of immune system and inflammation mediated by chemokine and cytokine pathway.

Conclusions: The collective data point to a significant alteration of histone acetylation patterns in SLE patients possibly mediated by the DNA specific autoantibodies. The results of the study offer additional insight into the genetics of SLE pointing to putative mechanisms of transcriptional dysregulation.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.5783

FRI0285

DETECTION OF OLIGOCLONAL B-CELL POPULATIONS BY SPECTRATYPING ANALYSIS IN THE RENAL TISSUE OF PATIENTS WITH ACTIVE LUPUS NEPHRITIS

P. Sfikakis¹, K. Kolovou², M. Roumelioti¹, D. Paleologou¹, M. Tektonidou¹, C. Kyrtsoni¹, J. Boletis¹, P. Panayiotidis¹, S. Marinaki². ¹First Department of Propaedeutic and Internal Medicine; ²Nephrology Department and Renal Transplantation Unit, Medical School, National and Kapodistrian University of Athens, Athens, Greece

Background: Previous studies have shown, using polymerase chain reaction (PCR), cloning, sequencing and analysis of rearranged immunoglobulin heavy-chain (Ig-V_H/D_H/J_H) genes, that clusters of clonally-related sequences are commonly found in the peripheral blood of patients with active lupus nephritis.

Objectives: Using an easy-to-perform method such as spectratyping analysis, to test the hypothesis that clonal B-cell populations are present in the renal tissue of lupus nephritis patients, induced perhaps as a result of local (auto)antigenic stimulation.

Methods: Genomic DNA extracted from renal biopsy samples from 18 patients with active lupus nephritis and 24 control patients with other (auto)immune-mediated glomerular diseases, as well as DNA from 25 paired peripheral blood samples, was subjected to multiplex PCR for the detection of Ig-V_H clonal rearrangement. PCR products were analysed by capillary electrophoresis according to the Biomed-2 standard guidelines for the definition of clonal B cell populations. Immunohistochemistry using the B-cell-specific L-26 antibody was also performed in available renal samples.

Results: Electrophoregrams of PCR products derived from patients with biopsy proven active lupus nephritis revealed the presence of oligoclonal B-cell populations among polyclonal B-cells in renal tissue of 6/18 patients. No associations with clinical or histology class were evident. Oligoclonal B-cell populations were also found in renal samples derived from patients with untreated focal segmental glomerulosclerosis (6 of 7), minimal change disease (1 of 3), membranous nephropathy (1 of 3) and IgA nephropathy (3 of 4), and not in patients with pauci-immune vasculitis (n=4) or membranoproliferative glomerulonephritis (n=3). Oligoclonal B-cell populations were not found in any of the paired peripheral blood samples derived from 13 patients having renal B-cell oligoclonality, suggesting the existence of local (auto)antigens leading to clonal expansion rather than B-cell transfer through peripheral circulation. Finally, spectratyping analysis identified polyclonal or oligoclonal B-cells in all renal tissues in the absence of detectable B-cells by immunohistochemistry in the same samples.

Conclusions: These novel findings show that spectratyping analysis can detect oligoclonal B-cell expansions in renal tissue from patients with active lupus nephritis and other (auto)immune-mediated glomerular diseases. Whether this standardised method can identify individual patients who could benefit from therapeutic B cell depletion deserves further study.

REFERENCE:

- [1] Sfikakis PP, et al. Clonal expansion of B-cells in human systemic lupus erythematosus: evidence from studies before and after therapeutic B-cell depletion. *Clin Immunol.* 2009 Jul;132(1):19–31.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2018-eular.2905

FRI0286

RANK-L IS EXPRESSED BY SALIVARY GLAND EPITHELIAL CELLS IN PRIMARY SJOGREN'S SYNDROME: A NOVEL ACTOR IN ECTOPIC LYMPHOID STRUCTURE NEOGENESIS

P.-M. DURET¹, R. VEBER², R. FELTEN¹, F. MONNEAUX², C. MUELLER², J. SIBILIA¹, H. DUMORTIER², J.-E. GOTTENBERG¹. ¹Rheumatology, Strasbourg University Hospital; ²Molecular and Cellular Biology, IBMC, Strasbourg, France

Background: Tertiary Lymphoid Organs (TLOs) are observed in target tissues of various immune-mediated inflammatory diseases (IMIDs) such as salivary glands in primary Sjögren's syndrome¹ (pSS). TLOs are mimicking secondary lymphoid organs (SLOs) architecture and strikingly share common features with lymph nodes.² SLOs organogenesis is coordinated by a complex stromal network that has not been fully characterised in TLOs yet. Although RANK-L (Receptor Activator of NF-κB Ligand) has been recently involved as a pivotal cytokine in precocious steps of lymph nodes development,³ notably through a stromal cell expression, its contribution in TLOs neogenesis remains unclear.

Objectives: To characterise stromal cells subsets within TLOs arising in the salivary glands and to determine whether RANKL is expressed or not in the target tissue of pSS.

Methods: Stromal cells and RANK-L expression were analysed in TLOs from salivary glands by immuno-fluorescence on frozen sections in the NZB/NZW F1 mouse model and in minor salivary gland biopsies of patients fulfilling 2016 ACR-EULAR Sjögren's syndrome criteria and by flow-cytometry after enzymatic digestion of NZB/NZW F1 salivary glands. RANK-L expression has also been assessed by Real Time quantitative Polymerase Chain Reaction (RT-qPCR) and immunofluorescence on primary cultures of salivary gland epithelial cells (SGECs) with or without IL-1b or Interferon alpha (INF-a) stimulation.

Results: Most of SLOs stromal cells populations: Fibroblastic Reticular Cells (FRCs), Follicular Dendritic Cells (FDCs), Lymphatic Endothelial Cells (LECs), Blood Endothelial Cells (BECs) and High Endothelial Venules (HEVs) were identified in salivary TLOs of both NZB/NZW F1 mice and patients with pSS. FRCs were the dominant subset in salivary TLOs and their proportion correlated with the degree of lymphocytic infiltration (r=0.7; p=0.007). In SLOs, RANK-L was mainly expressed by MRCs, whereas, none of them could be detected in salivary TLOs. However, despite the absence of MRCs in TLOs, RANK-L was still expressed by