

without SLE (640.98 ± 259.96 ng/ml) had relative lower serum calprotectin than patients with SLE (690.49 ± 268.22 ng/ml) ($p=0.047$, figure 1). The cutoff was set as 783.36 ng/ml. 93 patients (19.9%) were positive for calprotectin. The positivity of calprotectin was significantly associated with SLE ($p=0.044$), microangiopathy ($p=0.046$), non-vascular neurological manifestations ($p=0.047$), and lupus anticoagulant (LA) positivity ($p=0.017$). Livedo reticularis may also have association with calprotectin ($p=0.099$, table 1).

Conclusions Serum calprotectin elevates in aPLs positive patients, and could be a novel marker of microangiopathy in antiphospholipid syndrome patients. More studies are required to explore the association between calprotectin and microangiopathy in APS patients, as well as the clinical application value of calprotectin in the future.

2. SLE biomarkers

LP-009 IMMUNOGLOBULIN GAMMA-3 SUBCLASS IS A POTENTIAL BIOMARKER IN SERUMA, SALIVA, AND URINE OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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Background Immunoglobulin gamma-3 subclass, also called the immunoglobulin gamma 3 chain C (IGHG3), normally comprises 5%–8% of all IgG in humans. The salivary IGHG3 was increased in Korean patients with systemic lupus erythematosus (SLE). This study tried to assess the levels of IGHG3 in serum, saliva, and urine in patients with SLE.

Methods Serum, saliva, and urine samples were collected from 181 patients with SLE and 99 age- and sex-matched healthy controls (HCs) with clinical data. The levels of IGHG3 in each body fluid were measured and analyzed to assess their associations with clinical manifestations and disease activity of SLE.

Results Serum IGHG3 was 478.1 ± 160.9 and 364.4 ± 97.9 $\mu\text{g/mL}$ ($p<0.001$) in patients with SLE and HCs. Salivary IGHG3 was $3,078.9 \pm 2,473.8$ and $1,413.6 \pm 1,075.3$ ng/mL ($p<0.001$), and urinary IGHG3 was 64.0 ± 74.5 and 27.1 ± 16.2 ng/mL ($p<0.001$) in patients with SLE and HCs, respectively. Area under the receiver operating characteristic curve for diagnosis of SLE was 0.737 for serum IGHG3 (95% confidence interval (CI), 0.673–0.8), 0.755 for salivary IGHG3 (95% CI, 0.694–0.815), and 0.733 for urinary IGHG3 (95% CI, 0.67–0.795). Serum IGHG3 was correlated with leukocyte count ($r=-0.219$, $p=0.003$), lymphocyte count ($r=-0.221$, $p=0.03$), anti-dsDNA antibody ($r=0.22$, $p=0.003$), C3 ($r=-0.23$, $p=0.002$), salivary IGHG3 was correlated with ESR ($r=0.173$, $p=0.024$), and urinary IGHG3 was correlated with hemoglobin ($r=-0.183$, $p=0.021$), erythrocyte sedimentation rate ($r=0.204$, $p=0.01$), anti-dsDNA antibody ($r=0.262$, $p=0.001$), C3 ($r=-0.202$, $p=0.011$), and SLE disease activity index ($r=0.332$, $p<0.01$). In addition, urinary IGHG3 was higher in patients with nephritis compared in those not (119.55 ± 110.0 vs. 49.8 ± 54.4 , $p<0.01$).

Conclusions The levels of IGHG3 were significantly increased in serum, saliva and urine of patients with SLE, and urinary IGHG3 level was associated with disease activity and renal involvement of SLE.

LP-012 PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS AND HYPERPRODUCTION OF ANTIBODIES TO ANTI-U1RNP

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Background The presence of anti-U1RNP is associated with the features of different systemic rheumatic diseases (SLE, SSC, etc.), and it is also included in the criteria of the mixed connective tissue disease (MCTD). It is important to note that the MCTD may evolve into other rheumatic diseases over time and only a third of patients have a stable clinical picture for many years. The frequency of detection of anti-U1RNP in SLE according to various studies varies from 13 to 40%. Our aim was to study the frequency of SLE among patients positive for anti-U1RNP.

Methods The study included 60 patients (pts) who were positive for anti-U1RNP: 54 women and 6 men, mean age 52 ± 10 years, duration of the disease 10.6 ± 8 years. All pts were examined according to guidelines.

Results In study group all pts were positive for ANAs, anti-U1RNP and met the criteria of MCTD (R. Kasukawa, 1987). The frequency of anti-DNA was 42%, anti-Ro – 38%, RF in 31%, anti-Sm 11%, anti-La – 8%. The detection of anti-DNA was correlated with the presence of overlap syndrome ($r=0.3$, $p<0.05$), the median indicator was 16.7 (5.2; 29.5), the range of values ranged from 0.1 to 300 IU/ml, while high values were detected in pts with a cross with SLE. Leukopenia was detected in 8 pts (14%), anemia – 2 pts (3%), hypocomplementemia – 9 pts (15%), arthritis/arthralgia – 37 pts (62%), malar rash – 14 pts (24%). It turned out that 18 out of 60 (30%) pts with MCTD, it was possible to simultaneously establish the diagnosis of SLE (SLICC, 2012), thus the patients met the criteria for two different rheumatic diseases.

Conclusions 30% of patients positivity for anti-U1RNP simultaneously met the SLE criteria. This fact requires further study of this group of patients as a separate subtype of SLE.

LP-013 AUTOANTIBODY TRAJECTORIES ASSOCIATE WITH CLASSIFICATION AND TREATMENT RESPONSE IN LUPUS NEPHRITIS

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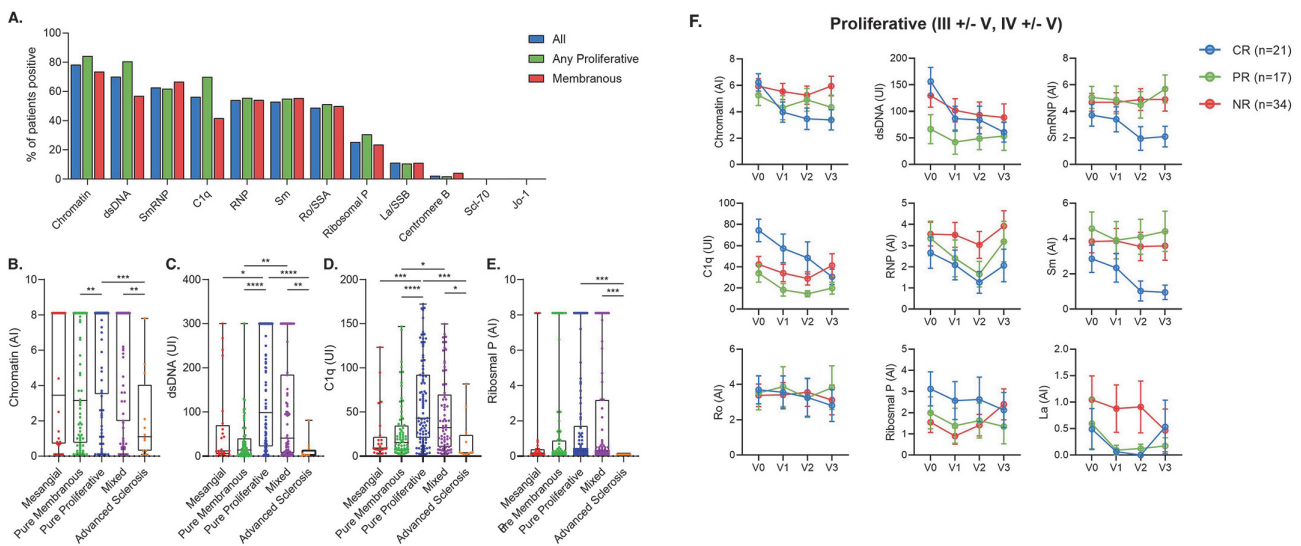
Background Autoantibodies are a hallmark of lupus nephritis (LN). While there is known heterogeneity in autoantibody expression among LN patients, the association of

autoantibodies with LN subtypes and the implications of longitudinal changes in LN are not entirely understood. In this study, we quantified circulating autoantibodies in the Accelerating Medicines Partnership (AMP) LN longitudinal cohort to identify novel serum biomarkers of LN classification and treatment response and to provide insights into the pathogenesis of LN.

Methods SLE patients meeting ACR or SLICC criteria (n=268) indicated for kidney biopsy by a urine protein/creatinine (UPCR) >0.5 were recruited for this study as part of the AMP. Kidney biopsies were evaluated by a renal pathologist according to ISN/RPS classification, and serum samples were collected at the time of diagnostic kidney biopsy and 3-, 6-, and 12-months post-biopsy. Serum autoantibodies against dsDNA, chromatin, ribosomal-P, Ro, La, Sm, SmRNP, RNP, Jo-1, Scl-70, and centromere-B were measured using the BioPlex 2200® ANA kit (Bio-Rad Technologies, Hercules, CA), while anti-C1q positivity was determined by ELISA (QUANTA Lite®, Werfen, Bedford, MA). Clinical response was

determined at 12 months using the Abatacept and Cyclophosphamide Combination Efficacy and Safety Study definitions for patients with ISN/RPS class III, IV, V, or a combination thereof and a baseline UPCR ratio >1.0.

Results Most LN patients exhibited autoantibodies against chromatin (78%) dsDNA (70%), SmRNP (63%), C1q (56%), RNP (54%), and Sm (52%) (figure 1A). Patients with proliferative LN (class III, IV, III+V, or IV+V) had higher positivity rates of several autoantibodies, including those against dsDNA, chromatin, and C1q, compared to patients with membranous LN (class V) (figure 1A). Similarly, patients with pure proliferative (class III or IV) and mixed (class III+V or IV+V) LN had significantly higher titers of these autoantibodies compared to those with mesangial (class I or II), membranous, and advanced sclerosis (class VI) LN (figure 1B-D). Furthermore, increased titers of these autoantibodies were associated with higher odds of having proliferative LN (table 1). Proliferative LN patients with a complete treatment response exhibited a significant decline in several autoantibodies including anti-



Abstract LP-013 Figure 1

Abstract LP-013 Table 1

	Any Proliferative					Pure Membranous					Others							
	OR	95% CI	PPV (%)	NPV (%)	AUC	OR	95% CI	PPV (%)	NPV (%)	AUC	OR	95% CI	PPV (%)	NPV (%)	AUC			
dsDNA	2.88	2.03, 4.345	****	75	55.15	0.73	0.35	0.21, 0.537	****	0	73.13	0.68	0.54	0.304, 0.847	*	0	86.57	0.66
Chromatin	1.79	1.39, 2.31	****	68.79	57.45	0.66	0.69	0.52, 0.897	**	0	73.03	0.61	0.59	0.412, 0.841	**	0	86.52	0.64
Ribosomal P	1.41	1.08, 1.90	*	59.93	0	0.64	0.85	0.618, 1.12	ns	0	73.41	0.58	0.54	0.252, 0.901	*	0	86.52	0.66
Ro	1.16	0.904, 1.48	ns	59.7	0	0.54	1.04	0.793, 1.36	ns	0	73.13	0.50	0.67	0.436, 0.975	*	0	86.57	0.59
La	0.92	0.724, 1.18	ns	0	40.3	0.51	1.00	0.749, 1.30	ns	0	73.13	0.50	1.15	0.822, 1.53	ns	13.43	0	0.52
Sm	1.26	0.981, 1.62	ns	59.55	0	0.55	0.87	0.655, 1.14	ns	0	73.03	0.50	0.79	0.535, 1.13	ns	0	86.52	0.60
SmRNP	1.10	0.861, 1.41	ns	59.55	0	0.52	1.00	0.762, 1.31	ns	26.97	0	0.52	0.82	0.574, 1.17	ns	0	86.52	0.58
RNP	1.16	0.905, 1.49	ns	59.7	0	0.54	1.03	0.784, 1.35	ns	0	73.13	0.52	0.67	0.436, 0.989	ns	0	86.57	0.60
Centromere B	0.93	0.716, 1.20	ns	50	40.15	0.50	1.16	0.902, 1.51	ns	50	73.48	0.50	0.62	0.0028, 1.18	ns	0	86.57	0.51
Scl-70	1.026	0.804, 1.36	ns	59.7	0	0.52	0.93	0.635, 1.21	ns	0	73.13	0.51	1.055	0.703, 1.39	ns	13.43	0	0.52
C1q	2.32	1.69, 3.30	****	71.95	59.62	0.71	0.56	0.384, 0.775	**	0	73.13	0.63	0.40	0.202, 0.682	**	0	86.57	0.71

dsDNA, C1q, chromatin, Smith, and ribosomal P (figure 1F). Autoantibody levels remained relatively stable in partial- and non-responder proliferative LN patients, as well as in patients with membranous LN.

Conclusions LN patients exhibit heterogeneous autoantibody profiles associated with ISN/RPS classification. Specifically, levels of autoantibodies against dsDNA, C1q, chromatin, and ribosomal P may serve as noninvasive biomarkers of proliferative LN. In patients with proliferative but not membranous LN, a decline in the titers of several autoantibodies, including many not routinely measured over time, such as anti-Sm, was associated with treatment response, suggesting a possible role in LN pathogenesis. In addition, these autoantibodies may serve as early biomarkers of treatment response.

LP-016 ANTI-HISTONE AND ANTI-NUCLEOSOME ANTIBODIES, RATHER THAN ANTI-DSDNA ANTIBODIES ARE ASSOCIATED WITH INTERFERON-INDUCED BIOMARKERS IN SUDANESE AND SWEDISH SLE PATIENTS

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Background In SLE, anti-dsDNA often exists together with autoantibodies against other chromatin components, like histones and nucleosomes. These antibodies can induce cytokines including interferon-alpha.

Methods We have measured ANA specificities and investigated their associations to inflammatory biomarkers. We included 93 Sudanese and 480 Swedish SLE patients. Serum levels of autoantibodies against dsDNA, Sm, the Sm/U1RNP complex, U1RNP, SSA/Ro52, SSA/Ro60, SSB/La, ribosomal P, PCNA and histones were quantified with a bead-based multiplex immunoassay. In the Swedish cohort also anti-nucleosome antibodies were investigated. Relative levels of 73 plasma biomarkers were determined with Proximity Extension Assay technique or ELISA. Adjusted p values were considered significant when <0.05.

Results Among Sudanese patients, levels of 5/73 biomarkers showed significant associations to ANA-associated antibodies. Anti-histone antibodies showed the strongest positive correlations with interferon-inducible factors MCP-1 and IP-10, and with MCP-3 and S100A12, and negative correlation with stem cell factor. Also anti-dsDNA antibodies associated with MCP-3, IP-10 and S100A12, but when combined in the same regression model, anti-dsDNA associations but not anti-histone lost significance.

Validation analyses among Swedish patients for MCP-1, IP-10, SA100A12 also demonstrated significantly stronger associations to anti-histone and anti-nucleosome antibodies respectively, compared to anti-dsDNA and other ANA specificities, and in combined regression models, anti-histone/

nucleosome showed the strongest associations. When excluding anti-histone or anti-nucleosome positive patients, the associations between interferon-inducible factors MCP-1/IP-10 and anti-dsDNA and were lost. In contrary, when excluding anti-dsDNA positive patients, associations with anti-histone and anti-nucleosome respectively remained significant. SA100A12 associations with anti-dsDNA antibodies remained significant after exclusion of anti-histone positive patients but lost significance when excluding anti-nucleosome positive patients.

Conclusions Levels of mainly IFN-induced inflammatory biomarkers correlate stronger with anti-histone and anti-nucleosome antibodies compared to other ANA specificities including anti-dsDNA. Our results suggest that autoantibodies against DNA-complexes or DNA-associated proteins rather than anti-dsDNA induce the interferon signature in SLE.

LP-203 THE NEW MARKERS OF SYSTEMIC LUPUS ERYTHEMATOSUS ACTIVITY: FOCUS ON INTERLEUKIN (IL)-1B AND SOLUBLE IL-2 RECEPTOR

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Background Systemic lupus erythematosus (SLE) is a systemic autoimmune disease with unknown etiology, characterized by the hyperproduction of autoantibodies to various components of the cell nucleus and the resulting immune-inflammatory damage to tissues. Current trends of personalization therapy require the search for new serum markers, the production of which reflects aberrant activation of the immune system with further formation of autoimmunity. These are cytokines, chemokines and their receptors. Our aim was to determine the levels of interleukin (IL)-1b and soluble IL-2 receptor (sIL-2R) in patients with SLE, to evaluate their association with clinical and laboratory disease manifestations.

Methods The study included 26 patients (21 women, 5 men) with a diagnosis of SLE meeting the criteria of SLICC 2012 and EULAR/ACR 2019. The mean age of the patients was 33 ±11 years and the median disease duration was 14 [4;144] months. Examination of patients included standard laboratory and instrumental diagnostics. Disease activity was assessed using the SLEDAI-2K index. Serum levels of IL-1b and sIL-2R were determined by enzyme immunoassay (Invitrogen, Australia).

Results In the study cohort median IL-1b and sIL-2R levels were 3,3 [2,5;4,6] ng/mL and 0,0065 [0,005;0,008] pg/mL, respectively. Only negative correlation of IL-1b level with glomerular filtration rate was found (R=-0,48, p<0,01). sIL-2R level was associated with SLEDAI-2K (R=0,53, p<0,005), anti-dsDNA (R=0,55, p<0,003), C3 (R=-0,56, p<0,003) and ferritin level (R=0,47, p<0,05), CRP (R=0,45, p<0,002), urinary casts (R=0,46, p<0,01), leukocyturia (R=0,42, p<0,03). There were no statistically significant differences in the concentrations of both studied immunological markers between patients with lupus nephritis (LN) (n=18) and without LN (n=8).

Conclusions The concentration of sIL-2R correlates with laboratory indicators of SLE, SLEDAI-2K and urine sediments, suggesting its promising potential for SLE activity evaluation.