there is an urgent need for non-invasive alternative biomarkers that can facilitate LN class diagnosis. Such biomarkers will be very useful in guiding intervention strategies to mitigate or treat patients with LN. The current study aims to explore new biomarker candidates for non-invasive diagnosis of LN and explore the pathogenic mechanisms that contribute to renal injury.

Materials and Methods A metabolomics approach using LC-QTOF-MS in both positive and negative electrospray ionization (ESI) modes and GC-QTOF-MS was developed for comparison of urine metabolic profile of 23 LN patients, 16 SLE patients, and 10 healthy controls (HCs). Differential metabolites were evaluated with univariate (UVA) and multivariate (MVA) analysis using a nonparametric t test, principal component analysis (PCA) and orthogonal partial least squares regression (OPLS-DA).

Results Both UVA and MVA showed a clear discrimination in the urinary metabolome between LN, SLE and HCs. The significant altered metabolites between LN and SLE correspond mainly to fatty acyls, amino acids, bile acids in particular methylglutamic acid, monopalmitin methyl-L-proline, 3-oxo-4-pentenoic acid, glutaric acid, 3-hydroxyglutaric acid, citraconic acid, glutamine, glycocholic acid and ureidoisobutyric acid. Analysis of metabolic pathways shows disturbances in biosynthesis of alanine, aspartate and glutamate metabolism, citrate cycle (TCA cycle) and glutamine and glutamate metabolism.

Conclusions The urinary metabolome of SLE and LN patients made it possible to determine metabolic alterations and discriminate LN patients from SLE patients. If confirmed in larger studies, these urine metabolites may serve as biomarkers to help discriminate between SLE with and without renal involvement.

PO.1.8 DISTINCT TRANSCRIPTOMIC SIGNATURE OF PERIPHERAL BLOOD IN NEUROPSYCHIATRIC LUPUS

[1]D Nikolopoulos*, [1]A Filia, [1]K Katsiki, [1]T Manolakou, [2]A Pieta, [2]N Kapsala, [3]G Bertsias, [2]A Fanouriakis, [2]D Boumpas. *[1]Laboratory of Autoimmunity and Inflammation, Biomedical Research Foundation of the Academy of Athens ~ Greece; [2]Rheumatology and Clinical Immunology Unit, 'Attikon' University Hospital, National and Kapodistrian University of Athens ~ Greece; [3]Rheumatology, Clinical Immunology and Allergy, University Hospital of Heraklion ~ Greece*

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Purpose We sought to identify distinct blood transcriptomic signatures of NPSLE patients that could serve as potential biomarkers and therapeutic targets.

Methods NPSLE was defined as patients with primary neuropsychiatric events (attributed to SLE) using a combination of multidisciplinary physician judgment with attribution models. Patients without neuropsychiatric events or secondary NPSLE (neuropsychiatric manifestations not attributed to SLE) were classified as non-NPSLE. Diagnosis of SLE was established by the Systemic Lupus Erythematosus International Collaborating Clinics (SLICC) 2012 criteria. RNA-sequencing was performed in peripheral blood from 172 individuals (54 NPSLE, 94 non-NPSLE and 24 healthy controls). Relative expression levels of transcripts and differentially expressed genes (DEGs) (FC >1.5, FDR <0.2) were calculated. Gene set enrichment analysis (GSEA; Preranked) and Gene ontology (GO; gprofiler) analyses were performed in RNA datasets.

Results Comparison of NPSLE with healthy controls revealed 103 DEGs mainly involved in inflammatory pathways (leukocyte cell-cell adhesion, regulation of leukocyte proliferation, neutrophil aggregation, complement and coagulation cascades, Toll-like receptor binding, NF-kappa B signaling pathway) suggesting that systemic inflammation is a key component in NPSLE pathogenesis. Comparison of NPSLE with non-NPSLE patients by GSEA analysis (FDR<0.25) revealed angiogenesis (FGFR1, LPL, PGLYRP1), complement (C3, ITGAM, CASP7), coagulation (VWF, ADAM9, CAPN2) G2M checkpoint (CHEK1, MKI67, CDKN3), MYC targets (XRCC6, PCNA, ILF2), E2F targets (CDK1, CKS1B, SMC3), estrogen response (MYB, CKB, SLC1A4), neutrophil degranulation (TNFAIP6, MMP8, LCN2) and PPAR signaling pathway (DBI, LPL, FABP5) being significantly enriched in NPSLE.

Conclusions NPSLE patients exhibit distinct transcriptomic signature compared to SLE patients without NP events. These data could facilitate the development of novel biomarkers and therapeutic targets.

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PO.1.9 SERUM SPHINGOLIPIDS AS A POTENTIAL BIOMARKER IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

[1]JW Kim, [1]CH Suh*, [2]SH Kim, [3]SJ Hong. *[1]Ajou University School of Medicine ~ Suwon ~ Korea, Republic of; [2]Keimyung University College of Medicine ~ Daegu ~ Korea, Republic of; [3]Kyung Hee University Hospital ~ Seoul ~ Korea, Republic of*

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Purpose Sphingolipids, an essential signaling molecules for the biological and structural functions of cells, are increasingly recognized as playing an important signaling role in the pathophysiology of chronic inflammatory diseases. We hypothesized that the pathogenesis of systemic lupus erythematosus (SLE), a chronic autoimmune disease, is related to altered composition and dysregulation of sphingolipids.

Methods We performed liquid chromatography tandem mass spectrometry to evaluate the levels of sphingolipids in plasma from 38 women with SLE, including 11 lupus nephritis, and 30 controls. The receiver operating characteristic curve (ROC) was analyzed to calculate the area under the curves (AUC) to determine whether sphingolipids can be efficiently used to diagnose SLE. Further, Pearson's correlation coefficient was used to analyze the correlation between sphingolipids and the disease activity markers.

Results The mean age of SLE patients was 44.5 years and the mean disease duration was 110.7 months. The levels of serum ceramide (Cer) and Cer to sphingosine-1-phosphate (S1P) ratio subspecies were increased in patients with SLE, while the levels of sphingomyelins were decreased compared to the controls. The ratio of Cer16:0 to S1P showed especially strong increments in patients with lupus nephritis, and the AUC value for discriminating lupus nephritis from controls was 0.739 (95% confidence interval, 0.581–0.898). In addition, their levels were associated with disease duration, anti-double stranded DNA antibody, SLE disease activity index 2000, and Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index.

Abstract PO.1.9 Table 1 Sphingolipid profiles in patients with systemic lupus erythematosus and controls

Sphingolipids (ng/mL)	SLE (n = 27)	LN (n = 11)	HC (n = 30)	p-value[1]	p-value[2]
S1P	707.44 ± 93.09	644.89 ± 114.86	710.55 ± 119.28	0.208	0.380
Sphingosine	3.92 ± 2.35	2.7 ± 1.02	3.25 ± 1.56	0.155	0.680
Cer14:0	7.04 ± 2.31	7.86 ± 1.91	7.07 ± 1.95	0.512	0.671
Cer16:0	184.05 ± 47.86	198.17 ± 33.24	177.86 ± 35.79	0.372	0.140
Cer18:0	98.96 ± 35.17	106.09 ± 27.83	94.02 ± 34.67	0.591	0.081
Cer18:1	18.05 ± 6.33	20.83 ± 5.81	18.9 ± 6.55	0.479	0.649
Cer20:0	116.7 ± 34.43	125 ± 30.49	120.31 ± 29.12	0.754	0.319
Cer24:0	2,197.34 ± 706.74	1,977.69 ± 545.01	2,314.07 ± 569.7	0.313	0.145
Cer24:1	770.97 ± 217.36	795.61 ± 149.6	720.48 ± 155.08	0.406	0.387
SM(d18:0/16:0)	25,902.07 ± 6,263.2	26,625.82 ± 4,281.66	27,659.76 ± 4,922.28	0.474	0.583
SM(d18:0/18:0)	5,894.02 ± 1,498.08	6,290.09 ± 1,070.86	6,554.73 ± 1,498.31	0.231	0.140
SM(d18:0/18:1)	58,766.05 ± 12,976.89	62,823.39 ± 11,531.87	63,925.33 ± 11,869.54	0.277	0.546
SM(d18:0/24:0)	17,126.86 ± 4,263.68	16,441.45 ± 5,358.13	19,453.68 ± 4,611.38	0.081	0.053
SM(d18:0/24:1)	34,201.36 ± 9,038.26	34,652.83 ± 6,113.78	34,414.91 ± 7,179	0.986	0.934
Cer14/S1P	0.010 ± 0	0.012 ± 0	0.010 ± 0	0.110	**0.031**
Cer16/S1P	0.27 ± 0.09	0.32 ± 0.09	0.26 ± 0.06	**0.027**	**0.019**
Cer18/S1P	0.14 ± 0.06	0.17 ± 0.07	0.13 ± 0.05	0.189	0.107
Cer18:1/S1P	0.03 ± 0.01	0.03 ± 0.01	0.03 ± 0.01	0.209	0.519
Cer20/S1P	0.17 ± 0.05	0.2 ± 0.07	0.17 ± 0.05	0.215	0.283
Cer24/S1P	3.12 ± 1	3.15 ± 1.14	3.35 ± 1.06	0.691	0.198
Cer24:1/S1P	1.11 ± 0.34	1.28 ± 0.37	1.04 ± 0.27	0.111	**0.031**

LN; lupus nephritis, HC; healthy control, Cer; ceramide, SM; sphingomyelin, SIP; sphingosine-1-phosphate
[1]SLE+LN vs. HC, [2]LN vs. HC. Bold values indicate significant P value.

Conclusions Serum sphingolipids can be a good candidate for SLE diagnostic markers, and in particular, Cer16/S1P has the best ability to distinguish against lupus nephritis.

PO.1.10 MULTICENTRE STUDY IN SLE PATIENTS WITH AND WITHOUT RENAL INVOLVEMENT BY LABEL FREE PROTEOMIC ANALYSIS OF 24H URINE

[1]N Rivera*, [2]E Ruiz, [3]J Calvo, [4]E Aurrecoechea, [4]L Riancho, [5]A De Diego-Sola, [6]M Diaz, [2]E Galindez, [1]O Fernandez, [1]I Torre, [1]E Cuende, [1]J Blanco, [1]A Intxaurbe, [1]R Exposito, [1]C Garcia, [1]L Vega, [2]M Enjuanes, [1]M Allande, [7]F Elortza, [7]I Iloro, [7]M Azkargorta, [2]M García-Vivar. *[1]ISS BIOCRUCES BIZKAIA ~ BARAKALDO ~ Spain; [2]Basurto University Hospital ~ Bilbao ~ Spain; [3]Araba University Hospital ~ Vitoria ~ Spain; [4]Sierrallana Hospital ~ Torrelavega ~ Spain; [5]Donostia University Hospital ~ Donostia ~ Spain; [6]Fundació PuigVert ~ Barcelona ~ Spain; [7]CIC bioGUNE ~ DERIO ~ Spain*

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Background Lupus nephropathy (LN) is an important cause of morbidity and mortality in patients with Systemic Lupus Erythematosus (SLE). Considering that renal biopsy is a specialized technique and not risk free, a proteomics study is proposed to determine biomarkers that may help us to differentiate patients diagnosed with SLE with and without renal involvement.

Abstract PO.1.10 Figure 1