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

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10.1136/lupus-2022-elm2022.44

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

Methods Prospective and multicentric study of proteomics was conducted in 24-hour urine from SLE patients with and without renal involvement, by label free nLC MS/MS analysis.

Results 124 patients were recruited from 5 centers: 49 patients with SLE and renal involvement and 73 patients with SLE without renal involvement. There were no differences between groups according to race, gender and age (Table 1).

A total of 718 proteins (identified with at least two peptides with a FDR<1%) were quantified and further considered in the analysis. The Student's T-test analysis reflected the differential presence of 518 proteins ($p<0.01$) between patients with and without renal involvement, being 58 more abundant in the urine of the patients with renal damage, whereas 460 showed the opposite pattern. Two diagrams (diagram 1 & 2) by biological process and protein class, show the results.

Conclusions In this multicentric study, a different protein pattern in urine (over or under expression) is observed between patients with and without renal involvement. It is necessary to continue with the study of the results in the context of cell biology, to know the basis of the deregulation of the proteins found among these groups of patients. On the other hand more studies are needed to know if proteomics analysis of urine could serve as diagnostic/prognostic tool of lupus patients with and without renal involvement.

PO.1.12 TRANSCRIPTOME PROFILING AND AUTOIMMUNITY-RELATED SEROLOGICAL MARKERS IDENTIFY TP53 AND C3AR AS DRUG TARGETS IN NEUROPSYCHIATRIC SYSTEMIC LUPUS ERYTHEMATOSUS

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10.1136/lupus-2022-elm2022.45

Purpose Involvement of the nervous system is a common but poorly understood manifestation of systemic lupus erythematosus (SLE), termed neuropsychiatric SLE (NPSLE). Although studies have reported varying prevalence estimates, NPSLE affects at least 20% of patients with SLE within the first years of the disease course. The management of NPSLE is poorly optimised and specific treatment is lacking. The aim of this study was to investigate expression quantitative trait loci (eQTLs), the transcriptome, and autoimmunity-related cytokines and autoantibodies in patients with central nervous system (CNS) lupus to gain insights into underlying genetics and biologic mechanisms towards identification of novel drug targets.

Methods We analysed differentially expressed genes (DEGs), pathways and their druggability via the Drug Gene Interaction database (DGIdb) in active CNS lupus (n=26) versus healthy controls (HC; n=497), and eQTLs in active or past CNS lupus (n=53), based on validated (identified in two independent SLE populations) DEGs in SLE (n=350) versus HC (n=497), in whole blood collected within the frame of the European PRECISESADS consortium. CNS lupus was defined according to SLE Disease Activity Index 2000 (SLEDAI-2K) CNS items or by CNS manifestations such as chorea, acute confusional state, transverse myelitis, and aseptic meningitis in the absence of predisposing conditions unrelated to SLE. Genome-wide RNA-sequencing and genotyping was previously performed by Illumina assays, and serum levels of 17 cytokines were analysed using a Luminex assay and ELISA (Barturen et al. 2021).

Results Among 5631 significant and validated DEGs in active CNS patients compared with HC, 1922 unique DEGs were tagged to 21 and 176 significant KEGG and Reactome pathways, respectively. Pathways included 'Interferon signalling', 'TNF signalling' and 'Toll-like Receptor Cascades'. The pathways included 29 of 59 DEGs with a fold change (FC) <0.66 or >1.5, 6 genes from 14 significant cis-eQTLs and 10 genes from 22 trans-eQTLs, and 2 genes from 8 cytokines that differed significantly between active CNS lupus and HC. These genes could be targeted by 496 different drugs, with the Bruton tyrosine kinase (BTK) inhibitor ibrutinib and the anti-CD20 B cell depleting monoclonal rituximab with ability to interfere with tumour protein P53 (TP53) activity, and a complement C3a Receptor (C3aR) antagonist being of particular interest.

Conclusions Integrated multilevel omics analysis revealed a set of enriched pathways of potential interest for future drug investigation in CNS lupus, including BTK and C3aR inhibition, and B cell depletion.

PO.1.13 PLASMA AND CEREBROSPINAL FLUID NEUROFILAMENT LIGHT CONCENTRATIONS REFLECT NEURONAL DAMAGE IN SYSTEMIC LUPUS ERYTHEMATOSUS

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10.1136/lupus-2022-elm2022.46

Purpose Neuronal damage in systemic lupus erythematosus (SLE) is common, but the extent and mechanisms are unclear. Neurofilament light (NfL) concentrations rise in plasma and cerebrospinal fluid (CSF) during neuronal damage in various neurological disorders. In this cross-sectional study, plasma and CSF concentrations of NfL were explored as a marker of neuronal damage in SLE.

Methods 72 consecutive SLE out-patients and 26 healthy controls, all female, aged <55 years, underwent magnetic resonance imaging (MRI) and neurocognitive testing. NfL concentrations in plasma from all individuals and in CSF from 32 patients were measured with single-molecule array technology. Patients were assessed by a rheumatologist and neurologist to define neuropsychiatric involvement (NPSLE) according to three attribution models: SLICC A, SLICC B and ACR.