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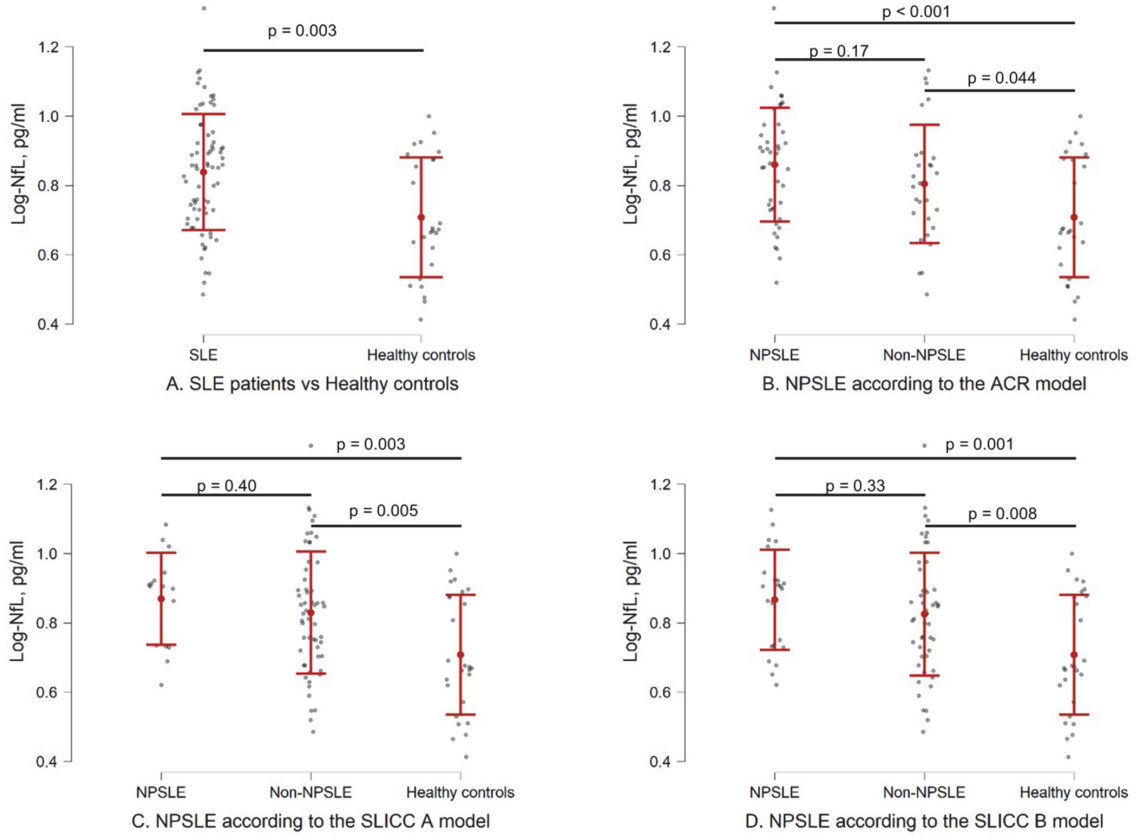
Purpose Neuronal damage in systemic lupus erythematosus (SLE) is common, but the extent and mechanisms are unclear. Neurofilament light (NfL) concentrations rise in plasma and cerebrospinal fluid (CSF) during neuronal damage in various neurological disorders. In this cross-sectional study, plasma and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



Abstract PO.1.13 Figure 1

Results Plasma and CSF NfL concentrations correlated strongly (r=0.72, p<0.001). Both NPSLE and non-NPSLE patients in all attribution models had higher plasma NfL concentrations compared with healthy controls (log-NfL, pg/ml, mean (SD); healthy controls (0.71 (0.17)); SLICC A model: NPSLE (0.87 (0.13), p=0.003), non-NPSLE (0.83 (0.18), p=0.005); SLICC B model: NPSLE (0.87 (0.14), p=0.001), non-NPSLE (0.83 (0.18), p=0.008); ACR model: NPSLE (0.86 (0.16), p<0.001), non-NPSLE (0.81 (0.17), p=0.044), see Figure 1). Plasma and CSF NfL concentrations did not differ between NPSLE and non-NPSLE patients. Higher plasma NfL concentrations correlated with larger CSF volumes on MRI (r=0.34, p=0.005), and was associated with poorer cognitive performance in the domains of simple attention, psychomotor speed and verbal memory. SLICC/ACR-Damage Index ≥1 was independently associated with higher plasma NfL concentrations (β=0.074, 95% CI 0.004–0.14, p=0.038). Higher plasma creatinine concentrations, anti-dsDNA-positivity, low complement C3 levels, or a history of renal involvement were associated with higher plasma NfL concentrations (β=0.003, 95% CI 0.001–0.006, p=0.009; β=0.072, 95% CI 0.005–0.14, p=0.031; β=0.077, 95% CI 0.009–0.15, p=0.027; β=0.069, 95% CI 0.001–0.14, p=0.047, respectively).

Conclusions Higher plasma NfL concentrations in NPSLE and non-NPSLE patients may indicate a higher degree of neuronal damage in SLE in general, corresponding to cognitive impairment and organ damage development. Furthermore, our results may indicate a higher degree of neuronal breakdown in patients with active SLE, also without overt clinical symptoms. NfL may serve as an indicator of neuronal damage in SLE in further studies.

PO.1.14 EVALUATION OF COGNITIVE IMPAIRMENT IN SLE – A COMPARISON OF TWO ASSESSMENT TOOLS

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Background, aims Cognitive impairment is estimated to occur in 10–30% of systemic lupus erythematosus (SLE) patients. Its screening and early recognition is not well established in routine clinical care. Assessment tools for common types of dementia are insufficient to detect early signs of cognitive dysfunction, furthermore, few tests have been studied specifically in SLE patients to screen and follow cognitive functions.

The aim of this study was to evaluate the efficacy of Quick mild cognitive impairment screen (Qmci) and the Montreal Cognitive Assessment (MoCA) to find a brief screening tool for the everyday practice. Furthermore, our aim was to analyse which cognitive functions are mostly affected in SLE patients compared to healthy controls to detect mild cognitive impairment early, before it progresses to dementia.

Methods We enrolled consecutive SLE patients aged < 65 years who met the Systemic Lupus International Collaborating Clinics (SLICC) 2012 classification criteria. Disease activity was measured by SLEDAI-2K. We evaluated the patients' cognitive function with the MoCA and Qmci tests. We recorded the patients' demographic, clinical, immunoserological parameters and data about education, social and health habits. We