O16 PQTL ANALYSIS OF FICOLIN-3 ACTIVITY REVEALS A LINK BETWEEN THE LECTIN PATHWAY OF COMPLEMENT AND HEMATOLOGICAL DISEASE MANIFESTATIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Objective The complement system plays a central role in the pathogenesis of Systemic Lupus Erythematosus (SLE), but most studies have focused on the classical pathway. Ficolin-3 is the main initiator of the lectin pathway of complement in humans, but its role in systemic autoimmune disease has not been conclusively determined. To address these questions, we performed a protein quantitative trait locus (pQTL) analysis to interrogate the contribution of ficolin-3 to SLE risk and disease manifestations.

Methods Ficolin-3 activity was measured in serum samples from Swedish SLE patients (n = 786) and controls matched for age and sex (n = 566). Genetic variants in an extended 300 kb genomic region spanning the *FCN3* gene encoding ficolin-3 were analyzed for their association with ficolin-3 activity and SLE manifestations in a Swedish multicenter cohort (n = 985).

Results 132 single nucleotide variants in the *FCN3* gene region were significantly associated with ficolin-3 activity in the pQTL analysis. Significant pQTLs mapped to an extended block of DNA in high linkage disequilibrium upstream of the *FCN3* gene, and were associated with low ficolin-3 activity in serum in SLE patients but not in controls. Patients carrying the lead pQTL variant associated with low ficolin-3 activity had a lower frequency of hematological disease (OR 0.67, p = 0.018) and lymphopenia (OR 0.63, p = 0.031) and fewer autoantibodies (p = 0.0019). In contrast, genetic variants in the *FCN3* gene were not associated risk to develop SLE. In agreement with the genetic data, patients with ficolin-3 activity in the highest tertile showed an inverse phenotype compared to pQTL carriers and had increased rates of hematological disease (OR 1.4, p = 0.078) and lymphopenia (OR 1.6, p = 0.039), and showed a strong enrichment in an SLE cluster defined by anti-Sm/DNA/nucleosome antibodies (OR 3.0, p <0.001).

Conclusion Overall, our results provide genetic and biochemical evidence that implicate the lectin pathway in hematological SLE manifestations. We also identify activation of the lectin pathway through ficolin-3 as a factor that contributes to the autoantibody response in SLE.

O17 SLESIS-R: AN IMPROVED SCORE FOR PREDICTION OF SERIOUS INFECTION IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS, DEVELOPED FROM RELESSER PROSPECTIVE DATABASE COHORT

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Objective Patients with Systemic lupus erythematosus (SLE) have a not uniform increased risk of serious infection. It is important to estimate the infection risk and balance the immunosuppression and infection risks in practice, but there is no evidence-based tool available to do it. SLESIS score, one score for prediction of severe infection, was previously developed by our group and validated in an external cohort.[1] The original score incorporated up to 7 predictors and only a moderate performance of SLESIS score was observed, with AUC of 0.633. The objective of our study was to improve the SLESIS score both, as a predictor of infection and in terms of feasibility.

Methods We used data from the prospective phase of RELESSER (RELESSER-PROS), the SLE register of the Spanish

Abstract O17 Table 1 SLESIS-R index calculator

Predictor	Score
Age (years) ≥60	4
Previous SLE-related hospitalization	4
Previous serious infection	4
GC doses	
>5 mg and <10 mg	2
≥10 mg and <30 mg	2
≥30 mg	5

SLESIS-R: Systemic Lupus Erythematosus Infection Score-Revised; SLE: systemic lupus erythematosus; GC: glucocorticoids

Society of Rheumatology. A multivariable logistic model was constructed taking into account the variables already forming the SLESIS score, plus all other potential predictors identified in a literature review. Performance was analyzed using the C statistic and the area under the ROC (AUROC). Internal validation was carried out using a 100-sample bootstrapping procedure. OR were transformed into score items, and the AUROC was used to determine performance.

Results A total of 1459 patients who had completed 1 year of follow-up were included (mean age, 49 ± 13 years; 90% females). Twenty-five (1.7%) had experienced ≥1 severe infection. According to the adjusted multivariate model, severe infection could be predicted from 4 variables: age (years) ≥60, previous SLE-related hospitalization, previous severe infection, and glucocorticoid dose. A score was built from the best model (table 1). AUROC:0.861 (0.777–0.946). The cut-off chosen was ≥6, which exhibited an accuracy of 85.9% and a positive LR of 5.48.

Conclusions SLESIS-R is an accurate and feasible instrument for predicting infections in SLE patients. SLESIS-R could help to make informed decisions on the use of immunosuppressants and the implementation of preventive measures.

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O18 DATA-DRIVEN CLUSTERING OF CEREBROSPINAL FLUID PROTEOME REFLECTS CLINICAL PHENOTYPES OF SYSTEMIC LUPUS ERYTHEMATOSUS

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Objective Neuropsychiatric (NP) symptoms are frequent in patients with systemic lupus erythematosus (SLE) and signs of neuronal damage can be present in patients without evident NP involvement. The cerebrospinal fluid (CSF) protein patterns may reveal insights to the pathogenesis of NPSLE. We applied a data-driven approach to investigate the clinical differences in patients with SLE, clustered by their CSF proteomic profile. In addition, we explored the association between groups of proteins and clinical and serological data.

Methods CSF samples from a cross sectional cohort of 29 female outpatients recruited irrespectively of disease activity and organ involvement, were analyzed using label-free quantification liquid chromatography tandem mass spectrometry. Hierarchical clustering of proteomic data was used to identify sample clusters and clusters were analyzed for variance of clinical traits using Kruskal-Wallis and Wilcoxon tests. Proteins were clustered in modules using Weighted Gene Co-expression Correlation Network Analysis (WGCNA). Protein modules were analyzed for correlation to clinical traits using Pearson correlation coefficient.

Results Patient cluster 1 showed highest frequency of nephritis, depression and cognitive impairment. Cluster 2 was characterized by alopecia, SSA-antibodies, and low frequency of cognitive impairment. Cluster 3 had a clinical profile of autonomic neuropathy, lupus headache and increased neurofilament light concentrations in CSF. The protein modules (M1-M6) were characterized by nervous tissue proteins (M1), lipid lifecycle proteins (M2), macrophage derived proteins (M3), plasma proteins (M4), immunoglobulins (M5), intracellular metabolic proteins (M6). Modules 1 and 2 were associated with nephritis, depression, longer disease duration and cognitive impairment, and this pattern was most pronounced in patient cluster 1. The opposite clinical profile was associated with M4 and M5, which showed inverse correlation to cognitive impairment and brain atrophy and was most distinct in patient cluster 2.

Conclusion Data-driven clustering of patients using their CSF proteome forms subgroups reflecting clinical phenotypes of SLE. Two clinical phenotypes appear, where age of disease onset, level of disease severity, renal involvement and degree of neuronal damage differentiates the phenotypes. Variances in CSF proteomic patterns may represent differences in the SLE disease process.

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O19 CHATSLE – CONSULTING CHATGPT FOR 100 FREQUENTLY ASKED LUPUS QUESTIONS

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Objective Lupus is a rare and complex disease that affects almost all aspects of life. Inevitably, patients are constantly confronted with questions about their disease. Nevertheless,