Disclosure of Interests: Carmen Álvarez-Reguera: None declared, Jorge Javier Gaitán-Valdizán: None declared, Raúl Fernández-Ramón: None declared, Rosalía Demetrio-Pablo: None declared, José Luis Martín-Varillas: None declared, Lara Sanchez-Bilbao: None declared, David Martínez-López: None declared, Iñigo González-Mazón: None declared, Miguel A. González-Gay Speakers bureau: Abbvie, Pfizer, Roche, Sanofi and MSD., Grant/research support from: Abbvie, MSD, Janssen and Roche., Ricardo Blanco Speakers bureau: Abbvie, Pfizer, Roche, Bristol-Myer, Janssen, Lilly and MSD., Grant/research support from: Abbvie, MSD and Roche.

DOI: 10.1136/annrheumdis-2021-eular.1930

POS0741 **HISTOPATHOLOGIC PATTERNS OF LUPUS NEPHRITIS PREDICT THE RISKS OF MORTALITY: A SINGLE-CENTER RETROSPECTIVE STUDY**

Y. W. Liao¹, W. T. Hung¹, Y. M. Chen¹, C. W. Hsieh¹, T. Y. Hsieh¹, Y. H. Chen¹, W. N. Huang¹. ¹Taichung Veterans General Hospital, Division of Allergy, Immunology and Rheumatology, Taichung, Taiwan, Republic of China

Background: Lupus nephritis is a significant complication of systemic lupus erythematosus and is associated with increased risks of end-stage kidney disease and mortality.

Objectives: The retrospective observational study aims to investigate which component of the National Institutes of Health activity and chronic indices of lupus nephritis can predict mortality.

Methods: We identified 528 SLE patients with biopsy-proven lupus nephritis between 2006 and 2019. Two patients with class VI lupus nephritis were excluded, and a total of 526 patients were analyzed. Serum creatinine, urine protein-to-creatinine ratio (UPCR), and serologic markers for SLE disease activity were measured at the time of the renal biopsy. The histopathologic findings of renal biopsies were classified by utilizing the International Society of Nephrology/Renal Pathology Society (ISN/RPS) classification.

Results: Among 526 patients enrolled, 64 expired, and 44 were female (68.8%, $p=0.004$). Class IV ($\pm$ V) comprised the most ($n=39$, 60.9%), followed by class V ($n=18$, 29.7%). Lower eGFR was observed in the death group, compared with the survival group (median: 24.7 vs. 80.5, $p<0.001$). There were no significant differences in UPCR and serologic markers for SLE (dsDNA, C3, and C4). Total scores of chronicity index and the scores for each index were higher in the death group. Interestingly, although total scores of activity index in death and survival groups did not differ significantly, the scores for cellular crescents tended to be higher in the death group (1.38 ± 1.77 vs. 0.72 ± 1.24 , $p=0.002$).

In the univariable analysis, age, male sex, eGFR, activity index scores, cellular crescents, chronicity index scores, and all CI components (global obsolete glomeruli, tubular atrophy, interstitial fibrosis, fibrous crescents) and tubulointerstitial nephritis were significantly associated with an increased risk of death. When patient characteristics and NIH activity/ chronicity indices were jointly examined in a multivariable analysis, fibrous crescents were significantly associated with increased risk of death in females (HR 5.23 [95% CI: 1.51, 18.09]) (Table 1). In males, the risks of death increased with cellular crescents (HR 1.73 [95% CI: 1.10, 2.73]) but decreased with global obsolete glomeruli (HR 0.12 [95% CI: 0.02, 0.91]).

Conclusion: In this single-center observational study, fibrous crescents in females and cellular crescents in males were significantly associated with increased risks of mortality.

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Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2006

POS0742 **SCREENING AND BIOINFORMATICS ANALYSIS OF HUB GENES AND PATHWAYS FOR PRIMARY SJÖGREN'S SYNDROME BASED ON GEO DATABASE**

T. Kong¹, S. X. Zhang^{2,3,4}, S. Song^{2,3,4}, X. Sun¹, C. Zheng¹, S. Feng⁵, L. Cheng¹, G. Shi⁶, X. Li^{2,3,4}, P. F. He⁷, Q. Yu^{1,7}. ¹Shanxi Medical University, School of Management, Taiyuan, China; ²The Second Hospital of Shanxi Medical University, Department of Rheumatology, Taiyuan, China; ³Shanxi Li Xiaofeng Medical Groups, Department of Rheumatology, Taiyuan, China; ⁴Ministry of Education, Key Laboratory of Cellular Physiology at Shanxi Medical University, Taiyuan, China; ⁵Shanxi Medical University, School of Humanities and Social Sciences, Taiyuan, China; ⁶Shanxi Medical University, Basic Medical College, Taiyuan, China; ⁷Shanxi Medical University, Institute of Medical Data Sciences, Taiyuan, China

Background: Primary Sjögren's syndrome (pSS) is an autoimmune disease that featured as lymphoplasmacytic infiltration of the exocrine glands leading to sicca symptoms¹. However, its underlying molecular mechanisms remain elusive.

Objectives: This study aims to identify differentially expressed genes (DEGs) and pathways associated with the progression of pSS using bioinformatics analysis and explore its pathogenesis.

Methods: The pSS-associated gene chip data set GSE66795 was obtained from the Gene Expression Omnibus (GEO) database, which included 131 cases of fully-phenotyped pSS patients' whole blood samples and 29 cases of control samples. DEGs were screened Using R software. Online tool Metascape² was used to make Gene Ontology (GO) and KEGG pathway enrichment. The PPI network was performed using String database. Hub genes were identified by Cytoscape.

Results: A total of 108 DEGs were captured, including 101 up-regulated genes and 7 down-regulated genes. GO enrichment showed that these DEGs were primarily enriched in defense response to virus, response to interferon-gamma, regulation of innate immune response, response to interferon-beta, double-stranded RNA binding, response to interferon-alpha. KEGG pathway enrichment analysis showed these DEGs were principally enriched in Influenza A, RIG-I-like receptor signaling pathway, necroptosis, Staphylococcus aureus infection. Finally, 9 hub genes (STAT1, IRF7, OAS2, GBP1, OAS1, IFIT3, IFIH1, OAS3, DDX60) had highest degree value.

Conclusion: The findings identified molecular mechanisms and the key hub genes that may involve in the occurrence and development of pSS.

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Table 1. Logistic regression of predictors for mortality in patients with lupus nephritis

	Univariable			Multivariable (Female)			Multivariable (Male)		
	HR	95% CI	p value	HR	95% CI	p value	HR	95% CI	p value
Age	1.03	(1.01-1.05)	0.002	1.02	(0.98-1.07)	0.267	1.01	(0.95-1.08)	0.670
Male sex	2.10	(1.23-3.55)	0.006						
UPCR	1.02	(0.95-1.09)	0.616						
eGFR	0.97	(0.96-0.99)	<0.001	0.99	(0.96-1.00)	0.183	0.98	(0.96-1.00)	0.086
Activity Index	1.06	(1.01-1.11)	0.027						
Cellular crescents	1.29	(1.12-1.50)	<0.001	1.03	(0.63-1.67)	0.917	1.73	(1.10-2.73)	0.017
Chronicity Index	1.16	(1.07-1.26)	<0.001						
global obsolete glomeruli	1.37	(1.08-1.76)	0.011	1.24	(0.55-2.77)	0.606	0.12	(0.02-0.91)	0.040
Tubular atrophy	1.65	(1.28-2.13)	<0.001	0.41	(0.06-2.82)	0.362	4.77	(0.30-75.32)	0.267
Interstitial fibrosis	1.71	(1.32-2.23)	<0.001	3.70	(0.52-26.24)	0.191	1.37	(0.07-27.40)	0.837
Fibrous crescents	2.38	(1.40-4.03)	0.001	5.23	(1.51-18.09)	0.009	0.00	(0-extremely large)	0.989
Tubulointerstitial nephritis	1.70	(1.03-2.80)	0.037						

Figure 1: (A) Heatmap of the top 50 up-regulated differentially expressed genes: Each small square represents a gene; the color indicates the expression level of the gene. Each column indicates the expression level of the genes in a sample; each row indicates the expression level of a gene in different samples; the right side is the gene name. (B) Volcano map of gene expression: The horizontal axis is $\log_2 FC$, the vertical axis is $\log_{10} \text{adj. P.Val.}$. Each dot represents a gene, blue indicates low expression genes, red indicates high. (C, D) Visualization of GO enrichment analysis and KEGG pathway enrichment analysis. (E, F) PPI network and hub gene identification: Top 9 hub genes in the PPI network were screened by Cytoscape plugin cytoHubba based on their degree value from red (high degree value) to yellow (low degree value).

Acknowledgements: This project was supported by National Science Foundation of China (82001740), Open Fund from the Key Laboratory of Cellular Physiology (Shanxi Medical University) (KLCP2019) and Innovation Plan for Postgraduate Education in Shanxi Province (2020BY078).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2021

POS0743

GENE EXPRESSION MICROARRAY IN LUPUS NEPHRITIS BY BIOINFORMATIC ANALYSIS

C. Wang^{1,2,3}, S. X. Zhang^{1,2,3}, S. Song^{1,2,3}, J. Qiao^{1,2,3}, R. Zhao^{1,2,3}, M. J. Chang^{1,2,3}, Y. Zhang^{1,2,3}, G. Y. Liu¹, P. F. He⁴, X. Li^{1,2,3}. ¹The Second Hospital of Shanxi Medical University, Department of Rheumatology, Taiyuan, China; ²Shanxi Li Xiaofeng Medical Groups, Department of Rheumatology, Taiyuan, China; ³Ministry of Education, Key Laboratory of Cellular Physiology at Shanxi Medical University, Taiyuan, China; ⁴Shanxi Medical University, Medical Data Sciences, Taiyuan, China

Background: Nephritis is one of the predominant causes of morbidity and mortality in patients with lupus^{1,2}. The lack of understanding regarding the molecular mechanisms of lupus nephritis (LN) hinders the development of specific targeted therapy for this progressive disease³.

Objectives: In this study, we use bioinformatics method to analyze the genes involved in regulating the potential pathogenesis of LN.

Methods: The expression profile of LN (GSE104948 and GSE32591) was obtained from the GEO database. GSE104948 was a memory chip, which included 32 LN glomerular biopsy tissues and 3 glomerular tissues from living donors. GSE32591 dataset included 32 LN glomerular biopsy tissues and 15 glomerular tissues from living donors. The Oligo package was used to process the data to obtain the expression matrix files of all the related genes. $P < 0.05$ and $|\log_2(FC)| > 2$ were set as cut-off criteria for the DEGs. Ggplot2, heatmap packages were used to DEGs visualization. Metascape online tool was used to annotating DEGs for Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analysis performed. We used STRING online database to construct protein-protein interaction (PPI) network. Hub genes were identified by Cytoscape.

Results: In differential expression analysis, 357 DEGs were identified, including 248 up-regulated genes and 109 down-regulated genes (Figure 1A, B). GO enrichment showed that these DEGs were primarily enriched in biological

pathways, cell localization and molecular function and revealed that LN-related genes mainly involved in immune response. KEGG pathway annotation enrichment analysis revealed these DEGs were closely associated with Staphylococcus aureus infection, Complement and coagulation cascades (Figure 1D). Fourteen hub genes (IFT3, IRF7, OAS3, GBP2, RSAD2, MX1, IFIT2, IFI6, MX2, ISF15, IFIT1, QAS2, OASL, OAS1) were identified from PPI network (Figure 1C, E).

Conclusion: Illuminating the molecular mechanisms of LN was help for deep understanding of LN.

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Figure 1: (A) Volcano plots of DEGs between LN and healthy controls. Each dot represents a gene, where red represent up-regulated, blue represent down-regulated genes, and black represent genes with no significant difference. (B) Heatmap of the top 50 up-regulated and 50 down-regulated DEGs. Red represent up-regulated, blue represent down-regulated genes. Each row represents the expression level of a gene in a sample, sample grouping information is on the right. Each column represents the expression level of a gene in different samples. (C) Heatmap of enriched terms across input gene lists, colored by p-values. (D, E) PPI network and hub gene identification. Top 14 hub genes in the PPI network were screened by Cytoscape plugin cytoHubba based on their degree value from red (high degree value) to yellow (low degree value).

Acknowledgements: This project was supported by National Science Foundation of China (82001740), Open Fund from the Key Laboratory of Cellular Physiology (Shanxi Medical University) (KLCP2019) and Innovation Plan for Postgraduate Education in Shanxi Province (2020BY078).

Disclosure of Interests: None declared

DOI: 10.1136/annrheumdis-2021-eular.2062

POS0744

A NEGATIVE INTERFERON BIOMARKER CD169 / SIGLEC-1 RULES OUT SYSTEMIC LUPUS ERYTHEMATOSUS

L. Zorn-Pauly¹, A. S. L. Von Stuckrad², J. Klotzsch³, T. Rose¹, T. Kallinich², F. Hiepe¹, P. Enghard⁴, L. Ostendorf⁴, T. Dörner¹, C. Meisel⁵, U. Schneider¹, N. Unterwiesing⁵, G. R. Burmester¹, T. Alexander¹, R. Biesen¹. ¹Charité - Universitätsmedizin Berlin, Rheumatology and Clinical Immunology, Berlin, Germany; ²Charité - Universitätsmedizin Berlin, Pediatric Pneumology and Immunology, Berlin, Germany; ³German Rheumatism Research Centre, Epidemiologic Unit, Berlin, Germany; ⁴Charité - Universitätsmedizin Berlin, Nephrology and Intensive Care Medicine, Berlin, Germany; ⁵Institute for Medical Immunology, Labor Berlin - Charité Vivantes, Immunology, Berlin, Germany

Background: While there have been advances in the therapy of systemic lupus erythematosus (SLE) in recent years, there have been no major new findings in SLE biomarkers [1, 2]. Type I interferon (IFN) plays a pivotal role in the pathogenesis of SLE [3]. In 2008, we first described CD169 / SIGLEC-1 (sialic acid-binding immunoglobulin-like lectin-1), an interferon-induced adhesion molecule on monocytes in SLE patients [4]. For over five years SIGLEC-1 has been routinely assessed in our clinic.

Objectives: To evaluate and compare the diagnostic utility of the type I IFN induced SIGLEC-1 with established biomarkers in the initial diagnosis of the disease.

Methods: We analyzed retrospectively 232 patients who were on suspicion of SLE at Charité University Hospital Berlin between October 2015 and September 2020. Patients underwent full clinical characterization, and biomarkers were