Supplementary Material

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Supplementary Table S1. Main inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
For all patients	**For all patients**

- Age ≥18 years
- Diagnosed according to the prevailing criteria for systemic lupus erythematosus (SLE)
- Informed consent signed
	- Pediatric lupus
	- Drug-induced lupus
	- Severe nephrotic syndrome with proteinuria ≥3.5 g/day
	- Patients with stable doses of prednisone equivalent >15 mg/day for the last 3 months or with IV corticosteroids in the last 3 months
	- Patients under immunosuppressant treatment in the last 3 months prior to recruitment and patients with combined therapy using two or more immunosuppressants:
	  Methotrexate ≥25mg/week
	  Azathioprine ≥2.5mg/kg/day
	  Cyclosporine A >3mg/kg/day
	  Mycophenolate mofetil >2g/day
	- Chronic HBV or HCV infection
	- Patients who are also diagnosed according to the prevailing criteria for one of the following autoimmune diseases:
	  Rheumatoid arthritis (RA)
	  Scleroderma or systemic sclerosis (SSc)
	  Primary Sjögren's syndrome (pSjS)
	  Primary antiphospholipid syndrome (pAPS)
	  Mixed connective tissue disease (MCTD)
	  Patients with undifferentiated connective tissue disease (UCTD) for over 1 year and that do not fulfill the diagnosis of any of the above diseases or SLE

	For controls
	- Individuals on chronic medication - Individuals suffering from any inflammatory autoimmune, allergic or infectious condition, and with a history of autoimmune disease, particularly thyroid disease or other diseases that may modify cellular profiles in blood

Adapted from "Integrative Analysis Reveals a Molecular Stratification of Systemic Autoimmune Diseases." Arthritis Rheum. 2021;73(6):1073-1085. Copyright 2021 by the American College of Rheumatology. Adapted with permission. IV: intravenous, HBV: hepatitis B virus, HCV: hepatitis C virus.

Supplementary Table S2. Modified STROBE statement checklist

Section(s)	Item No	Recommendation	Page No
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4–5
Objectives	3	State specific objectives, including any prespecified hypotheses	5
Methods			
Study design	4	Present key elements of study design early in the paper	5–8
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5–6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	5; Supplementary Material
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5–8
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement).	5–8
Bias	9	Describe any efforts to address potential sources of bias	6–8
Study size	10	Explain how the study size was arrived at (if applicable)	
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6–8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6–8
		(*b*) Describe any methods used to examine subgroups and interactions	7–8

		(*c*) Explain how missing data were addressed	
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	6–8
		(*e*) Describe any sensitivity analyses	
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analyzed	9–10; Supplementary Material
		(c) Use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	9
		(b) Indicate number of participants with missing data for each variable of interest	9; Supplementary Material
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	9-13; Supplementary Material
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9-13; Supplementary Material
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9-13; Supplementary Material
Discussion			
Key results	18	Summarise key results with reference to study objectives	13–22
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	21–22
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	13–22

Generalisability	21	Discuss the generalisability (external validity) of the study results	21–22

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Supplementary Table S3. Renal disease activity in LN subgroups

Target	lo-IFN subgroup N=13	im-IFN subgroup N=9	hi-IFN subgroup N=19	lo-IFN vs im-IFN *p* value	lo-IFN vs hi-IFN *p* value	im-IFN vs hi-IFN *p* value
rSLEDAI-2K	7.38□3.59	6.67□2.00	6.95□3.49	0.822	0.692	0.871

Data are presented as mean (standard deviation). All *p* values are derived from non-parametrical Mann-Whitney *U* tests. Statistically significant *p* values are in bold.

hi: high; IFN: interferon; im: intermediate; LN: lupus nephritis; lo: low; rSLEDAI-2K: renal SLE Disease Activity Index 2000.

Supplementary Table S4. Correlations between serological markers and z-scores of the "B cell" gene module in patients with LN

Serological marker	n	Coefficient	*p* value
anti-MDA IgM	31	0.09	0.612
anti-PC IgM	31	-0.07	0.717
BAFF	28	0.07	0.707
IL-6	28	0.13	0.523
TGF-ß	28	-0.17	0.376
TNF-α	28	0.21	0.282

Spearman's rank correlation coefficients of correlations between levels of different serological markers and Z-scores of the B cell gene module. The total number of patients with available data is indicated. Statistically significant *p* values are in bold. Only comparisons with sufficient numbers of observations (n≥10) are included.

BAFF: B cell activating factor belonging to the tumour necrosis factor family; Ig: immunoglobulin; IL-6: interleukin 6; LN: lupus nephritis; MDA: malondialdehyde; PC: phosphorylcholine; TGF-β: transforming growth factor β; TNF-α: transforming growth factor α.

Supplementary Table S5. Correlations between serological markers and z-scores of the "cell cycle, mitotic phase" gene module in patients with LN

Serological marker	n	Coefficient	*p* value
anti-MDA IgM	31	0.23	0.206
anti-PC IgM	31	0.04	0.850
BAFF	28	-0.13	0.525
IL-6	28	-0.02	0.930
TGF-ß	28	-0.12	0.534
TNF-α	28	-0.11	0.572

Spearman's rank correlation coefficients of correlations between levels of different serological markers and Z-scores of the cell cycle, mitotic phase gene module. The total number of patients with available data is indicated. Statistically significant *p* values are in bold. Only comparisons with sufficient numbers of observations (n≥10) are included.

BAFF: B cell activating factor belonging to the tumour necrosis factor family; Ig: immunoglobulin; IL-6: interleukin 6; LN: lupus nephritis; MDA: malondialdehyde; PC: phosphorylcholine; TGF-β: transforming growth factor β; TNF-α: transforming growth factor α.

Supplementary Table S6. Correlations between serological markers and z-scores of the "CORO1A-DEF6 network" gene module in patients with LN

Serological marker	n	Coefficient	*p* value
anti-MDA IgM	31	0.33	0.067
anti-PC IgM	31	-0.09	0.644
BAFF	28	0.16	0.407
IL-6	28	0.22	0.262
TGF-ß	28	-0.23	0.242
TNF-α	28	0.03	0.890

Spearman's rank correlation coefficients of correlations between levels of different serological markers and Z-scores of the CORO1A-DEF6 network gene module. The total number of patients with available data is indicated. Statistically significant *p* values are in bold. Only comparisons with sufficient numbers of observations (n≥10) are included.

BAFF: B cell activating factor belonging to the tumour necrosis factor family; CORO1A-DEF6: coronin 1A-differentially expressed in FDCP 6 homolog; Ig: immunoglobulin; IL-6: interleukin 6; LN: lupus nephritis; MDA: malondialdehyde; PC: phosphorylcholine; TGF-β: transforming growth factor β; TNF-α: transforming growth factor α.

Supplementary Table S7. Correlations between serological markers and z-scores of the "enriched in antigen presentation (III)" gene module in patients with LN

Serological marker	n	Coefficient	*p* value
anti-MDA IgM	31	0.10	0.575
anti-PC IgM	31	-0.13	0.477
BAFF	28	0.23	0.242
IL-6	28	0.26	0.177
TGF-ß	28	-0.02	0.910
TNF-α	28	0.30	0.115

Spearman's rank correlation coefficients of correlations between levels of different serological markers and Z-scores of the enriched in antigen presentation (III) gene module. The total number of patients with available data is indicated. Statistically significant *p* values are in bold. Only comparisons with sufficient numbers of observations (n≥10) are included.

BAFF: B cell activating factor belonging to the tumour necrosis factor family; Ig: immunoglobulin; IL-6: interleukin 6; LN: lupus nephritis; MDA: malondialdehyde; PC: phosphorylcholine; TGF-β: transforming growth factor β; TNF-α: transforming growth factor α.

Supplementary Table S8. Correlations between serological markers and z-scores of the "enriched in neutrophils (II)" gene module in patients with LN

Serological marker	n	Coefficient	*p* value
anti-MDA IgM	31	-0.10	0.588
anti-PC IgM	31	-0.30	0.101
BAFF	28	0.29	0.139
IL-6	28	0.08	0.674
TGF-ß	28	0.18	0.349
TNF-α	28	0.00	0.996

Spearman's rank correlation coefficients of correlations between levels of different serological markers and Z-scores of the enriched in neutrophils (II) gene module. The total number of patients with available data is indicated. Statistically significant *p* values are in bold. Only comparisons with sufficient numbers of observations (n≥10) are included.

BAFF: B cell activating factor belonging to the tumour necrosis factor family; Ig: immunoglobulin; IL-6: interleukin 6; LN: lupus nephritis; MDA: malondialdehyde; PC: phosphorylcholine; TGF-β: transforming growth factor β; TNF-α: transforming growth factor α.

Supplementary Table S9. Correlations between serological markers and z-scores of the "erythrocytes" gene module in patients with LN

Serological marker	n	Coefficient	*p* value
anti-MDA IgM	31	-0.32	0.082
anti-PC IgM	31	-0.22	0.244
BAFF	28	0.25	0.192
IL-6	28	-0.06	0.750
TGF-ß	28	-0.11	0.587
TNF-α	28	-0.10	0.600

Spearman's rank correlation coefficients of correlations between levels of different serological markers and Z-scores of the erythrocytes gene module. The total number of patients with available data is indicated. Statistically significant *p* values are in bold. Only comparisons with sufficient numbers of observations (n≥10) are included.

BAFF: B cell activating factor belonging to the tumour necrosis factor family; Ig: immunoglobulin; IL-6: interleukin 6; LN: lupus nephritis; MDA: malondialdehyde; PC: phosphorylcholine; TGF-β: transforming growth factor β; TNF-α: transforming growth factor α.

Supplementary Table S10. Correlations between serological markers and z-scores of the "extracellular matrix (I)" gene module in patients with LN

Serological marker	n	Coefficient	*p* value
anti-MDA IgM	31	0.20	0.274
anti-PC IgM	31	0.02	0.921
BAFF	28	0.01	0.974
IL-6	28	-0.01	0.965
TGF-ß	28	-0.16	0.423
TNF-α	28	0.00	0.982

Spearman's rank correlation coefficients of correlations between levels of different serological markers and Z-scores of the extracellular matrix (I) gene module. The total number of patients with available data is indicated. Statistically significant *p* values are in bold. Only comparisons with sufficient numbers of observations (n≥10) are included.

BAFF: B cell activating factor belonging to the tumour necrosis factor family; Ig: immunoglobulin; IL-6: interleukin 6; LN: lupus nephritis; MDA: malondialdehyde; PC: phosphorylcholine; TGF-β: transforming growth factor β; TNF-α: transforming growth factor α.

Supplementary Table S11. Correlations between serological markers and z-scores of the "extracellular region cluster" gene module in patients with LN

Serological marker	n	Coefficient	*p* value
anti-MDA IgM	31	0.03	0.858
anti-PC IgM	31	-0.13	0.477
BAFF	28	0.16	0.404
IL-6	28	0.14	0.479
TGF-ß	28	0.03	0.894
TNF-α	28	0.15	0.453

Spearman's rank correlation coefficients of correlations between levels of different serological markers and Z-scores of the extracellular region cluster gene module. The total number of patients with available data is indicated. Statistically significant *p* values are in bold. Only comparisons with sufficient numbers of observations (n≥10) are included.

BAFF: B cell activating factor belonging to the tumour necrosis factor family; Ig: immunoglobulin; IL-6: interleukin 6; LN: lupus nephritis; MDA: malondialdehyde; PC: phosphorylcholine; TGF-β: transforming growth factor β; TNF-α: transforming growth factor α.

Supplementary Table S12. Correlations between serological markers and z-scores of the "inflammation (IV)" gene module in patients with LN

Serological marker	n	Coefficient	*p* value
anti-MDA IgM	31	-0.11	0.558
anti-PC IgM	31	0.10	0.595
BAFF	28	-0.25	0.201
IL-6	28	-0.11	0.587
TGF-ß	28	0.00	0.998
TNF-α	28	-0.21	0.273

Spearman's rank correlation coefficients of correlations between levels of different serological markers and Z-scores of the inflammation (IV) gene module. The total number of patients with available data is indicated. Statistically significant *p* values are in bold. Only comparisons with sufficient numbers of observations (n≥10) are included.

BAFF: B cell activating factor belonging to the tumour necrosis factor family; Ig: immunoglobulin; IL-6: interleukin 6; LN: lupus nephritis; MDA: malondialdehyde; PC: phosphorylcholine; TGF-β: transforming growth factor β; TNF-α: transforming growth factor α.

Supplementary Table S13. Correlations between serological markers and z-scores of the "inflammation (VI)" gene module in patients with LN

Serological marker	n	Coefficient	*p* value
anti-MDA IgM	31	0.03	0.867
anti-PC IgM	31	-0.22	0.230
BAFF	28	0.26	0.184
IL-6	28	0.26	0.173
TGF-ß	28	0.02	0.927
TNF-α	28	0.20	0.304

Spearman's rank correlation coefficients of correlations between levels of different serological markers and Z-scores of the inflammation (VI) gene module. The total number of patients with available data is indicated. Statistically significant *p* values are in bold. Only comparisons with sufficient numbers of observations (n≥10) are included.

BAFF: B cell activating factor belonging to the tumour necrosis factor family; Ig: immunoglobulin; IL-6: interleukin 6; LN: lupus nephritis; MDA: malondialdehyde; PC: phosphorylcholine; TGF-β: transforming growth factor β; TNF-α: transforming growth factor α.

Supplementary Table S14. Correlations between serological markers and z-scores of the "inositol phosphate metabolism" gene module in patients with LN

Serological marker	n	Coefficient	*p* value
anti-MDA IgM	31	0.08	0.685
anti-PC IgM	31	0.07	0.692
BAFF	28	-0.18	0.359
IL-6	28	-0.05	0.816
TGF-ß	28	0.04	0.853
TNF-α	28	-0.21	0.292

Spearman's rank correlation coefficients of correlations between levels of different serological markers and Z-scores of the inositol phosphate metabolism gene module. The total number of patients with available data is indicated. Statistically significant *p* values are in bold. Only comparisons with sufficient numbers of observations (n≥10) are included.

BAFF: B cell activating factor belonging to the tumour necrosis factor family; Ig: immunoglobulin; IL-6: interleukin 6; LN: lupus nephritis; MDA: malondialdehyde; PC: phosphorylcholine; TGF-β: transforming growth factor β; TNF-α: transforming growth factor α.

Supplementary Table S15. Correlations between serological markers and z-scores of the "interferon" gene module in patients with LN

Serological marker	n	Coefficient	*p* value
anti-MDA IgM	31	0.12	0.513
anti-PC IgM	31	-0.06	0.742
BAFF	28	0.16	0.426
IL-6	28	0.26	0.175
TGF-ß	28	-0.06	0.771
TNF-α	28	0.32	0.100

Spearman's rank correlation coefficients of correlations between levels of different serological markers and Z-scores of the interferon gene module. The total number of patients with available data is indicated. Statistically significant *p* values are in bold. Only comparisons with sufficient numbers of observations (n≥10) are included.

BAFF: B cell activating factor belonging to the tumour necrosis factor family; Ig: immunoglobulin; IL-6: interleukin 6; LN: lupus nephritis; MDA: malondialdehyde; PC: phosphorylcholine; TGF-β: transforming growth factor β; TNF-α: transforming growth factor α.

Supplementary Table S16. Correlations between serological markers and z-scores of the "interferon (II)" gene module in patients with LN

Serological marker	n	Coefficient	*p* value
anti-MDA IgM	31	0.06	0.768
anti-PC IgM	31	-0.20	0.287
BAFF	28	0.26	0.180
IL-6	28	0.36	0.063
TGF-ß	28	0.00	0.993
TNF-α	28	0.41	0.033

Spearman's rank correlation coefficients of correlations between levels of different serological markers and Z-scores of the interferon (II) gene module. The total number of patients with available data is indicated. Statistically significant *p* values are in bold. Only comparisons with sufficient numbers of observations (n≥10) are included.

BAFF: B cell activating factor belonging to the tumour necrosis factor family; Ig: immunoglobulin; IL-6: interleukin 6; LN: lupus nephritis; MDA: malondialdehyde; PC: phosphorylcholine; TGF-β: transforming growth factor β; TNF-α: transforming growth factor α.

Supplementary Table S17. Correlations between serological markers and z-scores of the "MAPK, RAS signalling" gene module in patients with LN

Serological marker	n	Coefficient	*p* value
anti-MDA IgM	31	-0.14	0.440
anti-PC IgM	31	-0.16	0.388
BAFF	28	0.25	0.191
IL-6	28	0.00	0.987
TGF-ß	28	0.20	0.301
TNF-α	28	0.02	0.910

Spearman's rank correlation coefficients of correlations between levels of different serological markers and Z-scores of the MAPK, RAS signalling gene module. The total number of patients with available data is indicated. Statistically significant *p* values are in bold. Only comparisons with sufficient numbers of observations (n≥10) are included.

BAFF: B cell activating factor belonging to the tumour necrosis factor family; Ig: immunoglobulin; IL-6: interleukin 6; LN: lupus nephritis; MAPK: mitogen-activated protein kinase; MDA: malondialdehyde; PC: phosphorylcholine; TGF-β: transforming growth factor β; TNF-α: transforming growth factor α.

Supplementary Table S18. Correlations between serological markers and z-scores of the "monocytes" gene module in patients with LN

Serological marker	n	Coefficient	*p* value
anti-MDA IgM	31	0.07	0.712
anti-PC IgM	31	-0.12	0.532
BAFF	28	0.14	0.480
IL-6	28	0.42	**0.028**
TGF-ß	28	0.07	0.715
TNF-α	28	0.38	0.047

Spearman's rank correlation coefficients of correlations between levels of different serological markers and Z-scores of the monocytes gene module. The total number of patients with available data is indicated. Statistically significant *p* values are in bold. Only comparisons with sufficient numbers of observations (n≥10) are included.

BAFF: B cell activating factor belonging to the tumour necrosis factor family; Ig: immunoglobulin; IL-6: interleukin 6; LN: lupus nephritis; MDA: malondialdehyde; PC: phosphorylcholine; TGF-β: transforming growth factor β; TNF-α: transforming growth factor α.

Supplementary Table S19. Correlations between serological markers and z-scores of the "plasma cells, immunoglobulins" gene module in patients with LN

Serological marker	n	Coefficient	*p* value
anti-MDA IgM	31	0.14	0.461
anti-PC IgM	31	-0.09	0.635
BAFF	28	0.14	0.470
IL-6	28	0.39	0.039
TGF-ß	28	-0.06	0.765
TNF-α	28	0.39	0.041

Spearman's rank correlation coefficients of correlations between levels of different serological markers and Z-scores of the plasma cells, immunoglobulins gene module. The total number of patients with available data is indicated. Statistically significant *p* values are in bold. Only comparisons with sufficient numbers of observations (n≥10) are included.

BAFF: B cell activating factor belonging to the tumour necrosis factor family; Ig: immunoglobulin; IL-6: interleukin 6; LN: lupus nephritis; MDA: malondialdehyde; PC: phosphorylcholine; TGF-β: transforming growth factor β; TNF-α: transforming growth factor α.

Supplementary Table S20. Correlations between serological markers and z-scores of the "platelets" gene module in patients with LN

Serological marker	n	Coefficient	*p* value
anti-MDA IgM	31	-0.51	**0.003**
anti-PC IgM	31	-0.42	**0.019**
BAFF	28	0.29	0.128
IL-6	28	-0.02	0.916
TGF-ß	28	0.14	0.491
TNF-α	28	-0.05	0.791

Spearman's rank correlation coefficients of correlations between levels of different serological markers and Z-scores of the platelets gene module. The total number of patients with available data is indicated. Statistically significant *p* values are in bold. Only comparisons with sufficient numbers of observations (n≥10) are included.

BAFF: B cell activating factor belonging to the tumour necrosis factor family; Ig: immunoglobulin; IL-6: interleukin 6; LN: lupus nephritis; MDA: malondialdehyde; PC: phosphorylcholine; TGF-β: transforming growth factor β; TNF-α: transforming growth factor α.

Supplementary Table S21. Correlations between serological markers and z-scores of the "protein synthesis (I)" gene module in patients with LN

Serological marker	n	Coefficient	*p* value
anti-MDA IgM	31	0.16	0.380
anti-PC IgM	31	0.03	0.865
BAFF	28	0.08	0.692
IL-6	28	0.23	0.235
TGF-ß	28	-0.12	0.553
TNF-α	28	0.18	0.370

Spearman's rank correlation coefficients of correlations between levels of different serological markers and Z-scores of the protein synthesis (I) gene module. The total number of patients with available data is indicated. Statistically significant *p* values are in bold. Only comparisons with sufficient numbers of observations (n≥10) are included.

BAFF: B cell activating factor belonging to the tumour necrosis factor family; Ig: immunoglobulin; IL-6: interleukin 6; LN: lupus nephritis; MDA: malondialdehyde; PC: phosphorylcholine; TGF-β: transforming growth factor β; TNF-α: transforming growth factor α.

Supplementary Table S22. Correlations between serological markers and z-scores of the "regulation of antigen presentation and immune response" gene module in patients with LN

Serological marker	n	Coefficient	*p* value
anti-MDA IgM	31	0.18	0.337
anti-PC IgM	31	-0.01	0.973
BAFF	28	0.05	0.816
IL-6	28	0.13	0.500
TGF-ß	28	-0.18	0.362
TNF-α	28	0.14	0.484

Spearman's rank correlation coefficients of correlations between levels of different serological markers and Z-scores of the regulation of antigen presentation and immune response gene module. The total number of patients with available data is indicated. Statistically significant *p* values are in bold. Only comparisons with sufficient numbers of observations (n≥10) are included.

BAFF: B cell activating factor belonging to the tumour necrosis factor family; Ig: immunoglobulin; IL-6: interleukin 6; LN: lupus nephritis; MDA: malondialdehyde; PC: phosphorylcholine; TGF-β: transforming growth factor β; TNF-α: transforming growth factor α.

Supplementary Table S23. Correlations between serological markers and z-scores of the "regulation of transcription, transcription factors" gene module in patients with LN

Serological marker	n	Coefficient	*p* value
anti-MDA IgM	31	0.21	0.249
anti-PC IgM	31	0.17	0.355
BAFF	28	-0.16	0.413
IL-6	28	-0.17	0.377
TGF-ß	28	-0.13	0.503
TNF-α	28	-0.29	0.130

Spearman's rank correlation coefficients of correlations between levels of different serological markers and Z-scores of the regulation of transcription, transcription factors gene module. The total number of patients with available data is indicated. Statistically significant *p* values are in bold. Only comparisons with sufficient numbers of observations (n≥10) are included.

BAFF: B cell activating factor belonging to the tumour necrosis factor family; Ig: immunoglobulin; IL-6: interleukin 6; LN: lupus nephritis; MDA: malondialdehyde; PC: phosphorylcholine; TGF-β: transforming growth factor β; TNF-α: transforming growth factor α.

Supplementary Table S24. Z-scores of replicated gene modules in patients with LN and anti-βGPI IgG positivity versus negative patients

Gene module	anti-βGPI IgG (+) N=5	anti-βGPI IgG (-) N=26	*p* value
B cell	-1.54 (-2.61−-1.48)	-1.47 (-2.30−-0.32)	0.707
Cell cycle, mitotic phase	-0.23 (-0.86−-0.06)	-0.41 (-0.86−-0.12)	0.788
CORO1A-DEF6 network	-0.35 (-0.37−-0.06)	-0.07 (-0.18−0.02)	0.119
Enriched in antigen presentation (III)	-0.37 (-0.59−-0.17)	-0.39 (-0.53−0.03)	0.452
Enriched in neutrophils (II)	0.17 (-0.14−0.21)	0.06 (-0.08−0.18)	0.872
Erythrocytes	-0.23 (-0.30−0.19)	0.23 (-0.44−0.67)	0.707
Extracellular matrix (I)	-1.42 (-1.43−-1.15)	-0.74 (-1.12−-0.35)	0.060
Extracellular region cluster	-0.28 (-0.42−0.01)	-0.08 (-0.23−0.03)	0.259
Inflammation (IV)	0.25 (-0.11−0.49)	0.24 (-0.01−0.44)	0.872
Inflammation (VI)	0.08 (-0.50−0.34)	0.01 (-0.25−0.20)	1.000
Inositol phosphate metabolism	-0.13 (-0.55−0.68)	-0.05 (-0.38−0.26)	0.830
Interferon	0.76 (0.03−1.71)	1.41 (0.05−2.02)	0.830
Interferon (II)	0.23 (-0.27−0.93)	0.53 (0.24−0.70)	0.591
MAPK−RAS signalling	0.29 (-0.65−0.35)	-0.01 (-0.43−0.33)	0.957
Monocytes	0.38 (0.26−0.86)	0.26 (-0.15−0.92)	0.390
Plasma cells, immunoglobulins	0.04 (-0.24−1.06)	-0.16 (-0.70−0.56)	0.452
Platelets	-0.03 (-0.62−0.23)	0.13 (-0.35−0.65)	0.452
Protein synthesis (I)	-0.78 (-1.17−0.29)	-0.35 (-0.91−0.13)	0.667
Regulation of antigen presentation and immune response	-1.41 (-1.43−-0.86)	-0.73 (-1.26−-0.22)	0.334
Regulation of transcription, transcription factors	-0.82 (-0.92−-0.17)	-0.45 (-0.81−-0.10)	0.629

Data are presented as median (interquartile range). The total number of patients with available data is indicated. All *p* values are derived from non-parametrical Mann-Whitney *U* tests. Statistically significant *p* values are in bold.

βGPI: β_2 glycoprotein I; CORO1A-DEF6: coronin 1A-differentially expressed in FDCP 6 homolog; Ig: immunoglobulin; LN: lupus nephritis; MAPK: mitogen-activated protein kinase.

Supplementary Table S25. Z-scores of replicated gene modules in patients with LN and aCL IgG positivity versus negative patients

Gene module	aCL IgG (+) N=4	aCL IgG (-) N=27	*p* value
B cell	-1.51 (-1.97−-1.05)	-1.71 (-2.36−-0.43)	0.906
Cell cycle, mitotic phase	-0.15 (-0.56−0.16)	-0.43 (-0.87−-0.13)	0.480
CORO1A-DEF6 network	-0.21 (-0.45−-0.04)	-0.09 (-0.20−0.02)	0.289
Enriched in antigen presentation (III)	-0.48 (-0.88−-0.32)	-0.37 (-0.51−0.03)	0.289
Enriched in neutrophils (II)	0.02 (-0.25−0.19)	0.08 (-0.07−0.18)	0.680
Erythrocytes	-0.02 (-0.25−0.41)	0.21 (-0.49−0.65)	0.953
Extracellular matrix (I)	-1.28 (-1.61−-0.97)	-0.74 (-1.15−-0.36)	0.157
Extracellular region cluster	-0.20 (-0.47−0.03)	-0.08 (-0.25−0.02)	0.480
Inflammation (IV)	0.37 (0.16−0.70)	0.18 (-0.07−0.43)	0.377
Inflammation (VI)	-0.21 (-0.66−0.17)	0.02 (-0.24−0.22)	0.517
Inositol phosphate metabolism	0.28 (-0.23−0.78)	-0.07 (-0.39−0.25)	0.377
Interferon	0.39 (-0.01−0.99)	1.49 (0.05−2.12)	0.289
Interferon (II)	-0.02 (-0.29−0.41)	0.54 (0.24−0.73)	0.157
MAPK−RAS signalling	-0.15 (-0.78−0.40)	0.02 (-0.41−0.33)	0.768
Monocytes	0.32 (0.10−0.75)	0.26 (-0.10−0.92)	0.596
Plasma cells, immunoglobulins	-0.10 (-0.38−0.29)	-0.10 (-0.67−0.65)	0.953
Platelets	0.10 (-0.18−0.42)	0.01 (-0.37−0.63)	0.953
Protein synthesis (I)	-0.24 (-0.90−0.32)	-0.44 (-0.93−0.10)	0.860
Regulation of antigen presentation and immune response	-1.14 (-1.61−-0.63)	-0.80 (-1.35−-0.25)	0.517
Regulation of transcription, transcription factors	-0.50 (-0.85−-0.07)	-0.46 (-0.91−-0.13)	0.724

Data are presented as median (interquartile range). The total number of patients with available data is indicated. All *p* values are derived from non-parametrical Mann-Whitney *U* tests. Statistically significant *p* values are in bold.

aCL: anti-cardiolipin; CORO1A-DEF6: coronin 1A- differentially expressed in FDCP 6 homolog; Ig: immunoglobulin; LN: lupus nephritis; MAPK: mitogen-activated protein kinase.

Supplementary Table S26. Z-scores of replicated gene modules in patients with LN and low versus normal/high levels of C3c

Gene module	Low C3c N=10	Normal/high C3c N=21	*p* value
B cell	-1.03 (-2.54−-0.32)	-1.71 (-2.20−-0.68)	0.642
Cell cycle, mitotic phase	-0.47 (-0.88−0.38)	-0.32 (-0.76−-0.12)	0.899
CORO1A-DEF6 network	-0.07 (-0.18−0.10)	-0.12 (-0.28−0.00)	0.422
Enriched in antigen presentation (III)	-0.06 (-0.32−0.17)	-0.43 (-0.59−-0.24)	**0.031**
Enriched in neutrophils (II)	0.17 (0.08−0.20)	-0.03 (-0.14−0.14)	**0.010**
Erythrocytes	-0.24 (-0.50−-0.16)	0.33 (-0.23−0.72)	0.083
Extracellular matrix (I)	-0.52 (-0.79−-0.13)	-1.00 (-1.26−-0.58)	0.083
Extracellular region cluster	-0.01 (-0.12−0.13)	-0.10 (-0.27−-0.02)	0.099
Inflammation (IV)	-0.12 (-0.34−0.17)	0.33 (0.07−0.50)	**0.022**
Inflammation (VI)	0.23 (0.06−0.36)	-0.19 (-0.30−0.11)	**0.004**
Inositol phosphate metabolism	-0.25 (-0.57−0.36)	-0.03 (-0.28−0.28)	0.375
Interferon	1.73 (0.37−2.26)	0.76 (-0.06−1.74)	0.099
Interferon (II)	0.73 (0.38−0.98)	0.44 (-0.09−0.60)	**0.025**
MAPK−RAS signalling	0.29 (-0.13−0.33)	-0.35 (-0.68−0.36)	0.151
Monocytes	0.56 (0.11−1.06)	0.26 (-0.46−0.44)	0.353
Plasma cells, immunoglobulins	0.39 (-0.32−0.81)	-0.23 (-0.81−0.39)	0.205
Platelets	-0.21 (-0.50−0.19)	0.25 (-0.24−0.68)	0.083
Protein synthesis (I)	-0.73 (-1.07−0.11)	-0.18 (-0.90−0.16)	0.526
Regulation of antigen presentation and immune response	-0.99 (-1.16−-0.14)	-0.80 (-1.62−-0.29)	0.583
Regulation of transcription, transcription factors	-0.47 (-0.96−-0.09)	-0.46 (-0.82−-0.20)	0.833

Data are presented as median (interquartile range). The total number of patients with available data is indicated. All *p* values are derived from non-parametrical Mann-Whitney *U* tests. Statistically significant *p* values are in bold.

C3c: complement component 3c; CORO1A-DEF6: coronin 1A- differentially expressed in FDCP 6 homolog; Ig: immunoglobulin; LN: lupus nephritis; MAPK: mitogen-activated protein kinase.

Supplementary Table S27. Z-scores of replicated gene modules in patients with LN and low versus normal/high levels of C4

Gene module	Low C4 N=9	Normal/high C4 N=22	*p* value
B cell	-1.22 (-2.20−-0.91)	-1.76 (-2.55−-0.15)	0.761
Cell cycle, mitotic phase	-0.26 (-0.48−-0.06)	-0.44 (-0.98−-0.15)	0.240
CORO1A-DEF6 network	-0.01 (-0.17−0.07)	-0.11 (-0.29−0.00)	0.277
Enriched in antigen presentation (III)	-0.15 (-0.86−0.17)	-0.39 (-0.53−-0.15)	0.663
Enriched in neutrophils (II)	0.09 (0.00−0.19)	0.04 (-0.12−0.18)	0.572
Erythrocytes	-0.15 (-0.30−0.29)	0.20 (-0.42−0.71)	0.408
Extracellular matrix (I)	-0.55 (-0.85−-0.23)	-0.97 (-1.37−-0.51)	0.164
Extracellular region cluster	-0.08 (-0.14−0.03)	-0.09 (-0.28−0.02)	0.542
Inflammation (IV)	0.34 (-0.14−0.40)	0.21 (-0.01−0.48)	0.728
Inflammation (VI)	0.11 (0.01−0.36)	-0.04 (-0.27−0.18)	0.164
Inositol phosphate metabolism	0.05 (-0.36−0.45)	-0.08 (-0.40−0.19)	0.408
Interferon	1.71 (0.76−2.10)	0.88 (0.00−1.78)	0.408
Interferon (II)	0.60 (0.12−0.70)	0.45 (0.23−0.73)	0.632
MAPK−RAS signalling	-0.26 (-0.46−0.16)	0.16 (-0.47−0.37)	0.177
Monocytes	0.29 (0.25−1.09)	0.23 (-0.44−0.66)	0.240
Plasma cells, immunoglobulins	0.16 (-0.34−0.78)	-0.23 (-0.76−0.41)	0.317
Platelets	-0.18 (-0.53−0.28)	0.12 (-0.32−0.65)	0.486
Protein synthesis (I)	-0.18 (-0.46−0.31)	-0.55 (-1.00−0.03)	0.139
Regulation of antigen presentation and immune response	-0.85 (-1.15−0.02)	-0.83 (-1.65−-0.33)	0.296
Regulation of transcription, transcription factors	0.17 (-0.67−0.22)	-0.56 (-0.95−-0.35)	0.033

Data are presented as median (interquartile range). The total number of patients with available data is indicated. All *p* values are derived from non-parametrical Mann-Whitney *U* tests. Statistically significant *p* values are in bold.

C4: complement component 4; CORO1A-DEF6: coronin 1A- differentially expressed in FDCP 6 homolog; Ig: immunoglobulin; LN: lupus nephritis; MAPK: mitogen-activated protein kinase.

Supplementary Table S28. Z-scores of replicated gene modules in patients with LN and anti-chromatin positivity versus negative patients

Gene module	Anti-chromatin (+) N=8	Anti-chromatin (-) N=22	*p* value
B cell	-1.76 (-2.54−-0.71)	-1.35 (-2.37−-0.32)	0.743
Cell cycle, mitotic phase	-0.24 (-1.05−-0.06)	-0.46 (-0.84−-0.15)	0.963
CORO1A-DEF6 network	0.00 (-0.20−0.01)	-0.11 (-0.22−0.01)	0.574
Enriched in antigen presentation (III)	-0.43 (-0.54−-0.17)	-0.39 (-0.55−0.03)	0.851
Enriched in neutrophils (II)	-0.07 (-0.15−0.16)	0.09 (0.01−0.18)	0.373
Erythrocytes	0.62 (-0.28−0.80)	0.02 (-0.43−0.52)	0.260
Extracellular matrix (I)	-0.83 (-1.07−-0.64)	-0.69 (-1.35−-0.40)	0.815
Extracellular region cluster	-0.10 (-0.26−-0.01)	-0.09 (-0.28−0.02)	0.925
Inflammation (IV)	0.11 (0.00−0.30)	0.27 (-0.13−0.49)	0.511
Inflammation (VI)	-0.16 (-0.27−-0.01)	0.07 (-0.17−0.25)	0.205
Inositol phosphate metabolism	-0.17 (-0.39−0.16)	-0.06 (-0.39−0.39)	0.673
Interferon	0.88 (0.13−1.57)	1.70 (0.05−2.13)	0.606
Interferon (II)	0.41 (0.24−0.60)	0.57 (0.16−0.82)	0.511
MAPK−RAS signalling	-0.02 (-0.64−0.41)	0.02 (-0.33−0.33)	0.925
Monocytes	0.23 (-0.47−0.62)	0.28 (0.01−0.83)	0.851
Plasma cells, immunoglobulins	-0.49 (-0.93−0.02)	0.10 (-0.55−0.76)	0.133
Platelets	0.11 (-0.26−0.40)	-0.01 (-0.50−0.65)	0.606
Protein synthesis (I)	-0.35 (-0.93−-0.09)	-0.45 (-0.93−0.17)	0.888
Regulation of antigen presentation and immune response	-0.64 (-1.37−-0.38)	-0.96 (-1.42−-0.37)	0.778
Regulation of transcription, transcription factors	-0.45 (-0.73−-0.34)	-0.43 (-0.84−0.07)	0.673

Data are presented as median (interquartile range). The total number of patients with available data is indicated. All *p* values are derived from non-parametrical Mann-Whitney *U* tests. Statistically significant *p* values are in bold.

CORO1A-DEF6: coronin 1A- differentially expressed in FDCP 6 homolog; Ig: immunoglobulin; LN: lupus nephritis; MAPK: mitogen-activated protein kinase.

Supplementary Table S29. Z-scores of replicated gene modules in patients with LN and anti-dsDNA positivity versus negative patients

Gene module	anti-dsDNA (+) N=18	anti-dsDNA (-) N=13	*p* value
B cell	-1.03 (-2.30−-0.05)	-1.81 (-3.26−-1.48)	0.161
Cell cycle, mitotic phase	-0.41 (-0.69−-0.12)	-0.32 (-1.16−-0.06)	0.471
CORO1A-DEF6 network	-0.05 (-0.18−0.03)	-0.13 (-0.30−0.00)	0.401
Enriched in antigen presentation (III)	-0.16 (-0.45−0.14)	-0.44 (-0.56−-0.28)	0.093
Enriched in neutrophils (II)	0.09 (0.02−0.18)	-0.05 (-0.14−0.18)	0.337
Erythrocytes	-0.16 (-0.50−0.32)	0.57 (-0.23−0.79)	0.139
Extracellular matrix (I)	-0.52 (-1.12−-0.25)	-1.00 (-1.26−-0.74)	0.078
Extracellular region cluster	-0.05 (-0.15−0.03)	-0.14 (-0.40−-0.02)	0.186
Inflammation (IV)	0.24 (-0.18−0.44)	0.25 (0.06−0.49)	0.575
Inflammation (VI)	0.07 (0.00−0.24)	-0.25 (-0.30−0.20)	0.078
Inositol phosphate metabolism	-0.03 (-0.34−0.39)	-0.07 (-0.40−0.21)	0.936
Interferon	1.72 (0.05−2.22)	0.76 (-0.01−1.69)	0.246
Interferon (II)	0.62 (0.23−0.82)	0.44 (0.13−0.60)	0.186
MAPK−RAS signalling	0.09 (-0.28−0.33)	-0.37 (-0.68−0.37)	0.423
Monocytes	0.34 (0.04−0.95)	0.26 (-0.49−0.44)	0.471
Plasma cells, immunoglobulins	0.03 (-0.49−0.74)	-0.37 (-0.91−0.42)	0.262
Platelets	-0.10 (-0.39−0.51)	0.25 (-0.24−0.67)	0.378
Protein synthesis (I)	-0.45 (-0.88−0.11)	-0.13 (-1.03−0.17)	0.936
Regulation of antigen presentation and immune response	-0.85 (-1.16−-0.08)	-0.80 (-1.62−-0.44)	0.471
Regulation of transcription, transcription factors	-0.51 (-0.93−0.07)	-0.46 (-0.82−-0.35)	0.779

Data are presented as median (interquartile range). The total number of patients with available data is indicated. All *p* values are derived from non-parametrical Mann-Whitney *U* tests. Statistically significant *p* values are in bold.

CORO1A-DEF6: coronin 1A- differentially expressed in FDCP 6 homolog; Ig: immunoglobulin; LN: lupus nephritis; MAPK: mitogen-activated protein kinase.

Supplementary Table S30. Z-scores of replicated gene modules in patients with LN and anti-SSA-52 positivity versus negative patients

Gene module	anti-SSA-52 (+) N=5	anti-SSA-52 (-) N=19	*p* value
B cell	-2.33 (-3.17−-1.22)	-1.48 (-2.06−-0.43)	0.303
Cell cycle, mitotic phase	-0.76 (-1.15−-0.51)	-0.32 (-0.87−0.05)	0.126
CORO1A-DEF6 network	-0.13 (-0.17−-0.12)	-0.04 (-0.34−0.03)	0.546
Enriched in antigen presentation (III)	-0.45 (-0.59−-0.44)	-0.28 (-0.55−0.03)	0.374
Enriched in neutrophils (II)	0.08 (0.00−0.23)	0.09 (-0.10−0.18)	0.696
Erythrocytes	0.19 (-0.15−0.80)	-0.17 (-0.49−0.48)	0.271
Extracellular matrix (I)	-0.85 (-1.15−-0.58)	-0.74 (-1.21−-0.36)	0.499
Extracellular region cluster	-0.15 (-0.42−-0.08)	-0.09 (-0.27−0.06)	0.241
Inflammation (IV)	0.25 (-0.14−0.50)	0.12 (-0.06−0.36)	0.749
Inflammation (VI)	0.25 (-0.22−0.36)	0.02 (-0.22−0.15)	0.414
Inositol phosphate metabolism	-0.39 (-0.55−-0.03)	-0.10 (-0.38−0.44)	0.271
Interferon	1.71 (1.33−2.10)	0.58 (0.01−1.73)	0.271
Interferon (II)	0.70 (0.54−0.93)	0.28 (0.02−0.66)	0.166
MAPK−RAS signalling	0.16 (0.03−0.28)	-0.22 (-0.66−0.35)	0.696
Monocytes	0.25 (-0.20−0.38)	0.26 (0.02−0.92)	0.546
Plasma cells, immunoglobulins	-0.34 (-0.73−0.61)	-0.10 (-0.58−0.80)	0.644
Platelets	0.28 (0.23−0.67)	-0.18 (-0.46−0.25)	0.145
Protein synthesis (I)	-0.68 (-1.12−-0.18)	-0.44 (-0.91−0.23)	0.303
Regulation of antigen presentation and immune response	-1.15 (-1.17−-1.06)	-0.80 (-1.35−-0.04)	0.214
Regulation of transcription, transcription factors	-0.35 (-0.82−-0.26)	-0.44 (-0.96−0.11)	0.915

Data are presented as median (interquartile range). The total number of patients with available data is indicated. All *p* values are derived from non-parametrical Mann-Whitney *U* tests. Statistically significant *p* values are in bold.

CORO1A-DEF6: coronin 1A- differentially expressed in FDCP 6 homolog; Ig: immunoglobulin; LN: lupus nephritis; MAPK: mitogen-activated protein kinase.

Supplementary Table S31. Z-scores of replicated gene modules in patients with LN and anti-SSA-60 positivity versus negative patients

Gene module	anti-SSA-60 (+) N=5	anti-SSA-60 (-) N=19	*p* value
B cell	-2.33 (-3.17−-1.54)	-1.16 (-2.06−-0.10)	0.095
Cell cycle, mitotic phase	-0.51 (-1.15−-0.26)	-0.43 (-0.87, -0.09)	0.594
CORO1A-DEF6 network	-0.17 (-0.18−-0.13)	-0.04 (-0.23−0.03)	0.241
Enriched in antigen presentation (III)	-0.45 (-0.59−-0.14)	-0.37 (-0.55−0.03)	0.644
Enriched in neutrophils (II)	0.08 (0.00−0.23)	0.09 (-0.10−0.18)	0.644
Erythrocytes	-0.15 (-0.23−0.19)	-0.13 (-0.49−0.70)	0.972
Extracellular matrix (I)	-1.15 (-1.15−-0.85)	-0.63 (-1.13−-0.36)	0.214
Extracellular region cluster	-0.08 (-0.15−-0.03)	-0.10 (-0.28−0.02)	0.972
Inflammation (IV)	0.25 (-0.14−0.49)	0.12 (-0.06−0.36)	0.915
Inflammation (VI)	0.25 (-0.22−0.36)	0.02 (-0.22−0.15)	0.455
Inositol phosphate metabolism	-0.39 (-0.55−0.28)	-0.10 (-0.38−0.32)	0.644
Interferon	1.71 (1.33−2.10)	0.58 (0.04−1.73)	0.546
Interferon (II)	0.70 (0.54−0.93)	0.28 (0.13−0.66)	0.303
MAPK−RAS signalling	0.16 (-0.46−0.28)	0.03 (-0.59−0.35)	0.972
Monocytes	0.38 (0.25−1.09)	0.21 (-0.18−0.65)	0.303
Plasma cells, immunoglobulins	-0.34 (-0.73−0.61)	-0.10 (-0.58−0.73)	0.804
Platelets	0.28 (0.23−1.02)	-0.18 (-0.46−0.25)	0.110
Protein synthesis (I)	-0.68 (-1.12−-0.18)	-0.44 (-0.91−0.10)	0.499
Regulation of antigen presentation and immune response	-1.15 (-1.17−-1.06)	-0.80 (-1.35−-0.13)	0.455
Regulation of transcription, transcription factors	-0.82 (-0.85−-0.26)	-0.39 (-0.84−0.11)	0.644

Data are presented as median (interquartile range). The total number of patients with available data is indicated. All *p* values are derived from non-parametrical Mann-Whitney *U* tests. Statistically significant *p* values are in bold.

CORO1A-DEF6: coronin 1A- differentially expressed in FDCP 6 homolog; Ig: immunoglobulin; LN: lupus nephritis; MAPK: mitogen-activated protein kinase.

Supplementary Table S32. Z-scores of replicated gene modules in patients with LN and anti-U1RNP positivity versus negative patients

Gene module	Anti-U1RNP (+) N=5	Anti-U1RNP (-) N=20	*p* value
B cell	0.01 (-0.65−0.03)	-1.84 (-2.40−-1.11)	0.089
Cell cycle, mitotic phase	-0.76 (-1.05−-0.48)	-0.29 (-0.87−-0.01)	0.197
CORO1A-DEF6 network	-0.04 (-0.09−0.02)	-0.13 (-0.33−0.02)	0.342
Enriched in antigen presentation (III)	0.03 (-0.44−0.20)	-0.41 (-0.75−-0.15)	0.174
Enriched in neutrophils (II)	0.02 (-0.14−0.17)	0.09 (-0.07−0.19)	0.541
Erythrocytes	0.19 (-0.13−0.72)	-0.16 (-0.49−0.60)	0.248
Extracellular matrix (I)	-0.48 (-0.58−-0.33)	-0.80 (-1.30−-0.52)	0.221
Extracellular region cluster	-0.29 (-0.42−-0.25)	-0.09 (-0.26−0.05)	0.118
Inflammation (IV)	0.25 (-0.50−0.29)	0.14 (-0.04−0.41)	0.587
Inflammation (VI)	0.07 (-0.14−0.20)	0.01 (-0.26−0.21)	0.634
Inositol phosphate metabolism	-0.28 (-0.55−-0.11)	0.07 (-0.39−0.43)	0.118
Interferon	0.58 (0.30−1.71)	1.41 (0.04−2.25)	0.587
Interferon (II)	0.24 (0.13−0.76)	0.53 (0.20−0.69)	0.839
MAPK−RAS signalling	0.52 (0.36−0.55)	-0.27 (-0.68−0.29)	0.007
Monocytes	0.38 (0.09−0.38)	0.23 (-0.24−1.01)	0.684
Plasma cells, immunoglobulins	-0.23 (-0.55−-0.10)	-0.10 (-0.77−0.79)	0.786
Platelets	0.23 (0.01−0.67)	-0.10 (-0.43−0.31)	0.248
Protein synthesis (I)	-0.26 (-1.27−-0.04)	-0.45 (-0.92−0.20)	0.415
Regulation of antigen presentation and immune response	-0.64 (-1.12−-0.29)	-0.96 (-1.41−-0.17)	0.839
Regulation of transcription, transcription factors	-0.82 (-1.10−-0.35)	-0.42 (-0.72−0.11)	0.277

Data are presented as median (interquartile range). The total number of patients with available data is indicated. All *p* values are derived from non-parametrical Mann-Whitney *U* tests. Statistically significant *p* values are in bold.

CORO1A-DEF6: coronin 1A- differentially expressed in FDCP 6 homolog; Ig: immunoglobulin; LN: lupus nephritis; MAPK: mitogen-activated protein kinase.

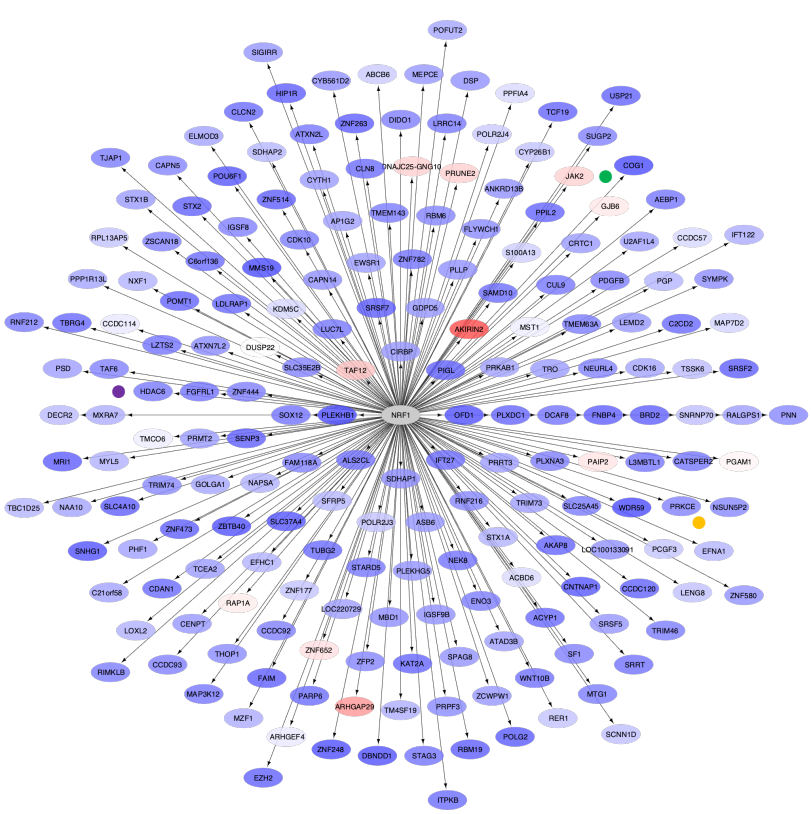
Supplementary Table S33. The most enriched signalling molecule networks in patients with LN

Regulator	Motif ID	AUC	NES	Targets	TFs
Interferon gene module					
STAT1	factorbook-STAT2	0.229	22.37	59	13
IRF8	taipale-NCGAAACCGAAACY-IRF8-DBD	0.207	20.12	57	8
STAT1	jaspar-MA0137.1	0.206	19.98	65	12
Interferon (II) gene module					
1RF9	taipale-AWCGAAACCGAAACY-IRF9-full	0.147	13.16	48	6
IRF8	taipale-NCGAAACCGAAACT-IRF8-full	0.140	12.47	47	6
IRF8	taipale-NCGAAACCGAAACY-IRF8-DBD	0.136	12.03	24	8
B cell gene module					
SOX10	tfdimers-MD00329	0.101	4.78	12	2
PRDM1	flyfactorsurvey-Blimp-1_SOLEXA_FBgn0035625	0.096	4.42	24	14
TBX2	taipale-NAGGTGTGAWN-TBX2-full	0.095	4.36	11	12
Plasma cells, immunoglobulins gene module					
TFDP3	transfac_pro-M00920	0.079	8.38	65	8
NFYC	yetfasco-1537	0.077	8.03	96	4
NFYC	jaspar-MA0316.1	0.076	7.91	95	4
Regulation of transcription, transcription factors					
YY1	flyfactorsurvey-phol_SOLEXA_5_FBgn0035997	0.162	8.83	18	3
YY1	flyfactorsurvey-phol_SANGER_5_FBgn0035997	0.149	8.04	9	2
YY1	factorbook-YY1	0.143	7.73	19	3
Cell cycle, mitotic phase gene module					
YY1	jaspar-PF0063.1	0.059	4.50	25	1
NANOS1	hdpi-NANOS1	0.058	4.40	9	1
YY1	flyfactorsurvey-phol_SOLEXA_5_FBgn0035997	0.057	4.32	39	3
Protein synthesis (I) gene module					
ZBTB33	jaspar-PF0008.1	0.030	3.91	143	1
ZBTB33	factorbook-UA1	0.029	3.56	108	1
ZBTB33	homer-M00076	0.029	3.54	135	1
Extracellular matrix (I) gene module					
NRF1	factorbook-NRF1	0.037	5.32	202	2
NRF1	swissregulon-NRF1.p2	0.036	5.09	131	2
ZSCAN10	jaspar-PF0001.1	0.036	4.91	191	3
Regulation of antigen presentation and immune response gene module					
PRDM2	yetfasco-1185	0.027	4.29	562	9
ZNF143	jaspar-PF0113.1	0.027	4.15	82	1
CUX1	homer-M00467	0.027	4.09	90	2

Genes in replicated gene modules with a mean |z-score| >1 in at least one LN patient subgroup were imputed in iRegulon through Cytoscape to generate signalling molecule networks and identify their chief regulators. The top chief regulators and enriched motifs are displayed.

AUC: area under the curve; LN: lupus nephritis; NES: normalised enrichment score; TFs: transcription factors.

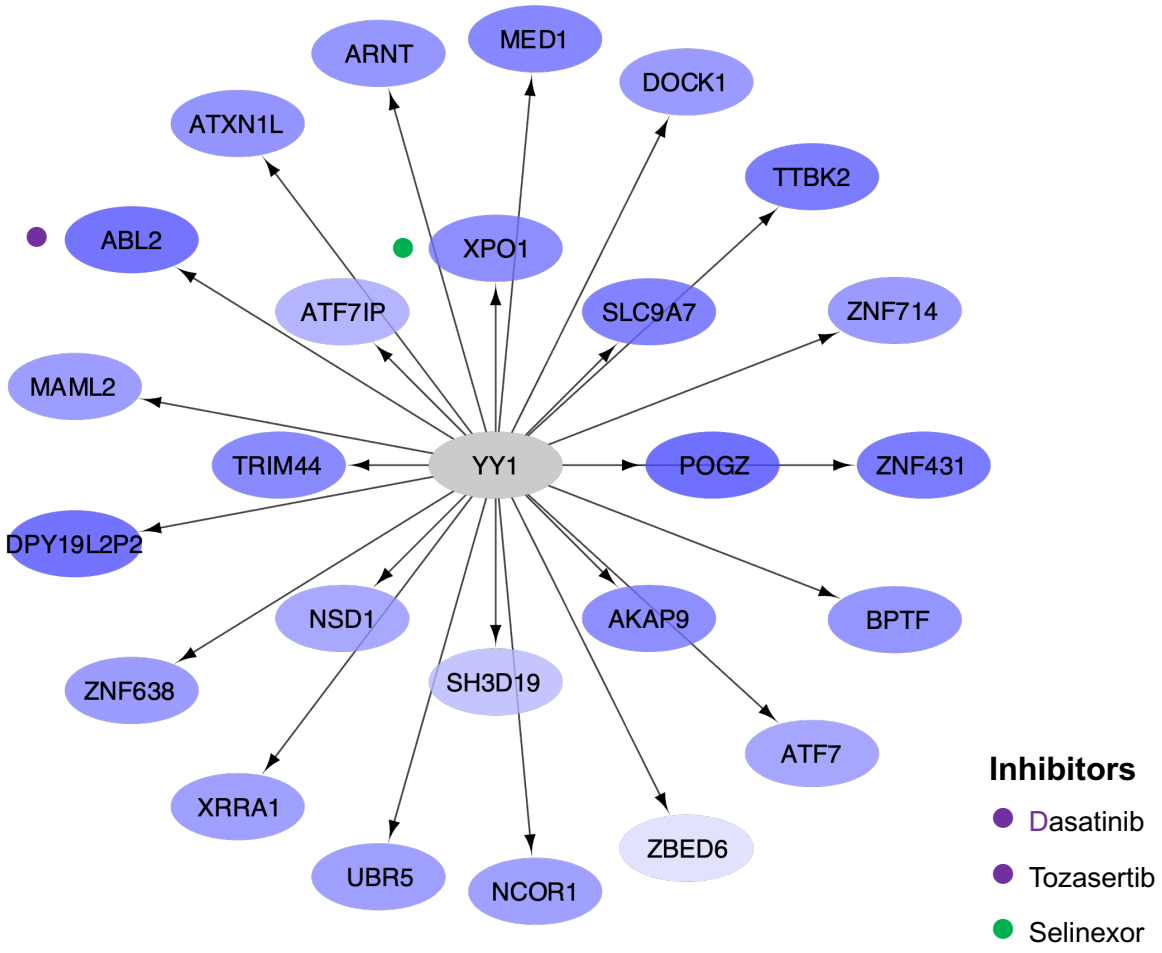
Supplementary Figure S1. The *NRF1* signalling molecule network and annotated drug targets in patients with lupus nephritis



Genes in the extracellular matrix (I) gene module were imputed in iRegulon through Cytoscape to generate signalling molecule networks and identify their chief regulators. One of the most enriched signalling molecule networks is plotted, with the chief regulator *NRF1* in the central node. The colour of the nodes ranges from light blue (downregulated genes) to increasing intensities of red (upregulated genes) based on the gene dysregulation (z-scores) in the lo-IFN patient subgroup. Inhibiting drugs and their upregulated targets are indicated by coloured dots.

IFN: interferon; lo; low.

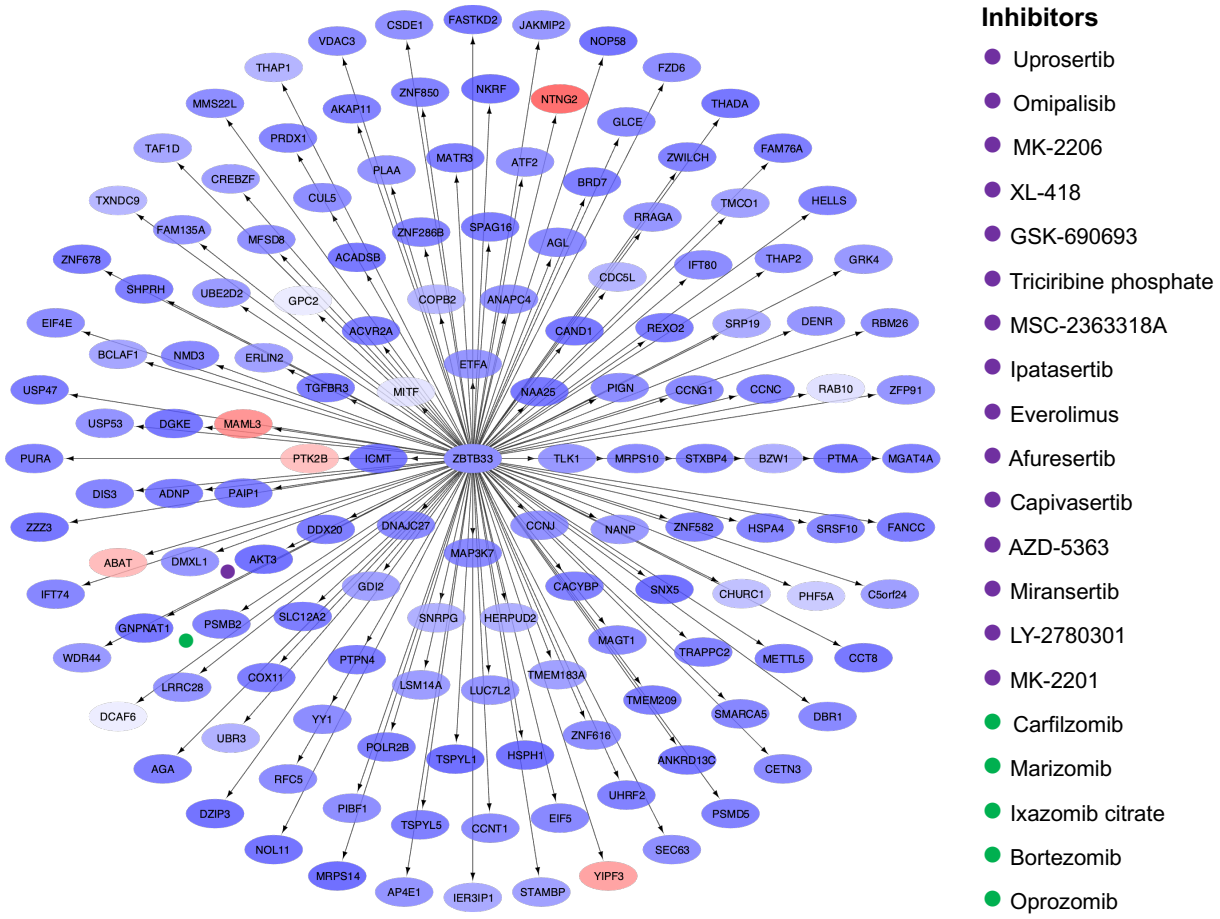
Supplementary Figure S2. The *YY1* signalling molecule network and annotated drug targets in patients with lupus nephritis



Genes in the cell cycle, mitotic phase gene module were imputed in iRegulon through Cytoscape to generate signalling molecule networks and identify their chief regulators. One of the most enriched signalling molecule networks is plotted, with the chief regulator *YY1* in the central node. The colour of the nodes ranges from light blue (downregulated genes) to increasing intensities of red (upregulated genes) based on the gene dysregulation (z-scores) in the lo-IFN patient subgroup. Inhibiting drugs and their upregulated targets are indicated by coloured dots.

IFN: interferon; lo; low.

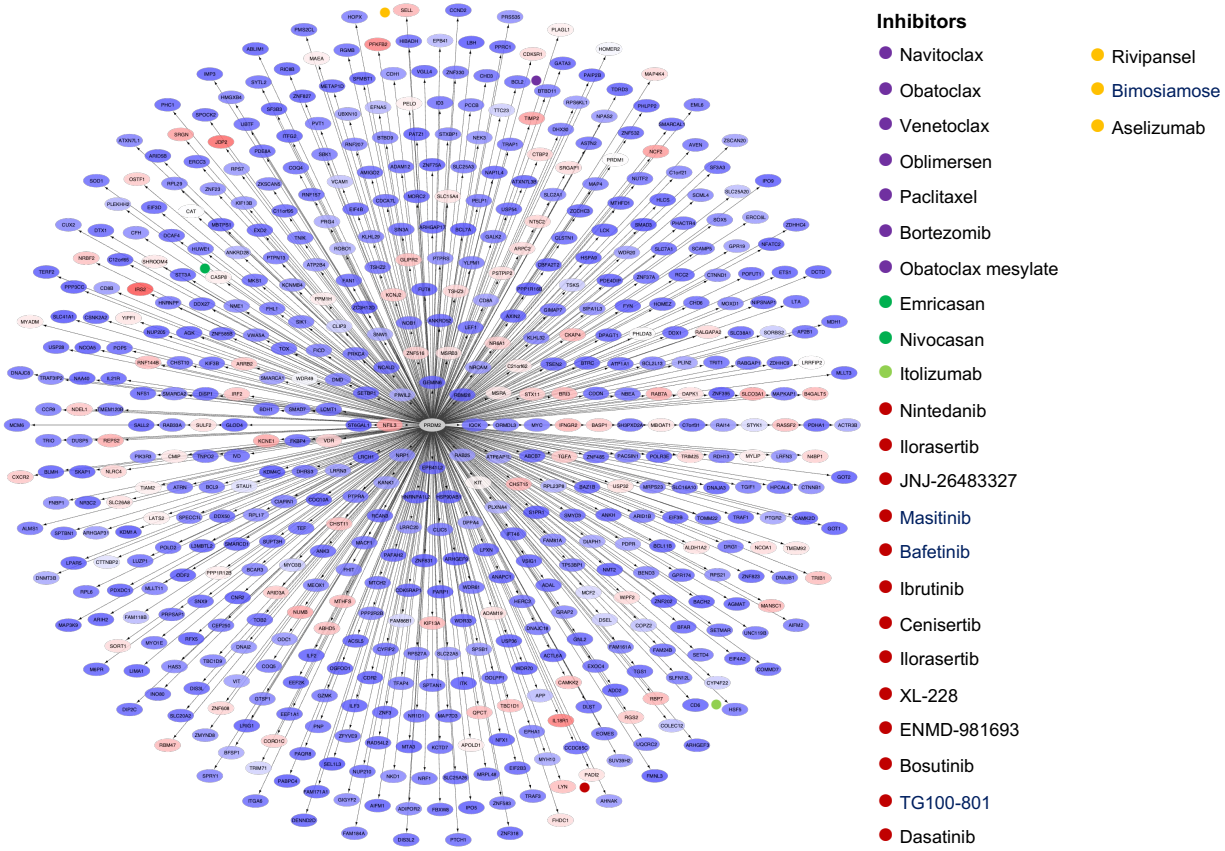
Supplementary Figure S3. The *ZBTB33* signalling molecule network and annotated drug targets in patients with lupus nephritis



Genes in the protein synthesis (I) gene module were imputed in iRegulon through Cytoscape to generate signalling molecule networks and identify their chief regulators. One of the most enriched signalling molecule networks is plotted, with the chief regulator *ZBTB33* in the central node. The colour of the nodes ranges from light blue (downregulated genes) to increasing intensities of red (upregulated genes) based on the gene dysregulation (z-scores) in the lo-IFN patient subgroup. Inhibiting drugs and their upregulated targets are indicated by coloured dots.

IFN: interferon; lo; low.

Supplementary Figure S4. The *PRDM2* signalling molecule network and annotated drug targets in patients with lupus nephritis



Genes in the regulation of transcription, transcription factors gene module were imputed in iRegulon through Cytoscape to generate signalling molecule networks and identify their chief regulators. One of the most enriched signalling molecule networks is plotted, with the chief regulator *PRDM2* in the central node. The colour of the nodes ranges from light blue (downregulated genes) to increasing intensities of red (upregulated genes) based on the gene dysregulation (z-scores) in the lo-IFN patient subgroup. Inhibiting drugs and their upregulated targets are indicated by coloured dots.

IFN: interferon; lo; low.

Supplementary Table S34. Response scores to selected targets in patients with LN

Target	lo-IFN subgroup N=13	im-IFN subgroup N=9	hi-IFN subgroup N=19	lo-IFN vs im-IFN *p* value	lo-IFN vs hi-IFN *p* value	im-IFN vs hi-IFN *p* value
IFNAR	0.58□ 0.05	0.55□0.03	0.60□0.05	0.133	0.309	**0.015**
CD22	0.07□0.01	0.08□0.00	0.08□0.01	0.077	**0.027**	0.539
BAFF	0.25□0.02	0.24□0.02	0.25□0.03	0.171	0.803	0.337
BAFF and APRIL	0.25□0.02	0.24□0.02	0.25□0.03	0.171	0.803	0.337
BAFFR	0.03□0.01	0.04□0.01	0.03□0.01	**0.010**	0.309	0.052
Calcineurin	0.07□0.01	0.05□0.01	0.05□0.01	**0.001**	**<0.001**	0.446
C5	0.01□0.00	0.01□0.00	0.01□0.00	0.217	0.454	0.363
CD19	0.18□0.08	0.26□0.03	0.22□0.04	**0.005**	0.328	**0.010**
CD38	0.36□0.02	0.40□0.05	0.40□0.03	**0.021**	**<0.001**	0.476
mTORC1	0.76□0.04	0.71□0.03	0.72□0.04	**0.001**	**0.003**	0.337
CCR1	0.00□0.00	0.00□0.00	0.00□0.01	N/A	0.408	0.491
BTK	0.14□0.02	0.17□0.01	0.16□0.01	**0.001**	**0.001**	**0.029**
Tyrosine kinase	0.81□0.04	0.75□0.02	0.76□0.05	**<0.001**	**0.016**	0.313
JAK1/JAK2	0.96□0.04	0.89□0.03	0.93□0.05	**0.001**	0.388	**0.022**

Data are presented as mean (standard deviation). All *p* values are derived from non-parametrical Mann-Whitney *U* tests. Statistically significant *p* values are in bold.

APRIL: a proliferation-inducing ligand; BAFF: B cell activating factor belonging to the tumour necrosis factor family; BAFFR; B cell activating factor belonging to the tumour necrosis factor family; BTK: Bruton's tyrosine kinase; C5: complement component 5; hi: high; IFN: interferon; IFNAR: interferon-α/β receptor; im: intermediate; N/A: not applicable; JAK: Janus kinase; LN: lupus nephritis; lo: low; mTORC1: mammalian target of rapamycin complex 1.

Supplementary Table S35. LN patients with anticipated response to selected drug targets

Target	lo-IFN subgroup	im-IFN subgroup	hi-IFN subgroup	lo-IFN vs im-IFN	lo-IFN vs hi-IFN	im-IFN vs hi-IFN
	N=13	N=9	N=19	*p* value	*p* value	*p* value
IFNAR	5 (38.5%)	1 (11.1%)	14 (73.7%)	0.333	0.104	**0.004**
CD22	4 (30.8%)	6 (66.7%)	14 (73.7%)	0.192	**0.041**	1.000
BAFF	7 (53.8%)	3 (33.3%)	10 (52.6%)	0.415	1.000	0.435
BAFF and APRIL	7 (53.8%)	3 (33.3%)	10 (52.6%)	0.415	1.000	0.435
BAFFR	6 (46.2%)	8 (88.9%)	12 (63.2%)	0.074	0.556	0.214
Calcineurin	12 (92.3%)	2 (22.2%)	5 (26.3%)	**0.001**	**0.001**	1.000
C5	4 (30.8%)	6 (66.7%)	10 (52.6%)	0.192	0.389	0.687
CD19	5 (38.5%)	8 (88.9%)	8 (42.1%)	**0.031**	1.000	**0.039**
CD38	0 (0.0%)	4 (44.4%)	13 (68.4%)	**0.017**	**<0.001**	0.409
mTORC1	10 (76.9%)	1 (11.1%)	5 (26.3%)	**0.008**	**0.014**	0.630
CCR1	0 (0.0%)	0 (0.0%)	1 (5.3%)	1.000	1.000	1.000
BTK	1 (7.7%)	9 (100.0%)	12 (63.2%)	**<0.001**	**0.003**	0.062
Tyrosine kinase	12 (92.3%)	1 (11.1%)	6 (31.6%)	**<0.001**	**0.002**	0.371
JAK1/JAK2	10 (76.9%)	0 (0.0%)	12 (63.2%)	**<0.001**	0.467	**0.003**

Data are presented as number (percentage). All *p* values are derived from Pearson's chi squared ($\chi 2$) or Fisher's exact tests. Statistically significant *p* values are in bold.

APRIL: a proliferation-inducing ligand; BAFF: B cell activating factor belonging to the tumour necrosis factor family; BAFFR; B cell activating factor belonging to the tumour necrosis factor family; BTK: Bruton's tyrosine kinase; C5: complement component 5; hi: high; IFN: interferon; IFNAR: interferon-α/β receptor; im: intermediate; JAK: Janus kinase; LN: lupus nephritis; lo: low; mTORC1: mammalian target of rapamycin complex 1.