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Reporting Summary

Nature Research wishes to improve the reproducibility of the work that we publish. This form provides structure for consistency and transparency in reporting. For further information on Nature Research policies, see Authors & Referees and the Editorial Policy Checklist.

Statistical parameters

When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. figure legend, table legend, main text, or Methods section).

n/a	Confirmed	
☐	☒	The exact sample size (*n*) for each experimental group/condition, given as a discrete number and unit of measurement
☐	☒	An indication of whether measurements were taken from distinct samples or whether the same sample was measured repeatedly
☐	☒	The statistical test(s) used AND whether they are one- or two-sided *Only common tests should be described solely by name; describe more complex techniques in the Methods section.*
☒	☐	A description of all covariates tested
☒	☐	A description of any assumptions or corrections, such as tests of normality and adjustment for multiple comparisons
☐	☒	A full description of the statistics including central tendency (e.g. means) or other basic estimates (e.g. regression coefficient) AND variation (e.g. standard deviation) or associated estimates of uncertainty (e.g. confidence intervals)
☒	☐	For null hypothesis testing, the test statistic (e.g. *F*, *t*, *r*) with confidence intervals, effect sizes, degrees of freedom and *P* value noted *Give P values as exact values whenever suitable.*
☒	☐	For Bayesian analysis, information on the choice of priors and Markov chain Monte Carlo settings
☒	☐	For hierarchical and complex designs, identification of the appropriate level for tests and full reporting of outcomes
☐	☒	Estimates of effect sizes (e.g. Cohen's *d*, Pearson's *r*), indicating how they were calculated
☐	☒	Clearly defined error bars *State explicitly what error bars represent (e.g. SD, SE, CI)*

Our web collection on statistics for biologists may be useful.

Software and code

Policy information about availability of computer code

Data collection	BD FACSDiva Software (v8.0.1), BD FACSChorus Software (v1.0) and Cytek SpectroFlo Software (v1.1) were used for flow data collection.
Data analysis	Statistical analysis was performed using GraphPad Prism v7.0. Flow cytometry data were analyzed with FlowJo v10.4.2. Microarray data were analyzed with GeneSpring v7.3.1. Softwares used in RNAseq and ATACseq data analysis: Trimmomatic (v0.33), Samtools (v0.1.19), bwa-mem (v0.7.12), MACS (v2.1.0), R (v3.3.1), DiffBind (v2.0.9), EdgeR (v3.14.0), HOMER (v4.6), IGV (v2.3.77) and DESeq2 (v1.16.1).

For manuscripts utilizing custom algorithms or software that are central to the research but not yet described in published literature, software must be made available to editors/reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research guidelines for submitting code & software for further information.

Data

Policy information about availability of data

All manuscripts must include a data availability statement. This statement should provide the following information, where applicable:

- Accession codes, unique identifiers, or web links for publicly available datasets
- A list of figures that have associated raw data
- A description of any restrictions on data availability

Gene expression (microarray data) from plasmacytoid Dendritic Cells (pDCs) is available at the Gene Expression Omnibus (GEO) GSE93679. Gene expression (RNAseq) data from in vitro generated CD4+ cells is available at the GEO database under GSE118951. Gene expression (RNAseq) data from ex vivo isolated CD4+ cells is available at the GEO database under accession GSE109843. ATAC-sequencing data is available at the GEO database under accession GSE110017. Uncropped data for Supplementary Fig. 2g can be accessed in Supplementary Fig. 8a. All other relevant data are available from the corresponding author directly.

Field-specific reporting

Please select the best fit for your research. If you are not sure, read the appropriate sections before making your selection.

☒ Life sciences ☐ Behavioural & social sciences ☐ Ecological, evolutionary & environmental sciences

For a reference copy of the document with all sections, see nature.com/authors/policies/ReportingSummary-flat.pdf

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	Samples were chosen based on availability of patient material. No sample size calculation was performed a priori. Up to eighty percent of pediatric SLE patients develop nephritis (LN). Thus, a sample size of 30 should include enough patients with and without this complication. We did enroll 27 pediatric SLE patients in our study. Twenty of them were diagnosed with LN and 7 did not. This number of patients enabled us to find statistically significant correlations with the cell populations of interest and the parameters that we analyzed.
Data exclusions	No data were excluded from the analyses.
Replication	All in vitro assays were performed at least three times with different donors. The data presented is representative of one assay. All attempts at replication were successful.
Randomization	SLE patients were allocated into different experimental groups according to the presence or absence of nephritis and the nephritis class defined by the International Society of Nephrology/Renal Pathology Society revised LN classification criteria.
Blinding	Kidney imaging acquisition and analyses were performed blinded in terms of Lupus nephritis class.

Reporting for specific materials, systems and methods

Materials & experimental systems

n/a	Involved in the study
☒	☐ Unique biological materials
☐	☒ Antibodies
☐	☒ Eukaryotic cell lines
☒	☐ Palaeontology
☒	☐ Animals and other organisms
☐	☒ Human research participants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☐	☒ Flow cytometry
☒	☐ MRI-based neuroimaging

Antibodies

Antibodies used	anti-CD4 PE-Cy7 (Clone SK3) - BD Biosciences – cat#557852 anti-CXCR5 AlexaFluor 647 (Clone RF8B2) - BD Biosciences – cat#558113 anti-CD45RA APC-H7 (Clone H100) - BD Biosciences – cat#560674 anti-PD1 Brilliant Violet 421 (Clone EH12.2H7) – Biolegend – cat#329919 anti-CD3 V500 (Clone RPA-T4) - BD Biosciences – cat#560770

anti-CXCR3 Brilliant Violet 785 (Clone GO25H7) – Biolegend – cat#353737
anti-CD21 FITC (Clone Bu32) – Biolegend – cat#354909
anti-CD27 PE (Clone M-T271) – Biolegend – cat#356405
anti-IgD PerCP Cy5.5 (Clone IA6-2) – Biolegend – cat#348207
anti-CD38 PE-Cy7 (Clone HB7) - BD Biosciences – cat#335790
anti-CD19 AF700 (Clone H1B19) – Biolegend – cat#302225
anti-CD11c V450 (Clone B-ly6) - BD Biosciences – cat#560369
anti-CD3 Brilliant Violet 650 (Clone OKT3) – Biolegend – cat#317323
anti-Lin1 FITC - BD Biosciences - cat #340546
anti-HLADR APC-H7 (Clone G46-6) - BD Biosciences – cat#561358
anti-CD11c APC (Clone S-HCL-3) - BD Biosciences – cat#340544
anti-CD123 PE (Clone 9F5) - BD Biosciences – cat#340545
anti-IgD APC (Clone IgD26) – Miltenyi – cat#130-099-221
anti-CD27 PE (Clone MT271) – Biolegend – cat#356405
anti-CD19 FITC (Clone H1B19) - BD Biosciences – cat#560994
anti-CD80 APC (Clone L307) - BD Biosciences – cat#561134
anti-CD86 PE (Clone FUN-1) - BD Biosciences – cat#555658
anti-CD83 FITC (Clone HB15e) – Biolegend – cat#305305
anti-CD40 PE (Clone 5C3) – Biolegend – cat#334307
anti-HLADR APC-H7 (Clone G46-6) - BD Biosciences – cat#561358
anti-CXCR4 PECy7 (Clone 12G5) – Biolegend – cat#306513
anti-CXCR3 Brilliant Violet 785 (Clone GO25H7) – Biolegend – cat#353737
anti-CCR7 APC (Clone 3D12) – Thermofisher – cat#17-1979-41
anti-IL10 APC (Clone JES3-19F1) – Biolegend – cat#506806
anti-IFNg PE-Cy7 (Clone B27) - BD Biosciences – cat#557643
anti-HIF1a antibody (Clone 546-16) – Biolegend– cat#359703
anti-Tbet antibody (Clone 4B10) – Biolegend – cat#644803

anti-PD1 antibody (clone EH12.2H7) – Biolegend – cat#329925
anti-CD3 (clone OKT3) – Biolegend – cat#317325
anti-CD28 mAb – Biolegend – cat#302933
anti-IL10 (clone JES3-9D7) – Biolegend – cat#501406
anti-SUCNR1/GPR91 - Novus Biological – cat#NBP1-00861SS
anti- IL21R (clone 17A12) – Biolegend – cat#359503

anti-p65 antibody – Abcam – cat#ab16502

anti-GAPDH (Cat # 2118; Cell Signaling)
anti-pRb Ser807/811 (Cat # 9308; Cell Signaling)
anti-Cyclin D1 (Cat # 2989; Cell Signaling)
anti-Cyclin D2 (Cat # 3741; Cell Signaling)
anti-Cyclin D3 (Cat # 2936; Cell Signaling)
anti-Nitrotyrosine (Cat # 9691; Cell Signaling)
anti-NDUFA9 (Cat # ab110412; Abcam)
anti-NDUFA8 (Cat # ab199681; Abcam)
anti-SDHA (Cat # ab110412; Abcam)
anti-UQCRC2 (Cat # ab110412; Abcam)
anti-ATP5A (Cat # ab110412; Abcam)

anti-CD3 (Clone OKT3; Biolegend) cat#317325
anti-IL10 (Clone A47-25-17; Abcam) cat#ab134742
anti-IFNg (Cat #ab25101; Abcam)
anti-Nitrotyrosine (Cat #ab42789; Abcam)
anti-CD20 (Clone EP459Y; Abcam) cat#ab78237
anti-CD4 (Clone EPR6855; Abcam) cat#ab133616
anti-PD1 (Clone EPR4877; Abcam) cat#ab137132
anti-Aquaporin1 (Clone B-11; SantaCruz) cat#sc-25287

Validation

Each antibody was validated accordingly to the manufacturer instructions. Were not stated differently, 1:1000 dilution for the antibodies was used.

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)

Human CD40L-transfected murine fibroblasts were obtained from the the laboratory of Dr. Jacques Banchereau. See Methods section for details.

Authentication

Cell lines were authenticated by assessing their ability to induce B cell proliferation and activation.

Mycoplasma contamination

All cell lines tested negative for mycoplasma contamination.

Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell lines were used.

Human research participants

Policy information about studies involving human research participants

Population characteristics	On average, our SLE patient population is 86% female and 14% male (female patients: age range: 8-17 y/o, with an average age of 14; 58% Hispanic/White, 35% non-Hispanic/African American, 5% non-Hispanic/White, 2% other; male patients: age range 9-17 y/o, with an average age of 12 years; 57% Hispanic/White, 14% non-Hispanic/African American, 2% other).
Recruitment	The SLE patient population was recruited from pediatric rheumatology clinics at Texas Scottish Rite Hospital for Children and Children's Medical Center, both in Dallas, Texas; and as such is representative of the lupus patients in that geographic region of the country.

Flow Cytometry

Plots

Confirm that:

☒ The axis labels state the marker and fluorochrome used (e.g. CD4-FITC).

☒ The axis scales are clearly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).

☒ All plots are contour plots with outliers or pseudocolor plots.

☒ A numerical value for number of cells or percentage (with statistics) is provided.

Methodology

Sample preparation	See Methods section for details.
Instrument	BD FascAria II, BD Fortessa, BD FacsCanto II and BD FacsMelody (BD Biosciences). Cytek Aurora (Cytek).
Software	BD FACSDiva Software (v8.0.1), BD FACSChorus Software (v1.0) and Cytek SpectroFlo Software (v1.1) were used for flow data collection. Flow cytometry data were analyzed with FlowJo v. 10.4.2.
Cell population abundance	See Main text and Methods sections for details.
Gating strategy	See Main text and Methods sections for details.

☒ Tick this box to confirm that a figure exemplifying the gating strategy is provided in the Supplementary Information.