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Reporting Summary

Nature Portfolio 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 Portfolio policies, see our <u>Editorial Policies</u> and the <u>Editorial Policy Checklist</u>.

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For	all statistical analyses, confirm that the following items are present in the 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
	A statement on 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 statistical parameters 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. <i>F</i> , <i>t</i> , <i>r</i>) with confidence intervals, effect sizes, degrees of freedom and <i>P</i> value noted <i>Give P values as exact values whenever suitable.</i>
\boxtimes	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 <i>d</i> , Pearson's <i>r</i>), indicating how they were calculated
	Our web collection on <u>statistics for biologists</u> contains articles on many of the points above.

Software and code

Policy information about availability of computer code

Data collection

JEOL JEM-1400 TEM (JEOL Ltd) with Gatan US1000 2k x 2k CCD camera (Gatan), FlowJo 10.7.1, Image J 1.53

Data analysis

Prism 8.2.0, Partek Flow v10.0, Custom scripts and in-house developed analysis software were used with R, Matlab or Circos tools for visualization.

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 and reviewers. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Portfolio 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 description of any restrictions on data availability
- For clinical datasets or third party data, please ensure that the statement adheres to our policy

The AIRR sequencing and RNA sequencing datasets for ASC populations were deposited at Genome Expression Omnibus under the accession number GSE235660. Source data are provided with this paper. Custom scripts and in-house developed analysis software were used with R, Matlab or Circos tools for visualization AIRR

Research involving	human	participants,	their data,	or biological	material

sequencing data, and the scripts are available on GitHub at https://github.com/chenwr56/airr.

Policy information about studies with <u>human participants or human data</u>. See also policy information about <u>sex, gender (identity/presentation)</u>, and sexual orientation and <u>race</u>, ethnicity and racism.

Reporting on sex and gender

Participants in this study are predominately female as SLE occurs much more frequent in women.

Reporting on race, ethnicity, or other socially relevant groupings

Our study population reflects the demographics of Atlanta, GA area and was predominately African American, a group that experiences higher SLE prevalence and severity. Both Black and white healthy control doors were used for comparison.

Population characteristics

Female, African American, age ranged from 22-65 years old.

Recruitment

SLE patients fulfilled four or more criteria of the modified American College of Rheumatology classification were recruited as active SLE patients, with less than four for SLE disease activity index were recruited as inactive SLE, both from Emory University Hospital and Grady Hospital. Healthy subject at steady state or post influenza vaccines were recruited based on matching gender, race and age with SLE patients.

Ethics oversight

All research was approved by the Emory University Institutional Review Board (Emory IRB numbers IRB00058515 and IRB00057983) and was performed in accordance with all relevant guidelines and regulations. Written informed consent was obtained from all participants.

Healthy donors (n = 45) were recruited using promotional materials approved by the Emory University Institutional Review Board. Healthy subjects received the influenza vaccinations (n = 24) as part of routine medical care. Subjects with systemic lupus erythematosus (n = 176) were recruited from Emory University Hospital and Grady Hospital in Atlanta, GA, USA. Peripheral blood mononuclear cells were isolated on days 6-7 after vaccination for all vaccinated subjects.

Note that full information on the approval of the study protocol must also be provided in the manuscript.

Field-specific reporting

Please select the one belo	w that is the best fit for your research.	If you	u 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 <u>nature.com/documents/nr-reporting-summary-flat.pdf</u>

Life sciences study design

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

Sample size We collected as many samples as we can that met our recruitment criteria for each group in the period of time of this study.

Data exclusions No data was excluded.

Flow cytometry experiments were conducted at least five human samples. Wright-Giemsa and electron microscopy were repeated for five times. ELISA were repeated for five times and each time with triplicate. ELISpot for cell survival experiments and neutralizing antibodies were conducted for five times and each time with triplicate. Attempts at replication were successful.

Randomization Sai

Samples of participants were assigned to specific group based on their vaccination status and disease severity (see information above in the Recruitment).

Blinding

Replication

Blinding was performed wherever possible. Number systems, rather than sample IDs, were used for assays such as ELISA and ELISpot, and microscopy experiments, and data analysis for flow cytometry. All data were quantified independently to minimize bias.

Reporting for specific materials, systems and methods

We require information from authors about some types of materials, experimental systems and methods used in many studies. Here, indicate whether each material, system or method listed is relevant to your study. If you are not sure if a list item applies to your research, read the appropriate section before selecting a response.

Materials & experime			
n/a Involved in the study	n/a Involved in the study		
Antibodies	ChIP-seq		
Eukaryotic cell lines	Flow cytometry		
Palaeontology and a			
Animals and other o	rganisms		
Clinical data			
Dual use research of	concern		
Plants			
Antibodies			
Antibodies used CD3-BV711 (clone: HIT3a, BD Biosciences, catalogue number: 740768, dilution at 1:20); CD14-BV711 (clone: M5E2, BD Biosciences, catalogue number: 740773, dilution at 1:20); IgD-FITC (IA6-2, BD Biosciences, catalogue number: 555778, dilution at 1:5); CD2 Cy7(clone: SJ25C1, BD Biosciences, catalogue number: 341093, dilution at 1:5); CD27-APC-eFluor780 (clone: O323, Invitrogen catalogue number: 50-161-60, dilution at 1:20); CD38-V450 (clone: HIT2, BD Biosciences, catalogue number: 561378, dilution 1:20); CD138-APC (clone: 44F9, Miltenyi Biotec, catalogue number: 130-127-977, dilution at 1:20); CXCR4-PE (clone: 12G5, BioLegend, catalogue number: 306506, dilution at 1:20); CXCR3-PE (clone: G025H7, BioLegend, catalogue number: 352706, dat 1:20); Blimp-1-PE (clone: 6D3, BD Biosciences, catalogue number: 564702, dilution at 1:10); BCMA-PE (clone: 19F2, BioLegend), dilution at 1:20); BCMA-PE (clone: 19F2, BioLege			
Validation	Antibodies were used for flow cytometry data analysis as well FACS sorting and data generated include Figure 1, 2, 3 (for analysis) and Figure 4, 5, 6 and 7 for sorting.		
Flow Cytometry			
Plots			
Confirm that:			
The axis labels state the	ne marker and fluorochrome used (e.g. CD4-FITC).		
The axis scales are cle	arly visible. Include numbers along axes only for bottom left plot of group (a 'group' is an analysis of identical markers).		
	lots with outliers or pseudocolor plots.		
	number of cells or percentage (with statistics) is provided.		
Methodology			
Sample preparation	Cells were isolated from peripheral blood using Ficoll density gradient centrifugation and perioheral blood mononuclear cells (PBMC) were stained with anti-human antibody staining reagents.		
Instrument	FACSAria II (BD Biosciences)		
Software	BD FACSDiva		
Cell population abundanc	e 1,000 to 5,000 were collected from sorting for each cell populations and post-sort purity analysis were performed to make sure the percentages of desired cells in specific sorting gate reach above 95%.		
Gating strategy	To delineate the peripheral blood ASC, we divided CD3- and CD14-negative lymphocytes, i.e., non-T cells, non-monocytes, into CD19+ and CD19- subpopulations, and then CD19+ cells were gated on IgD-negative cells to eliminate late transitional		

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

and naïve B cells, followed by a subsequent gate on cells that express high levels of CD27 and CD38 for CD19+ ASCs. CD19+ ASCs were further defined by the expression of CD138 and grouped into pop 2 (CD19+ CD138-) and pop 3 (CD19+ CD138+). Likewise, CD19- ASCs were gated and further divided into pop 4 (CD19- CD138-) and pop 5 (CD19- CD138+) (Fig. 1b).