

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 [Editorial Policies](#) and the [Editorial Policy Checklist](#).

Statistics

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. 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

Our web collection on [statistics for biologists](#) contains articles on many of the points above.

Software and code

Policy information about [availability of computer code](#)

Data collection	CellRanger (v6.0.6), BD Rhapsody Sequence Analysis Pipeline (v1.12)
Data analysis	Seurat (v4.3.0), FactoMineR (v2.9), miloR (v1.6.0), Enrichr (v3.1), Monocle3 (v1.3.1), and ggplot2 (v3.4.4) were R packages installed and used for analysis and visualization of scRNA-seq data. Seurat (v5.1.0), dbSCAN (v1.2-0), and scclusteval (v0.0.0.9000) were used for spatial transcriptome analysis. All functions were derived from these packages. Graphpad Prism (v10) were used for data visualization. The code is available at https://github.com/ShimagamiH/ShimagamiH_SSc_scRNAseq .

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](#)

Count matrix data of scRNA-seq is available at GEA with accession code E-GEAD-872. Fast-q files are also available at DNA Data Bank of Japan Sequence Read Archive with accession code DRA019274. The CosMX spatial transcriptomic data is provided as source data.

Research involving human participants, their data, or biological material

Policy information about studies with [human participants or human data](#). See also policy information about [sex, gender \(identity/presentation\), and sexual orientation](#) and [race, ethnicity and racism](#).

Reporting on sex and gender	In this study, the sex of the participants was determined based on self-report. Sex and gender analyses were not performed due to the small sample size.
Reporting on race, ethnicity, or other socially relevant groupings	Race, ethnicity, or any other socially relevant grouping was not used in this study. All patients or healthy donors recruited for this study were Japanese.
Population characteristics	21 patients with systemic sclerosis (16 females; median age, 64.0 years) and six healthy donors (four females; median age, 65.5 years) were recruited for CITE-seq experiments of peripheral blood mononuclear cells. Kidney samples were collected from three patients with scleroderma renal crisis and three healthy donors.
Recruitment	Patients with systemic sclerosis were recruited for scRNA-seq after informed consent was provided in accordance with the Declaration of Helsinki and with approval from the ethics review board of the Graduate School of Medicine, Osaka University, Japan (No. 855). There is no self-selection bias as all patients with systemic sclerosis without any immunosuppressive therapy, infection, or malignancy, who were admitted to or visited Osaka university hospital from August, 2021 to October, 2022 were recruited for the study. Samples for spatial transcriptomic analysis were collected in accordance with protocols approved by the ethics committee of Osaka University Hospital, Japan (No.11122 and No.18370).
Ethics oversight	Ethics review board of the Graduate School of Medicine, Osaka University, Japan (No. 855, No.11122, No.18370).

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 below that is 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/documents/nr-reporting-summary-flat.pdf](https://www.nature.com/documents/nr-reporting-summary-flat.pdf)

Life sciences study design

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

Sample size	The sample size was not predetermined and all patients with systemic sclerosis without any immunosuppressive therapy, infection, or malignancy, who were admitted to or visited Osaka university hospital from August, 2021 to October, 2022 were recruited for scRNA-seq. We recruited 21 patients with systemic sclerosis and six healthy donors. Sample size were sufficient to adequately detect compositional change of cell populations by clustering and differential abundance analysis.
Data exclusions	No data were excluded.
Replication	All findings were based on statistical analysis of a large patient cohort. There was no replication cohort. All data including multi-omics analyses were processed twice for quality control and all attempts at replication were successfully.
Randomization	We did not apply randomization of the samples because no intervention was conducted in this study.
Blinding	We did not apply blinding of the samples because no intervention was conducted in this study.

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 & experimental systems

n/a	Involved in the study
☐	☒ Antibodies
☒	☐ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☒	☐ Animals and other organisms
☐	☒ Clinical data
☒	☐ Dual use research of concern
☒	☐ Plants

Methods

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

Antibodies

Antibodies used	The antibodies for CITE-seq experiments conducted on the 10x chromium platform were obtained from BioLegend and are listed in Supplementary Table 11. The antibodies for Abseq experiments conducted on the BD Rhapsody Express System were obtained from BD Biosciences and are listed in Supplementary Table 13.
Validation	Antibodies used in CITE-seq experiments are validated by BioLegend, as stated in the website that they are tested by PCR and sequencing to confirm the oligonucleotide barcodes. Antibodies used in Abseq experiments are validated by BD Biosciences, as stated in the website with comprehensive performance data using human whole blood cells.

Clinical data

Policy information about [clinical studies](#)

All manuscripts should comply with the ICMJE [guidelines for publication of clinical research](#) and a completed [CONSORT checklist](#) must be included with all submissions.

Clinical trial registration	N/A
Study protocol	N/A
Data collection	N/A
Outcomes	N/A

Plants

Seed stocks	N/A
Novel plant genotypes	N/A
Authentication	N/A