

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 (<i>n</i>) 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 <i>Only common tests should be described solely by name; describe more complex techniques in the Methods section.</i>
☒	☒ 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>
☒	☐ 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 [statistics for biologists](#) contains articles on many of the points above.

Software and code

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

Data collection	NO software was used for single cell or spatial-seq data acquisition.
Data analysis	10X Genomics software cellranger (version 3.1.0), R package Seurat (version 5.0.1), monocle2 (version 2.28.0), CellChat (version 1.6.1) and NicheNet (version 2.0.6) were used to analyze the scRNA-seq data. Xenium Explore (version 2.0.0) was used to analyze the spatial-seq data.

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](#)

Provide your data availability statement here.

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	The sex information is reported in supplemental table S1. Sex or gender was not considered in the study design.
Reporting on race, ethnicity, or other socially relevant groupings	Race and Ethnicity information is reported in supplemental table S1. It was not considered in the study design.
Population characteristics	Skin biopsy specimens were obtained from patients with generalized pustular psoriasis at University of Michigan-Ann Arbor. The population characteristics, including age and background disease, are reported in supplemental table S1.
Recruitment	Patients with generalized pustular psoriasis are seen at hospital of University of Michigan-Ann Arbor. No self-selection bias was presented in this study.
Ethics oversight	Informed written consent was obtained from human subjects under a protocol approved by the institutional review boards of University of Michigan-Ann Arbor.

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

Life sciences study design

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

Sample size	Thirteen patients with generalized pustular psoriasis (GPP) and 4 healthy control donors were recruited for single cell RNA sequencing, and additional 3 GPP patients were recruited for spatial sequencing.
Data exclusions	Cells with less than 500 transcripts or 100 genes, or more than 10% of mitochondrial expression were filtered out as low-quality cells in scRNA-seq analysis. After initial clustering of the remaining cells, clusters showing high mitochondrial expression were excluded.
Replication	The samples in the same disease condition can be considered biological replicates. There are in total 4 healthy and 13 generalized pustular psoriasis samples in scRNA-seq. There are 3 healthy and 3 generalized pustular samples in spatial-seq.
Randomization	Not applicable. No comparison of experimental groups is performed.
Blinding	Not applicable in the context of scRNA-seq and spatial-seq due to the technical complexity and exploratory nature of the techniques. Each cell serves as a data point, and blinding to the identity or condition of individual cells within the dataset is not practical.

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	Antibodies used include: anti-MPO (ThermoFisher Scientific, PA5-16672), anti-CASPASE8 (Abcam, ab220171), anti-TL1A (Abcam,
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ab234300), anti-DR3 (R&D Systems, MAB943), anti-TL1A (R&D Systems, 1319-TL-010). All primary antibody mentioned above were diluted at 1:100. Alexa Fluor 594 conjugated anti-rabbit IgG (Jackson Immuno Research, 711-585-152) and Alexa Fluor 488 conjugated anti-mouse IgG (Jackson Immuno Research, 715-545-151). Appropriate negative: rabbit IgG (Abcam, ab172730), mouse IgG1 (Abcam, ab280974).

Validation

Antibodies validated by the manufacturer were used.

Eukaryotic cell lines

Policy information about [cell lines and Sex and Gender in Research](#)

Cell line source(s)	N/TERT-2G, an immortalized keratinocytes cell line, was used with permission from James G. Rheinwald, Department of Dermatology, Brigham and Women's Hospital, Harvard Skin Disease Research Center, Boston, MA, United States.
Authentication	The N/TERT-2G line was developed in 2000(PMID:10648628). It has been validated to express key epithelial differentiation markers.
Mycoplasma contamination	N/TERT-2G was tested negative for Mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	This is a keratinocytes cell line, and there are no misidentified lines.

Plants

Seed stocks	<i>Report on the source of all seed stocks or other plant material used. If applicable, state the seed stock centre and catalogue number. If plant specimens were collected from the field, describe the collection location, date and sampling procedures.</i>
Novel plant genotypes	<i>Describe the methods by which all novel plant genotypes were produced. This includes those generated by transgenic approaches, gene editing, chemical/radiation-based mutagenesis and hybridization. For transgenic lines, describe the transformation method, the number of independent lines analyzed and the generation upon which experiments were performed. For gene-edited lines, describe the editor used, the endogenous sequence targeted for editing, the targeting guide RNA sequence (if applicable) and how the editor was applied.</i>
Authentication	<i>Describe any authentication procedures for each seed stock used or novel genotype generated. Describe any experiments used to assess the effect of a mutation and, where applicable, how potential secondary effects (e.g. second site T-DNA insertions, mosaicism, off-target gene editing) were examined.</i>