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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 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	scRNA sequencing data were generated by the Illumina HiSeq 2500 instrument. RT-qPCR data was collected using Quantstudio TM 12K Flex Real-time PCR system. Flow cytometry analysis were performed using a 3-laser Sony SA3800 Spectral Analyzer. Multiplexed immunofluorescence images were collected by the Vectra Polaris Automated Quantitative Pathology Imaging System (AKOYA).
Data analysis	For scRNA-Seq, 10× Genomics Cell Ranger software (version 3.1.0) was used to convert raw BCL files to FASTQ files, alignment and counts quantification. The cell by gene matrices for each sample were individually imported to Seurat version 3.1.1 for downstream analysis. For multiplexed immunofluorescence staining, spatial distance between target cells were measured by HALO-link platform. The statistical analysis were performed using GraphPad Prism (version 9.0) or SPSS (version 27) software.

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 raw scRNA and TCR sequence data reported in this paper have been deposited in the Genome Sequence Archive (Genomics, Proteomics & Bioinformatics 2021) in National Genomics Data Center (Nucleic Acids Res 2022), China National Center for Bioinformation / Beijing Institute of Genomics, Chinese Academy of Sciences (GSA-Human: HRA004050) that are publicly accessible at https://bigd.big.ac.cn/gsa-human/browse/HRA004050. The remaining data are available within the Article, Supplementary Information. Source data are provided with this paper.

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/ gender of human participants was determined based on self-reporting. The human participants providing samples for our study were broadly age- and sex-matched and are detailed in Supplemental Table 1 and Supplemental Table 4. Written informed consent were obtained from all participants.
Reporting on race, ethnicity, or other socially relevant groupings	Only Chinese patients (Shenzhen) are included.
Population characteristics	See Supplemental Table 1 and Supplemental Table 4.
Recruitment	See Patient inclusion and exclusion criteria in the Method part.
Ethics oversight	This study was approved by the Ethic Committee of Southern Medical University (NYSZYYEC20190017), and the Ethics Committee of SHSMU on Laboratory Animal Care (No. 2022-157).

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	No statistical method was used to predetermine sample size. Sample size was determined based on common standard in research field, ensuring a minimum of n=3 biological replicates for in vitro experiments and a minimum of n=5 animals for in vivo studies with sufficient reproducibility.
Data exclusions	P1T sample data were excluded due to a library exception (average: >7,000 genes per cell).
Replication	For in vivo study, at least two batch animals were used and the results were successfully replicated. For in vitro experiments, flow cytometry analysis were performed at lease three times and the results were successfully replicated. For human sample studies, a minimum of n=10 patient in each group was adopted to ensure sufficient reproducibility.
Randomization	For in vivo study, 5 male and 5 female mice were randomly allocated into each group to exclude the gender-specific effects. For human sample studies, eligible female and male participants were randomly enrolled.
Blinding	For eligible participants who were recruited for endoscopy examination, the endoscopic performance of stomach tissues was determined by two experienced gastrointestinal (GI) endoscopists. Animal studies were not blinded during samples collection as the researcher need to make sure the grouping was correct. For in vitro assays, experiments were not conducted in blind as we performed the experiments using the same protocol.

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	Primary antibodies we used for multiplexed immunofluorescence staining were anti-CD45 (HUABIO, EM1708-69), anti-HLA-DR/DP/DQ (ThermoFisher scientific, MA1-80678), anti-CD86 (Abcam ab220188), anti-CD4 (Abcam, ab133616), anti-CD68 (ZSGB-bio, ZM-0060), anti-CTLA4 (Abcam, ab237712), anti-CD8 (ThermoFisher scientific, MA1-80231). Primary antibodies and reagents used for flow cytometry were Fixable Viability Stain 450 (FVS450) (BD, 562247), Zombie NIR™ Fixable Viability Kit (Biolegend, 423105), CD45-AF532 (Thermo Fisher, 58-0451-82), CD11b-PE-Cy7 (BD, 552850), CD172a-APC (Biolegend, 144013), Ly-6G -BV421 (Biolegend, 127627), I-A I-E-PerCP-Cy5.5 (BD, 562363), F4/80-BV605 (BD, 743281), CD11c-APC (Biolegend, 117309), Alexa Fluor® 532 anti-human CD3 (eBioscience, 58-0038-42), PerCP/Cyanine5.5 anti-human CD4 (Biolegend, 300529), PE anti-human CD8 (Biolegend, 344705), APC anti-human CD152 (CTLA-4) (Biolegend, 349907), Brilliant Violet 605™ anti-human HLA-DR (Biolegend, 307640), PE anti-human CD11c (Biolegend, 371503), Alexa Fluor® 700 anti-human CD11b (Biolegend, 301355), Brilliant Violet 421™ anti-human CD1c (Biolegend, 331525), FITC anti-human CD19 (Biolegend, 302205), Human TruStain FcX™ (Biolegend, 422301), and APC Mouse IgG1, κ Isotype Ctrl (FC) (Biolegend, 400121).
Validation	All antibodies used in this study were commercially available and were validated by the manufactures, validation statements are available on the manufacturer's website.

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	THP-1 cells (TIB-202) were purchased from ATCC (ATCC, TIB-202). Murine dendritic cell line DC2.4 cells (Millipore, SCC142) were purchased from Millipore.
Authentication	THP-1 cells are authenticated by ATCC. DC2.4 cells are authenticated by Millipore.
Mycoplasma contamination	The cells lines used in this study are tested periodically for Mycoplasma infection and were negative.
Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell lines were used in this study.

Animals and other research organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research, and Sex and Gender in Research

Laboratory animals	C57BL/6 mice were used in this study. Mice were housed under 12-hour light/dark cycles in a pathogen-free room with clean bedding and free access to food and water, and temperature and humidity were kept at 22-26°C, 55%±5%. Cage and bedding changes were performed each week.
Wild animals	No wild animals were used in this study.
Reporting on sex	For mice study, 5 males and 5 females mice were randomly allocated into each group to exclude the gender-specific effects.
Field-collected samples	No field-collected samples were used in this study.
Ethics oversight	All animal studies were performed in accordance with the guidelines approved by the Animal Experimentation Ethics Committee of Southern Medical University (No. 2022-157).

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

Plants

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

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	Fresh gastric biopsies were endoscopically acquired from participants' mucosae or in either antrum or corpus, then washed with PBS and cut into approximately 1-mm3 pieces. Tissue digestion was performed in digestive enzyme mixture containing 2 ml pre-warmed RPMI-1640 (ThermoFisher scientific), 2 mg/ml dispase II (Solarbio, D6430), 1 mg/ml type IV collagenase (Solarbio, 17104019) and 2 mg/ml DNase I (Solarbio, D8070) for 30 min at 37 ℃, then deactivated with Fetal bovine Serum (FBS, Gibco, 16140071). Digested tissues were gently triturated with a 20 ml syringe plunger on a 70 μm cell-strainer (BD, 352350) until uniform cell suspensions were obtained. The suspended cells were centrifuged at 400 g for 6 min at 4 ℃, and washed with PBS. Cell pellets were re-suspended in autoMACS Rinsing solution. Single living immune cells (CD45+) were obtained using human CD45 microbeads (Miltenyi Biotec, 130-045-801) according to the manufacturer's instructions.
Instrument	3-laser Sony SA3800 Spectral Analyzer
Software	FlowJo V10.1
Cell population abundance	Cells were run to achieve > 10,000 events in the gated cell population.
Gating strategy	Gating was performed based on identifying a distinct population in FSC vs SSC plots.

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