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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	Flow cytometric analysis was performed on a LSR II Analyzer (BD Biosciences). Cell sorting was performed on the FACS Aria II cell sorter (BD Biosciences). ELISA data was collected by Multiscan FC(Thermo Fisher). RNAseq libraries were sequenced on the Illumina NovaSeq 6000. Immunofluorescence images were obtained by a fluorescence microscope (Nikon, Tokyo, Japan).
Data analysis	All statistical analyses were performed using R version 4.1.0 (R Core Team, Vienna, Austria), Python version 3.8.10 (Python Software Foundation, Beaverton, OR), SPSS version 25.0 (IBM Corporation, Chicago, IL)and GraphPad Prism software version 9 (GraphPad Software, San Diego, CA).

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 scRNA-seq data generated in this study are deposited at the NCBI Gene Expression Omnibus (GEO) with accession codes GSE221297. We confrm that our study is compliant with the "Guidance of the Ministry of Science and Technology (MOST) for the Review and Approval of Human Genetic Resources. The data have been deposited in the OMIX, China National Center for Bioinformation/Beijing Institute of Genomics, Chinese Academy of Sciences (https://ngdc.cncb.ac.cn/omix: accession no.OMIX005173). 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 of the study participants was determined through self-report during the initial demographic data collection.
Reporting on race, ethnicity, or other socially relevant groupings	All participants, of Asian ethnicity, were drawn from various rural and urban regions throughout China.
Population characteristics	Cohort I consisted of 9 T1D patients (5 new-onset and 4 in remission) and 3 HDs for single-cell sequencing. Cohort II consisted of 90 T1D patients at different stages (21 new-onset T1D, 34 T1D in remission, and 35 post-remission T1D patients) and 35 controls for the in vitro validation experiments. Cohort III included 70 T1D patients who were followed up for 24 months for establishing predictive models with machine learning.
Recruitment	All patients with T1D were enrolled at the Second Xiangya Hospital of Central South University (Changsha, Hunan, China) from December 2020 to July 2022. The diagnosis of T1D was made according to the International Society for Pediatric and Adolescent Diabetes (ISPAD) guidelines and our inclusion criteria were defined as follows: (i) insulin dependence from the time of disease onset, (ii) positivity for at least 1 of the 3 islet autoantibodies measured (glutamic acid decarboxylase antibody [GADA], insulinoma associated protein 2 antibody [IA-2A], and zinc transporter 8 antibody [ZnT8A]), (iii) disease duration of less than 2 years, and (iv) regular follow-up to measure fasting C-peptide (FCP), PCP, insulin dosage (INS dose), body mass index (BMI) or BMI z-score (BMI z), and HbA1c, enabling the identification of PR status. The definition of PR in this study was based on either mixed meal tolerance test (MMTT)-stimulated C-peptide levels (≥300 pmol/L) or the index of insulin dose adjusted HbA1c (IDAA1c) (IDAA1C = HbA1c [%] + 4* daily insulin dose/kg ≤9). When C-peptide values were missing, IDAA1C values were used to define the PR. Participants were classified into three subgroups according to their status: (i) patients with diabetes for less than 3 months who did not meet the definition of PR were classified as 'new-onset', (ii) patients currently in the PR stage were grouped into the 'PR' group, and (iii) patients whose PR phase had ended were defined as 'post-PR'. All participants enrolled in this study were uniformly managed by a diabetes clinical care team consisting of a physician, nurse educator, dietitian and pharmacist (and often including a kinesiologist and a psychologist or mental health specialist). The treatment regimens were guided by the same clinical team, ensuring standardised care across all study participants. Healthy controls were recruited through a recruitment advertisement at a local preschool education institution and local medical centers. All controls underwent oral glucose tolerance test (OGTT) screening, and their medical history was collected to exclude those with a positive family history of diabetes, infection, autoimmune disease, severe liver and kidney damage, or steroid hormone therapy.
Ethics oversight	Informed consent was provided by all subjects, and the study was approved by the Ethics Committee of the Second Xiangya Hospital of Central South University (SQ2016YFSF110035).

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	We performed sample size calculation using PASS 15 software (NCSS, Kaysville, UT, USA), with α=0.05 and 1–β=0.8, which indicated a required sample size of 16 individuals per group (Cohort II). Our actual sample size has exceeded expectations. For the remaining analysis, sample sizes are indicated in the figure legends.
Data exclusions	No data was excluded from the analysis.
Replication	All experiments were performed in at least three biological replicates and specific sample sizes are mentioned in the figure legends. Most experiments contain statistical analysis and significances of the results are indicated.
Randomization	For animal models, all mice used in this study were divided into different groups randomly. For cell culture, ELISA assay, and Flow cytometry, cells were divided into each plates and assigned into different treatments groups randomly.
Blinding	The investigators were not blinded to group allocation due to fixed experimental groups used for comparison.

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

1. Treg subsets identification
   - CD4: PerCP-Cy5.5, Clone SK3, Vendor BioLegend, Catalog# 980810, Dilution 1:20
   - CD25: BB515, Clone 2A3, Vendor BD Pharmingen, Catalog# 564467, Dilution 1:20
   - CD127: PE, Clone A109D5, Vendor BioLegend, Catalog# 986002, Dilution 1:20
   - CCR7: PE-Cy7, Clone G043H7, Vendor BioLegend, Catalog# 353226, Dilution 1:20
   - TIGIT: BV785, Clone A15153G, Vendor BioLegend, Catalog# 372736, Dilution 1:20
   - FOXP3: APC, Clone PCH101, Vendor eBioscience™, Catalog# 15-4776-42, Dilution 1:20
   - IL-10: BV421, Clone JES3-9D7, Vendor BioLegend, Catalog# 501422, Dilution 1:20
   - TGF-β1: FITC, Clone S20006A, Vendor BioLegend, Catalog# 300010, Dilution 1:20
   - granzyme B: BV510, Clone GB11, Vendor BD Pharmingen, Catalog# 563388, Dilution 1:20
   - KI67: BV650, Clone B56, Vendor BD Pharmingen, Catalog# 563757, Dilution 1:20

2. $CD8^+$ T cell subsets identification
   - CD4: FITC, Clone SK3, Vendor BioLegend, Catalog# 980802, Dilution 1:20
   - CD8: BB700, Clone G42-8, Vendor BD Pharmingen, Catalog# 745850, Dilution 1:20
   - CCR7: PE-Cy7, Clone G043H7, Vendor BioLegend, Catalog# 353226, Dilution 1:20
   - CD226: APC, Clone 11A8, Vendor BioLegend, Catalog# 338311, Dilution 1:20

3. $CD8^+$ T cell subsets phenotypes
   - Same as identification list above with additional:
   - TIGIT: BV785, Clone A15153G, Vendor BioLegend, Catalog# 372736, Dilution 1:20
   - CD127: PE, Clone A019D5, Vendor BioLegend, Catalog# 986002, Dilution 1:20
   - CD62L: Brilliant Violet 510™, Clone DREG-56, Vendor BD Pharmingen, Catalog# 563203, Dilution 1:20
   - CTLA-4: Brilliant Violet 711™, Clone BNI3, Vendor BioLegend, Catalog# 369632, Dilution 1:20

4. $CD8^+$ T cell subsets functions
   - Same as identification list above with additional:
   - TNF: PE/Dazzle™ 594, Clone MAb11, Vendor BioLegend, Catalog# 502946, Dilution 1:20

- IL-17A: PE, Clone SCPL1362, Vendor BD Pharmingen, Catalog# 560436, Dilution 1:5
- granzyme B: BV510, Clone GB11, Vendor BD Pharmingen, Catalog# 563388, Dilution 1:20

5. Anti-mouse antibodies
- CD226: Monoclonal antibody, Clone 10E5, Vendor Thermo Fisher, Catalog# 16-2261-85
- CD4: FITC, Clone GK1.5, Vendor BioLegend, Catalog# 100405, Dilution 1:20
- CD8: AF700, Clone 53-6.7, Vendor BioLegend, Catalog# 100730, Dilution 1:20
- CD226: BV605, Clone TX42.1, Vendor BioLegend, Catalog# 133613, Dilution 1:40
- TIGIT: PE, Clone 1G9, Vendor BioLegend, Catalog# 142103, Dilution 1:20
- CD25: BV711, Clone PC61, Vendor BioLegend, Catalog# 102049, Dilution 1:160
- CD127: APC-Cy7, Clone A7R34, Vendor BioLegend, Catalog# 135040, Dilution 1:80
- CCR7: PE-Cy7, Clone 4B12, Vendor BioLegend, Catalog# 120124, Dilution 1:20
- Ki-67: BV650, Clone 11F6, Vendor BioLegend, Catalog# 151215, Dilution 1:80
- IFN-r: PE-Cy7, Clone XMG1.2, Vendor BD Pharmingen, Catalog# 557649, Dilution 1:160
- IL-17A: APC, Clone TC11-18H10.1, Vendor BioLegend, Catalog# 506916, Dilution 1:80
- Granzyme B: BV421, Clone QA18A28, Vendor BioLegend, Catalog# 396414, Dilution 1:20

Validation

Antibodies were purchased from the above stated companies. Antibodies are well described and published elsewhere. Information can be sought from the manufactures website under the respective catalogue number.

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	Wild-type C57BL/6 mice (male, 6–8 weeks old) and NOD/ShiLtj mice (female, 4–6 weeks old) were purchased from GemPharmatech (JiangSu, China).
Wild animals	No wild animals were involved in this study.
Reporting on sex	In this study, the C57 mice were all male, and the NOD mice were all female.
Field-collected samples	This study does not include any field collected samples.
Ethics oversight	All animal experiments were performed according to the protocol approved by the Animal Ethics Committee of Central South University (protocol No. 2021sydw0252).

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

Clinical data

Policy information about clinical studies

All manuscripts should comply with the ICMJEguidelines for publication of clinical research and a completedCONSORT checklist must be included with all submissions.

Clinical trial registration	n/a
Study protocol	All patients with T1D were enrolled at the Second Xiangya Hospital of Central South University (Changsha, Hunan, China) from December 2020 to July 2022. The diagnosis of T1D was made according to the International Society for Pediatric and Adolescent Diabetes (ISPAD) guidelines and our inclusion criteria were defined as follows: (i) insulin dependence from the time of disease onset, (ii) positivity for at least 1 of the 3 islet autoantibodies measured (glutamic acid decarboxylase antibody [GADA], insulinoma associated protein 2 antibody [IA-2A], and zinc transporter 8 antibody [ZnT8A]), (iii) disease duration of less than 2 years, and (iv) regular follow-up to measure fasting C-peptide (FCP), PCP, insulin dosage (INS dose), body mass index (BMI) or BMI z-score (BMI z), and HbA1c, enabling the identification of PR status. HD were recruited through a recruitment advertisement at a local preschool education institution and local medical centers. All controls underwent oral glucose tolerance test (OGTT) screening, and their medical history was collected to exclude those with a positive family history of diabetes, infection, autoimmune disease, severe liver and kidney damage, or steroid hormone therapy. We also enrolled 20 T2D patients defined according to the American Diabetes Association (ADA) criteria with different blood glucose controls : (i) HbA1c <7.5% (n = 11) , and (ii) HbA1c ≥7.5% (n = 11).
Data collection	Regular follow-ups to collect demographic information, physical examination data, clinical data, and to draw 5 ml of venous blood; no pharmacological interventions are involved.
Outcomes	The primary outcome event is the end of the PR period; the secondary outcome event is CP-AUC failure. The definition of PR in this study was based on either mixed meal tolerance test (MMTT)-stimulated C-peptide levels (≥300 pmol/L) or the index of insulin dose adjusted HbA1c (IDAA1c) (IDAA1C = HbA1c [%] + 4* daily insulin dose/kg ≤9). When C-peptide values were missing, IDAA1C values were used to define the PR. Participants were classified into three subgroups according to their status: (i) patients with diabetes for less than 3 months who did not meet the definition of PR were classified as "new-onset", (ii) patients currently in the PR stage were grouped into the "PR" group, and (iii) patients whose PR phase had ended were defined as "post-PR".

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 venous blood samples were drawn into sodium heparin tubes from fasting subjects and processed within two hours. PBMCs were isolated by standard Ficoll-Paque Plus density-gradient centrifugation. The spleens or PLN of mice were collected and processed to obtain single-cell suspensions using a 40-µm cell strainer (352340, Corning, USA). Splenic erythrocytes were lysed with a red blood cell lysis buffer (SigmaAldrich, St. Louis, MO, USA), and T cells were enriched using nylon wool (18369-50, Polysciences, USA).
Instrument	LSR II instrument (BD Biosciences); Aria II cell sorter (BD Biosciences).
Software	FlowJo V10.8.1 (Treestar, San Carlos, CA, USA).
Cell population abundance	Populations were sorted at 95% purity, determined by flow cytometric analysis of post-sort samples.
Gating strategy	Gating strategies are included in the Supplementary Figures.

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