nature portfolio

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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	Data were collected from an excel sheet
Data analysis	Data analysis were performed using the factor analysis model MOFA https://biofam.github.io/MOFA2/.

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 research data associated with this paper, including gene expression data, frequencies of circulating immune cell subsets, levels of serum metabolic hormones, and MOFA scores, from which the figures are derived, are accessible at https://figshare.com/s/4324fbd6cd9d779a6c24 without any access restrictions. RNA-sequencing FastQ data have been deposited in the Gene Expression Omnibus (GEO) database and are publicly accessible under the accession code GSE287275.

Additionally, the codes utilized for the MOFA analysis are also accessible at https://biofam.github.io/MOFA2/tutorials.html. All other data are available from the corresponding author on reasonable request.

Human research participants

Policy information about studies involving human research participants and Sex and Gender in Research.

Reporting on sex and gender	Sex was included as a factor in our study design. However, no significant differences were observed between sexes within our patient population. Therefore, we conclude that our findings are applicable to both sexes.
Population characteristics	Co-variates used in this study are: age, sex, family history of T1D, T1D genetic predisposition (GRS-2), percentile of BMI (BMIp), presence of diabetic ketoacidosis (DKA), C-peptide levels, proinsulin and C-peptide ratio, neutrophil count and insulin dose adjusted HbA1c (idda1c). They are indicated in the manuscript
Recruitment	A cohort of 194 pediatric new-onset type 1 diabetes patients, hospitalized in the Pediatric Department of the IRCCS Ospedale San Raffaele (OSR), Milan (Italy), was enrolled from October 2018 to October 2022. Blood samples were prospectively collected between 5 and 10 days after diagnosis. Selection criteria were applied (see the manuscript for details) leading to the selection of 174 patients. Based on the availability of at least one layer of information among immunome, transcriptome and metabolic hormones data, a final cohort of n=146 patients was included in the study. A selection bias is evident in our study due to restrictions on the age range. Very young children were excluded due to limitations on the volume of blood that could be withdrawn. Similarly, patients aged 5-6 years old are underrepresented for the same reason.
Ethics oversight	The study was approved by the OSR Ethics Committee (protocol #TIGET004-DRI003).

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	NA. Preliminary data using these assays and this technique of analysis were unavailable to allow sample size calculations.
Data exclusions	Exclusion criteria were: 1) treatment with drugs including antibiotics, steroids, non-steroidal anti-inflammatory drugs and immunosuppressive agents, 2) sign of infection (fever, cough, rhinitis) over the last two weeks prior the blood withdrawal, 3) monogenic diabetes.
Replication	Several MOFA models were tested from 5 to 15 factors and all of them showed superimposable results
Randomization	NA. There is only one experimental group
Blinding	NA. There is only one experimental group

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

Methods

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

Antibodies

Antibodies used	All the details, including clones, supplier, catalogue number, and concentration used, are available here: doi: 10.3389/fimmu.2022.1026416
Validation	All the details can be found here: doi: 10.3389/fimmu.2022.1026416

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	This was an observational study with no need for registration
Study protocol	The study protocol was submitted at the local ethics committee.
Data collection	A cohort of 194 pediatric new-onset type 1 diabetes patients, hospitalized in the Pediatric Department of the IRCCS Ospedale San Raffaele (OSR), Milan (Italy), was enrolled from October 2018 to October 2022. Blood samples were prospectively collected between 5 and 10 days after T1D diagnosis.
Outcomes	No primary or secondary outcomes were set for this study