

Reporting Summary

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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

The following scRNA-seq datasets have been used in this study:

- Human Malaria associated B-cells : described in [42] containing 7,044 cells over 19,374 genes.
- Mouse Visual Cortex : described in [43] containing 65,540 cells over 25,187 genes.
- Human Cell Line: described in [32] containing 902 cells over 16,468 genes from three different human cell lines (H1975, H2228, HCC827).
- mESC Cell Cycle: described in [44] containing 275 cells over 23,506 genes, each gene is labeled according to its cell cycle state (G1, G2/M, S).
- Glioblastoma Multiforme (GBM) mouse model: described in [30] containing 9,175 cells over 18,531 genes from control and treatment (inhibition of P-selectin) samples.
- Usoskin's Dorsal Root Ganglia: described in [31] containing 799 cells over 25,334 genes from the dorsal root ganglia of the mouse identified by known markers associated with their function.
- Glioma tumor-reactive CD8+ T cells: as described in [45], this dataset contains 4,231 T cells over 14,202 genes from the mouse Glioma tumor microenvironment. All T cells were H-2Kb-SIINFEKL dextramer-positive (Dext+).

Data analysis

scNET is available for download via the git repository <https://github.com/madilabcode/scNET> including all the necessary files and conda environment.

In addition, the following packages and versions were used: scanpy==1.9.1, torch==2.2.1, torch-geometric==2.1.0.post1, networkx==2.8.6, gseapy==1.0.4, scipy==1.9.1, scikit-learn==1.0.2, pandas==1.5.0, umap-learn==0.5.3, numpy==1.23.2, scGPT=0.2.1, R=4.3.3, SAVER=1.1.2, DEEPIMPUTE=1.0, scLINE=0.1.0, CSCORE=0.0.0.9

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](#)

In this study, we utilized publicly available datasets as detailed in the Methods section, accessible through Gene Expression and ArrayExpress. The specific datasets used are: Malaria-associated B-cells dataset (GSE149729), Mouse visual cortex dataset (GSE102827), Human cell line dataset (GSE118767), mESC Cell cycle dataset (E-MTAB-2805), Glioblastoma dataset (GSE156663), Usoskin's Dorsal Root Ganglia dataset (GSE59739), and the Glioma tumor active CD8 T-cells dataset (GSE154795).

Human research participants

Policy information about [studies involving human research participants and Sex and Gender in Research](#).

Reporting on sex and gender

na

Population characteristics

na

Recruitment

na

Ethics oversight

na

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

Data exclusions

na

Replication

na

Randomization

na

Blinding

na

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