nature portfolio

Corresponding author(s): Aleksandrina Goeva, Evan Macosko

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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	No software was used for data collection.
Data analysis	Data analysis was carried out by custom code utilizing standard functions from Seurat v3, scanpy v1.9.3, scipy v1.11.0, and sklearn v1.2.2. Code and scripts to reproduce analyses presented here are available on Github at https://github.com/tudaga/LabelCorrection.

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 endothelial single-nucleus RNA-seq data used in this study are available in the GEO database under accession code GSE276570 [https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE276570].

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	not applicable
Reporting on race, ethnicity, or other socially relevant groupings	Published human research data (GSE193531) was used under a Non Human Subjects Research determination for this project NHSR-7271.
Population characteristics	not applicable
Recruitment	not applicable
Ethics oversight	not applicable

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	Sample size for the remyelination dataset generation was determined from prior studies. No statistical method was used to predetermine the sample size in the publicly available datasets.
Data exclusions	No datapoint (n=lesion from a single animal) was excluded from the demyelination dataset. No data was excluded from public datasets beyond standard preprocessing practice (see online Methods and reproducibility code).
Replication	Our sample represented n=3 separate animals case and control. We did not perform any direct further replication although follow up was performed using in situ hybridization. For the public datasets, reproducibility was examined using different hyperparameter values and we provide jupyter notebooks which allow recovering reported results.
Randomization	Littermates were randomly assigned to case (demyelination) or control (PBS) conditions. The publicly available datasets did not require randomization.
Blinding	All animal handling was performed blind to treatment condition. Although condition status was obvious during the extraction of lesions from frozen brains, samples were randomly labeled and the experimenter was blinded for all subsequent single-nucleus RNA sequencing and in situ hybridization experiments.

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

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/6J from Jackson labs (cat# 000664). All mice were housed on a 12-h light/dark cycle between 68°F and 79°F and 30–70% humidity.
Wild animals	None
Reporting on sex	All animals were males
Field-collected samples	None
Ethics oversight	All animal work was approved by the Broad's Institutional Animal Care and Use Committee (IACUC).

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

Plants

Seed stocks	not applicable
Novel plant genotypes	not applicable
Authentication	not applicable

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	Nuclei were extracted as per the protocol described in the paper
Instrument	Sony SH800
Software	Sony SH800 software
Cell population abundance	Approximately 30% of isolated nuclei were DAPI-positive
Gating strategy	We selected DAPI-positive nuclei, therefore we only gated on the DAPI signal and took the large singlet peak. Please note that a further description of the dataset will be included in a forthcoming paper.

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