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	Images were collected using the Leica Stellaris 8 DIVE confocal microscope with LAS X (Version: 4.8.0.28989). RNA-seq libraries were sequenced using the Illumina NovaSeq6000.
Data analysis	Confocal images were analyzed with Fiji (v2.14.0/1.54f). Statistical analysis was performed using GraphPad Prism (v10.3.0 (507)). Raw single nuclei RNA-seq data was demultiplexed to fastq files using Illumina's bcl2fastq (v2.20.0.422). Alignment for single nuclei data was performed using Cell Ranger (v6.0.1), and for single cell data, Cell Ranger (v7.2.0) was used. For mouse single cell/nuclei samples, CellBender (v0.3.0) was used to remove technical artifacts. Analysis was performed with the following packages: Python (v3.11.11), R (v4.4.0), Scanpy (v1.10.1), sysVI cross-species-integration tool (v0.0.0), scVI-tools (v1.1.1), Matplotlib (v.3.10.0), Upsetplot (v0.9.0), Venn (0.1.3), ggplot2 (v3.5.1), fgsea (v1.30.0). Examples of the code used are available on https://github.com/AdamsLabNotreDame/Aboelnour_et_al and archived on Zenodo (https://zenodo.org/records/19075392).

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

Single nuclei data generated in this study are deposited in GEO (GSE293850). Published available single cell mouse data are accessible on GEO (GSE182846) and (GSE148676). Raw human MS data are deposited to European Genome-Phenome Archive (EGA) as dataset EGA: EGAD00001009169, and the cleaned, annotated counts matrix is available on Zenodo (DOI: 10.5281/zenodo.8338963).

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	n/a
Reporting on race, ethnicity, or other socially relevant groupings	n/a
Population characteristics	n/a
Recruitment	n/a
Ethics oversight	n/a

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 methods were used to pre-determine sample sizes, instead, sample size was determined based on previous reports for similar experiments.
Data exclusions	No exclusions were made.
Replication	All transcriptomic mouse data were collected with at least 2 replicates per treatment and time point. RNAscope experiments were done as independent validations of the single cell/nuclei mouse data. RNAscope was performed in at least 4 independent biological replicates.
Randomization	Mice were randomly assigned to different experimental groups.
Blinding	Investigators were blinded while acquiring and analyzing data from different experimental groups. Once the analysis was completed, the group allocation was revealed.

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: rabbit anti-Olig2 (Millipore AB9610, 1:300), goat anti-Olig2 (R&D Systems AF2418, 1:100), goat anti-Cd206 (R&D Systems AF2535, 1:400), rat anti-Cd31 (BD Pharmingen 550274, 1:100), rabbit anti-Apoe (Cell Signaling 49285T, 1:100), rat anti-Cd11b (Biorad MCA74G, 1:250), rabbit anti-Iba1 (Wako 019-19741, 1:200), donkey anti-rabbit IgG Alexa Fluor 488 (Jackson ImmunoResearch 711-545-152, 1:500), donkey anti-rabbit IgG Alexa Fluor 594 (Jackson ImmunoResearch 711-585-152, 1:500), donkey anti-goat IgG Alexa Fluor 594 (Jackson ImmunoResearch 705-585-147, 1:500), donkey anti-rat IgG Alexa Fluor 488 (Jackson ImmunoResearch 712-545-150, 1:500), donkey anti-rat IgG Alexa Fluor 647 (Jackson ImmunoResearch 712-605-153, 1:500)

Validation: All antibodies have been validated for use in immunohistochemistry for use on mice, and additional information and citations can be found at the manufacturers website.

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: Species: Mus musculus, strains: C57Bl6/J (strain #000664)

Wild animals: n/a

Reporting on sex: Both male and female mice were used in our single nuclei RNA-seq analysis, and immunohistochemical studies.

Field-collected samples: n/a

Ethics oversight: All animal procedures were approved by the Institutional Animal Care and Use Committee (IACUC) of the Children's National Health System (protocol #30578) and of the University of Notre Dame (protocol #23-01-7578).

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