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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	N/A
Data analysis	GraphPad Prism 9 software (GraphPad Software Inc.)

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 data that support the findings of this study are available from the corresponding author upon reasonable request.

Field-specific reporting

Life sciences study design

All studies must disclose on these points even when the disclosure is negative.

Sample size	Statistical evaluations were performed using the Student's t-test or one- or two-way ANOVA or repeated-measures ANOVA, as indicated in the figure legends. The multiple comparisons adjustment was made using the Bonferroni correction. For behavioral analyses, the number of mice per group was >8, which represents a >98% probability of detecting a significant change if alpha is set at 0.05 and standard deviations (SDs) are 20% of average. Histological and immunohistochemical comparisons were performed using unpaired Student's t-test (2 groups) or a one-way (>2 groups) ANOVA, followed by post hoc correction. At least 4 mice per condition were used. This represents a >98% probability of detecting a significant change if alpha is set at 0.05 and SDs are 8% of average. Statistical powers were calculated using the maximum SD observed in our previous studies. For the in vitro experiments, the values of 3 wells were averaged for each tested condition and the experiments repeated three times.
Data exclusions	No data were excluded from the analyses.
Replication	Experiments were repeated on several animals for each group (n is indicated in the legends). All experiments were reproducible.
Randomization	Negative control groups (e.g. genotype, vehicle treatment) were included in all experiments. Male and female mice were randomly assigned (in equal numbers) to control and treatment groups.
Blinding	All quantifications were done blind with respect to the identity of the animals. Behavioral testing was carried out by a blinded investigator.

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
[ ]	[x] Antibodies
[ ]	[x] Eukaryotic cell lines
[x]	[ ] Palaeontology and archaeology
[ ]	[x] Animals and other organisms
[x]	[ ] Human research participants
[x]	[ ] Clinical data
[x]	[ ] Dual use research of concern

Methods

n/a	Involved in the study
[x]	[ ] ChIP-seq
[ ]	[x] Flow cytometry
[x]	[ ] MRI-based neuroimaging

Antibodies

Antibodies used	Primary antibodies used for immunofluorescence in this study are of the following sources (catalog numbers in parentheses) and were used at the indicated dilutions: rat anti-BrdU (1:750, Abcam, ab6326), rat anti-C3 (1:100, Abcam, ab11862), mouse anti-CC1 (1:500, Abcam, ab16794), rat anti-CD11b (1:250, AbD Serotec, MCA711), rabbit anti-Fos (1:500, Cell signaling, #2250), mouse anti-GalC (1:800, Millipore, MAB342), goat anti-Iba1 (1:1500, Novus Biologicals, NB100-1028), goat anti-IL-1α (1:100 dilution, R&D Systems, AF-400-NA), rabbit anti-Ki67 (1:200, Abcam, ab15580), rabbit anti-laminin (1:1000, Dako, Z0097), rat anti-Ly6G (1:2000, BD Biosciences, #551459), rat anti-NG2 (1:200, R&D Systems, MAB6689), mouse anti-O4 (1:400, R&D Systems, MAB1326), goat anti-Olig2 (1:400, R&D Systems, AF2418), rabbit anti-P2ry12 (1:500, AnaSpec, AS-55043A), goat anti-Sox9 (1:250, R&D Systems, AF3075), and rabbit anti-Sox9 (1:1000, Millipore, AB5535). Antibodies used for flow cytometry are from BD Biosciences (catalog and clone numbers in parentheses) and were used at the indicated dilutions: PerCP-conjugated anti-CD45 (1:50 dilution), Alexa 700-conjugated anti-CD11b (1:50), BD HorizonTM V450-conjugated anti-Ly6C (1:83), and PE-Cy7-conjugated anti-Ly6G (1:50).
Validation	The antibodies used in this study were chosen based on their extensive use in the literature (supported by the references available on the supplier's website) and a significant amount of experiments in our hands (see the references provided in the Methods section).

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	Primary oligodendrocyte precursor cells (OPCs) were isolated from the brain of postnatal day 7-9 (P7-P9) mice. Pro-oligodendrocytes were isolated from adult brains (6-8 weeks old mice). Microglia were isolated from the adult mouse spinal cord at 8 weeks of age. Endothelial cells were isolated from brain capillaries of 6-8 weeks old mice. Primary astrocytes were isolated from the cortex of P0-P2 mouse pups.

Authentication	Morphology and immunophenotypic characterization were performed to assess the purity of the cultures.
Mycoplasma contamination	The cell lines were not tested for mycoplasma contamination.
Commonly misidentified lines (See ICLAC register)	N/A

Animals and other organisms

Policy information about studies involving animals; ARRIVE guidelines recommended for reporting animal research

Laboratory animals	Mice were purchased from Charles River Laboratories, The Jackson Laboratory or Taconic or obtained from in-house colonies maintained at the Animal Research Facility of the Centre de recherche du Centre hospitalier universitaire de Québec–Université Laval.
Wild animals	N/A
Field-collected samples	N/A
Ethics oversight	All animal procedures were approved by the Université Laval Animal Care Committee and conducted in compliance with relevant ethical regulations and guidelines of the Canadian Council on Animal Care.

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

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	The sample preparation is described in the "Methods" subsection "Automated blood cell count, flow cytometry and cell sorting".
Instrument	FACS LSRII or FACSAria II flow cytometer, both from BD Biosciences.
Software	FlowJo software (v. 9.2; Tree Star Inc.).
Cell population abundance	The different cell populations evaluated are described in the "Methods" subsection "Automated blood cell count, flow cytometry and cell sorting". The abundance of each cell population is represented as an absolute cell number in each graph (see Supplementary Figure 6d).
Gating strategy	FACS sorting was used to isolate either oligodendrocyte lineage cells, microglia, endothelial cells or astrocytes needed for DNA and mRNA analyses by means of quantitative real-time PCR (qPCR) and RT-PCR (qRT-PCR).

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