nature portfolio

Corresponding author(s): Aletta van den Bosch

Last updated by author(s): 02-02-2024

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.

Please do not complete any field with "not applicable" or n/a. Refer to the help text for what text to use if an item is not relevant to your study.
For final submission: please carefully check your responses for accuracy; you will not be able to make changes later.

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	Qupath (version 0.4.3) used for quantification of immunohistochemistry
Data analysis	Performed in RStudio (version 1.2.5033; Boston, MA, USA) for R (version 4.2.0) using key packages ggplo2, lme4, plyr, ggpubr, ggpubr, Hmisc, corrplot

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 sequencing data generated in this study have been deposited in the Gene Expression Omnibus (GEO) database under accession code GSE234700. (https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE234700). The immunohistochemistry data generated in this study are provided in the Source data file.

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	Sex has been reported, not gender. Sex was both self-reported as assigned and there were no discepencies.
Reporting on race, ethnicity, or other socially relevant groupings	Information on race or ethnicity is not available at the Netherlands Brain Bank
Population characteristics	MS: 5M/2F, average age 66 ± 12, MS type 6SP/1PP. Stroke: 4M/3F, average age 80 ± 10
Recruitment	Performed by the Netherlands Brain Bank
Ethics oversight	Medical ethics committee of the VU medical center (Amsterdam, The Netherlands)

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 pathology analysis (n=167) based on total MS-cohort of NBB. Sample size for RNA sequencing and IHC (MS n=7, stroke n=7) based on tissue availability and maximum number of tissue blocks approved by the tissue advisory board of the NBB. No sample size calculation was performed.
Data exclusions	Three samples were excluded from sequencing analysis due to low quality of the sample
Replication	Due to scarcity of tissue and limitations on number of tissue blocks approved by the NBB no validation cohort was set up. Data was validated with IHC.
Randomization	Samples were sequenced, stained and analysed in random order
Blinding	During analysis of sequencing and IHC data, investigators were blinded to the group of each sample

Behavioural & social sciences study design

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

Study description	
Research sample	
Sampling strategy	
Data collection	
Timing	
Data exclusions	
Non-participation	
Randomization	

Ecological, evolutionary & environmental sciences study design

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

Study description	
Research sample	
Sampling strategy	
Data collection	
Timing and spatial scale	
Data exclusions	
Reproducibility	
Randomization	
Blinding	

Did the study involve field work? ☐ Yes ☐ No

Field work, collection and transport

Field conditions	
Location	
Access & import/export	
Disturbance	

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

Validation

Antigen	Supplier (cat#)	Clone	Dilution	Antigen retrieval	Validation statement
C1qB	Abcam (ab92508)	EPR2981	1:100*	Tris EDTA buffer pH9	Validated by manufactorer for IHC-P and WB for human samples
C3d	Dako (A0063)	Polyclonal	1:300	Citrate buffer pH6	Validated by manufactorer for human samples
C5b9	Dako (M077701-8)	aE11	1:100	Citrate buffer pH6	Validated by the manufactorer for IHC, reacts both with soluble and solid form
CD138	BioRad (MCA2459T)	B-A38	1:250	Citrate buffer pH6	Validated by the manufactorer for IHC for human samples
CD20	Dako (M0755)	L26	1:100	Citrate buffer pH6	Validated by the manufactorer for IHC for human samples
CD3	Dako (A0452)	Polyclonal	1:100	Citrate buffer pH6	Validated by the manufactorer for IHC for human samples
CD38	Atlas antibodies (HPA022132)	Polyclonal	1:3000	Citrate buffer pH6	Validated by the manufactorer for IHC for human samples
CD4	Dako (M7310)	4B12	1:100	Tris EDTA buffer pH9	Validated by the manufactorer for IHC, IP, WB, Flow for human samples
CD8	BD Biosciences (641400)	SK1	1:500	Citrate buffer pH6	Validated by the manufactorer for flow cytometry, used by us for IHC: (Fransen et al, Brain, 2020, doi: 10.1093/brain/awaa117
DAGLB	Atlas Prestige (HPA069377)	Polyclonal	1:50*	PBS pH7.6	Validated by the manufactorer for IHC for human samples
E06	Avanti (330002S)	T15	1:100	PBS pH7.6	Validated by the manufactorer for IHC, ELISA, WB for human samples
FABP5	RabMab (ab255276)	EPR22552-64	1:2000	Tris EDTA buffer pH9	Validated by the manufactorer for IHC, WB, ICC/IF for human samples
HLA-DR	Dako (M0775)	CR3	1:100	Citrate buffer pH6	Validated by the manufactorer for IHC for human samples
IAH1	Invitrogen (PA5-65270)	Polyclonal	1:50*	PBS pH7.6	Validated by the manufactorer for IHC for human samples
Iba1	Wako (019-19741)	Polyclonal	1:500	Citrate buffer pH6	Validated by the manufactorer for ICC for human samples, used by us for IHC: (Hendrickx et al, Journal of Neuroimmunology, 2017, doi: 10.1016/j.jneuroim.2017.04.007
IGG	Abcam (ab218427)	Polyclonal	1:100	Citrate buffer pH6	Validated by the manufactorer for Protein Array, IHC for human samples
LAMP1	Abcam (ab24170)	Polyclonal	1:200	Citrate buffer pH6	Validated by the manufactorer for IHC and WB for human samples
MBP	Sigma (AB980)	Polyclonal	1:200	Citrate buffer pH6	Validated by the manufactorer for IHC and WB for human samples
PCNA	Santa Cruz (sc-25280)	PC10	1:1000	Citrate buffer pH6	Validated by the manufactorer for IHC, WB and ELISA for human samples
PLP	Secotec (MCA839G)	plpc1	1:3000	Citrate buffer pH6	Validated by the manufactorer for IHC, flow cytometry, WB for human samples
SMI312	Eurogentec (SMI-312R)	SMI-312R	1:6000	Citrate buffer pH6	Validated by the manufactorer for IHC and WB for human samples
STARD13	Invitrogen (PA5-63622)	Polyclonal	1:300*	PBS pH7.6	Validated by the manufactorer for IHC for human samples
Tomm20	RabMab (ab186735)	EPR15581-54	1:100*	Citrate buffer pH6	Validated by the manufactorer for IHC, ICC, WB, Flow Cyt for human samples
VWF	Atlas antibodies (AMAb90928)	CL1950	1:500*	Citraconic anhydride pH6	Validated by the manufactorer for IHC for human samples

Eukaryotic cell lines

Policy information about cell lines and Sex and Gender in Research

Cell line source(s)	
Authentication	
Mycoplasma contamination	
Commonly misidentified lines (See ICLAC register)	

Palaeontology and Archaeology

Specimen provenance	
Specimen deposition	
Dating methods	

☐ Tick this box to confirm that the raw and calibrated dates are available in the paper or in Supplementary Information.

Ethics oversight	

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

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	
Wild animals	
Reporting on sex	
Field-collected samples	
Ethics oversight	

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

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	
Study protocol	
Data collection	
Outcomes	

Dual use research of concern

Policy information about dual use research of concern

Hazards

Could the accidental, deliberate or reckless misuse of agents or technologies generated in the work, or the application of information presented in the manuscript, pose a threat to:

No	Yes	
☐	☐	Public health
☐	☐	National security
☐	☐	Crops and/or livestock
☐	☐	Ecosystems
☐	☐	Any other significant area

Experiments of concern

Does the work involve any of these experiments of concern:

No	Yes	
☐	☐	Demonstrate how to render a vaccine ineffective
☐	☐	Confer resistance to therapeutically useful antibiotics or antiviral agents
☐	☐	Enhance the virulence of a pathogen or render a nonpathogen virulent
☐	☐	Increase transmissibility of a pathogen
☐	☐	Alter the host range of a pathogen
☐	☐	Enable evasion of diagnostic/detection modalities
☐	☐	Enable the weaponization of a biological agent or toxin
☐	☐	Any other potentially harmful combination of experiments and agents

Plants

Seed stocks

Novel plant genotypes

Authentication

ChIP-seq

Data deposition

☐ Confirm that both raw and final processed data have been deposited in a public database such as GEO.

☐ Confirm that you have deposited or provided access to graph files (e.g. BED files) for the called peaks.

Data access links
May remain private before publication.

Files in database submission

Genome browser session
(e.g. UCSC)

Methodology

Replicates

Sequencing depth

Antibodies

Peak calling parameters

Data quality

Software

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

Instrument

Software

Cell population abundance

Gating strategy

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

Magnetic resonance imaging

Experimental design

Design type

Design specifications

Behavioral performance measures

Imaging type(s)

Field strength

Sequence & imaging parameters

Area of acquisition

Diffusion MRI ☐ Used ☐ Not used

Preprocessing

Preprocessing software

Normalization

Normalization template

Noise and artifact removal

Volume censoring

Statistical modeling & inference

Model type and settings

Effect(s) tested

Specify type of analysis: ☐ Whole brain ☐ ROI-based ☐ Both

Statistic type for inference

(See Eklund et al. 2016)

Correction

Models & analysis

n/a	Involved in the study
☐	☐ Functional and/or effective connectivity
☐	☐ Graph analysis
☐	☐ Multivariate modeling or predictive analysis

Functional and/or effective connectivity

Graph analysis

Multivariate modeling and predictive analysis