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Reporting Summary

Nature Research 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 Research policies, see Authors & Referees and the Editorial Policy Checklist.

Statistical parameters

When statistical analyses are reported, confirm that the following items are present in the relevant location (e.g. 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
☐	☒	An indication of 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 statistics 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
☐	☒	Clearly defined error bars *State explicitly what error bars represent (e.g. SD, SE, CI)*

Our web collection on statistics for biologists may be useful.

Software and code

Policy information about availability of computer code

Data collection	Nikon NIS Elements software AR 4.6.
Data analysis	GraphPad_Prism (version 7.0); Image J; Image Pro Plus (version 6.0); Excel 2013; Adobe Illustrator CC 2015; Adobe photoshop CS3; NIS Elements AR software AR 4.6.

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/reviewers upon request. We strongly encourage code deposition in a community repository (e.g. GitHub). See the Nature Research 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 list of figures that have associated raw data
- A description of any restrictions on data availability

All data supporting the findings of the current study are available from the corresponding author.

Field-specific reporting

Please select 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/authors/policies/ReportingSummary-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 and our sample size was chosen according to standard practices in the field.
Data exclusions	No data were excluded from our studies.
Replication	All attempts at replication were successful. Experiments were carried out at least three times unless otherwise indicated.
Randomization	Litter mates were ear tagged and randomly assigned to different experimental groups.
Blinding	All results from animal work were evaluated independently from two blinded experienced researchers. Quantification of microvessels diameter was performed independently by two blinded experienced researchers.

Reporting for specific materials, systems and methods

Materials & experimental systems

n/a	Involved in the study
☒	☐ Unique biological materials
☐	☒ Antibodies
☐	☒ Eukaryotic cell lines
☒	☐ Palaeontology
☐	☒ Animals and other organisms
☒	☐ Human research participants

Methods

n/a	Involved in the study
☒	☐ ChIP-seq
☐	☒ Flow cytometry
☒	☐ MRI-based neuroimaging

Antibodies

Antibodies used	Anti-CD31(#550274; 1:100 for IF) was from BD Biosciences (Franklin Lakes, NJ). Anti-MBP (ab40390; 1:200 for IF; 1:1,000 for ELISA),anti-Ki-67 (ab15580; 1:200 for IF), anti-CD11b (ab133357; 1:100 for IF), anti-Von Willebrand Factor (vWF; ab11713; 1:100 for IF), anti-α-SMA (ab124964; 1:400 for IF), anti-fibronectin (ab23750; 1:200 for IF; 1:1,000 for WB), anti-collagen I (ab34710; 1:200 for IF), anti-GFAP (#ab53554, 1:400and GAPDH (ab181602; 1:3,000 for WB) were purchased from Abcam (Cambridge, MA). The antibodies against LC3 (#4108; 1:100 for IF; WB 1:1,000), Atg5 (D5F5U, #12994, 1:1000 for WB), Rab5 (#3547; 1:50 for IF), Rab7 (#9367; 1:100 for IF) and GABARAP (#13733; 1:200 for IF)were purchased from Cell Signaling Technology (Danvers, MA). Another anti-MBP(MAB386; 1:1,000 for ELISA) was purchased from Millipore (Billerica, MA), anti-VCAM-1 (sc-8304; 1:250 for WB) was purchased from Santa Cruz Biotechnology (Dallas, TX) and anti-Lamp1 (1D4B; 1:25 for IF) was from Developmental Studies Hybridoma Bank.Anti-tubulin (DM1A; 1:5,000 for WB) was from Sigma-Aldrich (St. Louis, MO). Anti-p62 (PM045; 1:1,000 for WB) was from MBL (Woburn, MA). Anti-ubiquitin (FK2, #BML-PW8810-0500; 1:200 for IF) was from ENZO Life Sciences.Anti-Iba-1 (#019-19741, 1:200 for IF) was from FUJIFILM Wako Pure Chemical Corporation (Osaka, Japan). F4/80 and Mac-2 antibodies were produced by hybridoma cell lines (HB-198 for F4/80; TIB-166for Mac-2) from American Tissue Culture Collection (ATCC, Manassas, VA). VEGF neutralizing antibody (#AF-493-NA,20µg/ml for neutralization) and pan-TGF-β neutralizing antibody (#MAB1835R-100, 20µg/ml for neutralization) were from R&D Systems (Minneapolis, MN). Alexa Fluor 488, 555, 647-conjuated secondary antibodies (1:600 for IF) and HRP-conjugated secondary antibody (1:3,000 for ELISA) were purchased from Invitrogen.IRDye-800CW or IRDye-680LT-conjugated secondary antibodies (1:20,000 for WB) were from LI-COR Bioscience.
Validation	The antibodies used in the manuscript are all commercially available. All the antibodies used here have been well characterized and validated by the providers or previous publications. Below are the providers' links to the antibody information and relevant publications. anti-CD31 (#550274; 1:100 for IF) was from BD Biosciences (Franklin Lakes, NJ). (http://www.bdbiosciences.com/us/applications/research/stem-cell-research/cancer-research/mouse/purified-rat-anti-mouse-cd31-mec-133/p/550274)

anti-MBP (ab40390; 1:200 for IF; 1:1,000 for ELISA) (https://www.abcam.com/myelin-basic-protein-antibody-ab40390.html#top-300)

anti-Ki-67 (ab15580; 1:200 for IF) (https://www.abcam.com/ki67-antibody-ab15580.html)

anti-CD11b (ab133357; 1:100 for IF) (https://www.abcam.com/cd11b-antibody-epr1344-ab133357.html)

anti-Von Willebrand Factor (vWF; ab11713; 1:100 for IF) (https://www.abcam.com/von-willebrand-factor-antibody-ab11713.html)

anti-α-SMA (ab124964; 1:400 for IF) (https://www.abcam.com/alpha-smooth-muscle-actin-antibody-epr5368-ab124964.html)

anti-fibronectin (ab23750; 1:200 for IF; 1:1,000 for WB) (https://www.abcam.com/fibronectin-antibody-ab23750.html)

anti-collagen I (ab34710; 1:200 for IF) (https://www.abcam.com/collagen-i-antibody-ab34710.html)

anti-GFAP (#ab53554, 1:400)(https://www.abcam.com/gfap-antibody-ab53554.html)

anti-GAPDH (ab181602; 1:3,000 for WB) (https://www.abcam.com/gapdh-antibody-epr16891-loading-control-ab181602.html)

anti-LC3 (#4108; 1:100 for IF; WB 1:1,000)(https://www.cellsignal.com/products/primary-antibodies/lc3a-b-antibody/4108)

anti-Atg5 (D5F5U, #12994, 1:1000 for WB)(https://www.cellsignal.com/products/primary-antibodies/atg5-d5f5u-rabbit-mab/12994)

anti-Rab5 (#3547; 1:50 for IF) (https://www.cellsignal.com/products/primary-antibodies/rab5-c8b1-rabbit-mab/3547)

anti-Rab7 (#9367; 1:100 for IF) (https://www.cellsignal.com/products/primary-antibodies/rab7-d95f2-xp-rabbit-mab/9367)

anti-GABARAP (#13733; 1:200 for IF)(https://www.cellsignal.com/products/primary-antibodies/gabarap-e1j4e-rabbit-mab/13733)

another anti-MBP (MAB386; 1:1,000 for ELISA) (http://www.emdmillipore.com/US/en/product/Anti-Myelin-Basic-Protein-Antibody-a.a.-82-87,MM_NF-MAB386)

anti-VCAM-1 (sc-8304; 1:250 for WB) (https://www.scbt.com/scbt/product/vcam-1-antibody-h-276)

anti-Lamp1 (1D4B; 1:25 for IF) (http://dshb.biology.uiowa.edu/LAMP-1)

anti-tubulin (DM1A; 1:5,000 for WB) (https://www.sigmaaldrich.com/catalog/search?interface=All&term=DM1A%20anti-%CE%B1-tubulin&N=0&focus=product&lang=en&region=US)

anti-p62 (PM045; 1:1,000 for WB) (Woburn, MA)(https://www.mblintl.com/products/pm045)

anti-ubiquitin (FK2, #BML-PW8810-0500; 1:200 for IF) (http://www.enzolifesciences.com/BML-PW8810/mono-and-polyubiquitinylated-conjugates-monoclonal-antibody-fk2/)

anti-Iba-1 (#019-19741, 1:200 for IF) (http://www.e-reagent.com/uh/Shs.do?dspWkfcode=019-19741&_ga=2.114949767.1613726397.1542898843-1335469264.1542898843)

F4/80 and Mac-2 antibodies were produced by hybridoma cell lines (HB-198 for F4/80; TIB-166 for Mac-2) from American Tissue Culture Collection (ATCC, Manassas, VA).

VEGF neutralizing antibody (#AF-493-NA, 20μg/ml for neutralization)(https://www.rndsystems.com/cn/products/mouse-vegf-164-antibody_af-493-na)

pan-TGF-β neutralizing antibody (#MAB1835R-100, 20μg/ml for neutralization) (https://www.rndsystems.com/cn/products/tgf-beta1-2-3-antibody-1d11r_mab1835r)

Eukaryotic cell lines

Policy information about cell lines

Cell line source(s)	The mouse brain microvascular endothelial cell line (bEnd.3, CRL2299) and Neuro-2a (N2A, CCL-131) were purchased from American Tissue Culture Collection (ATCC).
Authentication	The endothelial nature of bEnd3 was confirmed by the observed expression of von Willebrand factor and CD31, morphology and uptake of fluorescently labeled low density lipoprotein (LDL). The nature of neuro-2a cell line was verified by its differentiation ability into neuronal cells.
Mycoplasma contamination	The cell lines were tested negative for mycoplasma contamination by using MycoScope Mycoplasma PCR Detection Kit (Cat# MY 01050, Genlantis)

Commonly misidentified lines (See ICLAC register)	No commonly misidentified cell lines were used.

Animals and other organisms

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

Laboratory animals	C57BL/6J, C57BL/6-Tg(ACTB-EGFP)1Osb/J and C3Fe.SWV-MBPshi/J mice were purchased from Jackson Laboratory and maintained in pathogen-free animal facility. All are female mice for in vivo assays and primary cell cultures. Myelin debris was isolated from 8-10 weeks old C57BL/6J and C3Fe.SWV-MBPshi/J mice brains, respectively. Bone marrow-derived macrophages were generated from 6-8 weeks old C57BL/6J mice. Primary astrocytes were isolated from 2-3 days old C57BL/6 mice. Thoracic spinal cord contusion injuries were performed on 8-10 week old C57BL/6J mice. 7-8 week old female C57BL/6J mice were used for EAE induction. Bone marrow cells from 8 weeks old C57BL/6-Tg(ACTB-EGFP)1Osb/J mice were transplanted to pre-iradiated C57BL/6J mice to generate GFP + bone marrow chimeras. All animal experiments were approved by Florida State University Animal Care and Use Committee (ACUC).
Wild animals	This study did not involve wild animals.
Field-collected samples	This study did not involve samples collected from field.

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	Primary endothelial cells or cell line were laden with CFSE-labeled myelin debris. The remaining or non-ingested myelin debris was removed. Cell were then trypsinized and resuspended in PBS for FACS detection. For FACS sorting of Atg5 KO EC clone, ECs were transfected with a CRISPR-Cas9 vector expressing EGFP. After 48 hr, cells were trypsinized into single cells and sorted by FACS.
Instrument	BD FACSCanto
Software	BD FACSDiva
Cell population abundance	Primary endothelial cells are pure after verifying two endothelial-specific markers CD31 and vWF. The cell line of endothelial cells is purchased from ATCC and has been well characterized. For Atg5 KO EC clone, single cell was sorted and sorted cells were enough to be seeded on 96-well plate for colony expansion.
Gating strategy	Low FSC/SSC population were identified as cell debris and non-ingested myelin debris by preliminary experiments and excluded in next cell phagocytosis experiments. CFSE-myelin positive cells were gated through FITC channel. Atg5 KO EC single cell was sorted according to the expression of EGFP.

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