

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 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

Wireless readout and stimulation was performed using a 13.56 MHz desktop reader/writer with built-in antenna (233015, Gao RFID). Software provided by the vendor (DevMgr, Gao RFID) was used to control the readout sampling interval and data storage.

Data analysis

For the open-field test for mice with and without the smart bandage, the recorded videos were analyzed using the DeepLabCut (v. 2.2) deep learning architecture to measure the total travel distances for each group. For the excisional splinted wound model, wound area was determined using ImageJ software (v. 10.2) by a blinded observer (NIH, Bethesda, MD). For the contact burn model, photographs of burns were analyzed using ImageJ software (v. 10.2).

For the parabiosis model, flow cytometry data was analyzed using FlowJo (v. 10.5.3) (Becton Dickinson, San Jose, CA).

For tissue analysis, Image J (v. 10.2) was used to binarize images taken with the same settings, and intensity thresholds were used to quantify staining based upon pixel-positive area averaged over three high power fields. ImageJ (v. 10.2) was also used to quantify dermal thickness.

For dermal collagen analysis, the CT-FIRE algorithm (v. 2.0) was used to analyze individual fiber metrics such as length, width, angle, and curvature. CurveAlign 4.0 was also used to quantify all fiber angles and strength of alignment within an image. Complexity and heterogeneity were measured using the ImageJ plug-in FracLac (v. 2.5). Lastly, MatFiber was used to further quantify fiber alignment, reported as mean vector length.

For the alignment/migration study of HUVEC cells, live cells were imaged in real time using a Leica TCS SP8 confocal microscope (Leica) and analyzed using ImageJ (v. 10.2) software.

For single cell RNA-seq data processing, normalization, and cell cluster identification, raw unique molecular identifier counts were normalized and subsequently natural log transformed with a pseudocount of 1 using the R package Seurat (version 3.1.1). Cell annotations were ascribed using the SingleR package (version 3.11) against the ImmGen database. Louvain clustering was performed using a resolution of 0.5 and 15

nearest neighbors. Cell-type markers were generated using Seurat's native FindMarkers function.

For pseudotime analysis, the Monocle 3 package in R (version 3.0.2.0) was used. The principal GraphTest function using the Moran's I statistic was also employed to identify correlated genes on trajectory embedded in the manifold.

For RNA velocity analysis, scVelo (v. 0.5.5) was used.

CytoTRACE (Cellular Trajectory Reconstruction Analysis using gene Counts and Expression) was also used to infer the cell differentiation trajectories.

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 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

The authors declare that all data supporting the findings of this study are available within the paper and its supplementary information.

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](https://www.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 was determined by the number of biological and technical replicates necessary for each experiment. The number of biological replicates was a minimum of 3, with several technical replicates in each sample, sufficient to satisfy criteria for statistical analyses on the resulting data collected. Specifically, sample sizes were determined empirically based on the authors' extensive experience with scRNA-seq, from which we and the broader community have found that minimum n=3 biological replicates is almost always appropriate for syngeneic animal studies. ARRIVE 2.0 guidelines (Animal Research: Reporting of In Vivo Experiments) were used to maximize quality and reliability of research reported.
Data exclusions	No data were excluded from the analyses.
Replication	All experimental findings, including chemical synthesis, material characterizations, and animal experiments, were reliably reproduced with time intervals over at least three months.
Randomization	Experimental groups were formed based on what was being tested with random selection. Mice within one experiment were of the same strain, batch, and birthday. Mice were allocated to different experimental arms of a study using the ARRIVE 2.0 guidelines (Animal Research: Reporting of In Vivo Experiments).
Blinding	All histology and immunofluorescent images shown are representative images of multiple experiments and were performed by a blinded observer. Wound area in the excisional splinted wound model was determined using ImageJ software by a blinded observer (NIH, Bethesda, MD). For the rest of the experiments listed in our study, investigators were blinded to group allocation during data collection and analysis.

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

Methods

n/a	Involved in the study
☒	☒ Antibodies
☒	☒ Eukaryotic cell lines
☒	☐ Palaeontology and archaeology
☐	☒ Animals and other organisms
☒	☐ Human research participants
☒	☐ Clinical data
☒	☐ Dual use research of concern

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

Antibodies

Antibodies used

Primary antibodies used in this work include PE/Cy7 rat anti-mouse CD11b antibody (101216, 1:100, Biolegend), PE rat anti-mouse CD163 antibody (156704, 1:100, Biolegend), and APC rat anti-mouse F4/80 antibody (123116, 1:100, Biolegend). For CD31 (ab28364, Abcam), α -SMA (ab5694, Abcam), CD206 (ab64693, Abcam), and CD163 (ab182422, Abcam). DAPI (ab104139, Abcam) was used to stain for nuclei. Secondary antibodies used in this work include Goat anti-Mouse IgG (H+L) Highly Cross-Adsorbed Secondary Antibody, Alexa Fluor Plus 488, A32723, 1:250, Thermo-Fisher; Goat anti-Rabbit IgG (H+L) Highly Cross-Adsorbed Secondary Antibody, Alexa Fluor Plus 647, A32733, 1:250, Thermo-Fisher.

Validation

Validation for primary antibodies can be found on the BioLegend and Abcam websites, including: <https://www.biolegend.com/en-us/products/pe-cyanine7-anti-mouse-human-cd11b-antibody-1921?GroupID=BLG10427> for PE/Cy7 rat anti-mouse CD11b, <https://www.biolegend.com/en-us/products/pe-anti-mouse-cd163-antibody-19309?GroupID=GROUP564> for PE rat anti-mouse CD163, <https://www.biolegend.com/en-us/products/apc-anti-mouse-f4-80-antibody-4071?GroupID=BLG5319> for APC rat anti-mouse F4/80, <https://www.abcam.com/cd31-antibody-ab28364.html> for CD31, <https://www.abcam.com/alpha-smooth-muscle-actin-antibody-ab5694.html> for α -SMA, <https://www.abcam.com/mannose-receptor-antibody-ab64693.html> for CD206, <https://www.abcam.com/cd163-antibody-epr19518-ab182422.html> for CD163, and <https://www.abcam.com/mounting-medium-with-dapi-aqueous-fluoroshield-ab104139.html> for DAPI.

The antibody for PE/Cy7 rat anti-mouse CD11b has been used in previous publications including Myelin oligodendrocyte glycoprotein-specific antibodies from multiple sclerosis patients exacerbate disease in a humanized mouse model in *J Autoimmun*, PMID: 28964723; A Three-Day Consecutive Fingolimod Administration Improves Neurological Functions and Modulates Multiple Immune Responses of CCI Mice in *Mol. Neurobiol.*, PMID: 27924525; and Inhibition of Endosteal Vascular Niche Remodeling Rescues Hematopoietic Stem Cell Loss in AML in *Cell Stem Cell*, PMID: 29276143.

The vendor for the antibody for PE rat anti-mouse CD163 did not provide information about its prior use in publication. We validated the efficacy of the antibody according to the vendor's instruction.

The antibody for APC rat anti-mouse F4/80 has been used in previous publications including Macrophages produce IL-33 by activating MAPK signaling pathway during RSV infection in *Mol Immunol*, PMID: 28531812; Differential expression of Cathepsin E in transthyretin amyloidosis: from neuropathology to the immune system in *J Neuroinflammation*, PMID: 28583160; and Dectin-2 is a primary receptor for NLRP3 inflammasome activation in dendritic cell response to *Histoplasma capsulatum* in *PLoS Pathog*, PMID: 28671985.

The antibody for CD31 has been used in previous publications including Stem Cell/Oxygen-Releasing Microparticle Enhances Erectile Function in a Cavernous Nerve Injury Model in *Tissue Eng Part A*, PMID: 32122268; Construction and Optimization of an Endometrial Injury Model in Mice by Transcervical Ethanol Perfusion in *Reprod Sci*, PMID: 32939736; and Dilated microvessel with endothelial cell proliferation involves intraplaque hemorrhage in unstable carotid plaque in *Acta Neurochir (Wien)*, PMID: 32995934.

The antibody for α -SMA has been used in previous publications including Photobiomodulation and estrogen stabilize mitochondrial membrane potential in angiotensin-II challenged porcine aortic smooth muscle cells in *J Biophotonics*, PMID: 32888351; Elimination of NF- κ B signaling in Vimentin+ stromal cells attenuates tumorigenesis in a mouse model of Barrett's Esophagus in *Carcinogenesis*, PMID: 33068426; and Downregulating long non-coding RNA PVT1 expression inhibited the viability, migration and phenotypic switch of PDGF-BB-treated human aortic smooth muscle cells via targeting miR-27b-3p in *Hum Cell*, PMID: 33106979.

The antibody for CD206 has been used in previous publications including Mono-macrophage-Derived MANF Protects Against Lipopolysaccharide-Induced Acute Kidney Injury via Inhibiting Inflammation and Renal M1 Macrophages in *Inflammation*, PMID: 33145627; Targeting the RNA-Binding Protein HuR Alleviates Neuroinflammation in Experimental Autoimmune Encephalomyelitis: Potential Therapy for Multiple Sclerosis in *Neurotherapeutics*, PMID: 33200288; and Macrophage polarization in peri-implantitis lesions in *Clin Oral Investig.*, PMID: 32886246.

The antibody for CD163 has been used in previous publications including Immune response drives outcomes in prostate cancer: implications for immunotherapy in *Mol Oncol.*, PMID: 33338321; The Paradox Effect of Calcification in Carotid Atherosclerosis: Microcalcification is Correlated with Plaque Instability in *Int J Mol Sci.*, PMID: 33401449; and A partially demineralized allogeneic bone graft: in vitro osteogenic potential and preclinical evaluation in two different intramembranous bone healing models in *Sci Rep.*, PMID: 33649345.

The antibody for DAPI has been used in previous publications including Strain Specific Responses in a Microbead Rat Model of Experimental Glaucoma in *Curr Eye Res.*, PMID: 32842792; The potential use of tideglusib as an adjuvant radio-therapeutic treatment for glioblastoma multiforme cancer stem-like cells in *Pharmacol Rep.*, PMID: 33140310; and Dynamic changes in the systemic immune responses of spinal cord injury model mice in *Neural Regen Res.*, PMID: 32859802.

Validation for secondary antibodies can be found on the Thermo Fisher website, including <https://www.thermofisher.com/antibody/product/Goat-anti-Mouse-IgG-H-L-Highly-Cross-Adsorbed-Secondary-Antibody-Polyclonal/A32723> and <https://www.thermofisher.com/antibody/product/Goat-anti-Rabbit-IgG-H-L-Highly-Cross-Adsorbed-Secondary-Antibody-Polyclonal/A32733>.

The Goat-anti-Mouse antibody has been used in previous publications including Permanent Whisker Removal Reduces the Density of c-Fos+ Cells and the Expression of Calbindin Protein, Disrupts Hippocampal Neurogenesis and Affects Spatial-Memory-Related Tasks in Front Cell Neurosci., PMID: 29867365; Paricalcitol accelerates BACE1 lysosomal degradation and inhibits calpain-1 dependent neuronal loss in APP/PS1 transgenic mice in EBioMedicine, PMID: 31303501; and Nexilin/NEXN controls actin polymerization in smooth muscle and is regulated by myocardin family coactivators and YAP in Sci Rep., PMID: 30158653.

The Goat-anti-Rabbit antibody has been used in previous publications including Region-Specific Reductions in Morphometric Properties and Synaptic Colocalization of Astrocytes Following Cocaine Self-Administration and Extinction in Front Cell Neurosci., PMID: 30147645; Arkadia/RNF111 is a SUMO-targeted ubiquitin ligase with preference for substrates marked with SUMO1-capped SUMO2/3 chain in Nat Commun., PMID: 31417085; and Precise inhibitory microcircuit assembly of developmentally related neocortical interneurons in clusters in Nat Commun., PMID: 28703129.

Eukaryotic cell lines

Policy information about [cell lines](#)

Cell line source(s)	Human Umbilical Vein Endothelial Cells (HUVEC) were obtained from Sigma-Aldrich (catalog #C-12203)
Authentication	According to the vendor, rigid quality control tests are performed for each lot of Endothelial Cells from large vessels. They are tested for cell morphology, adherence rate, and cell viability. Flow cytometric analyses for cell-type specific markers, e.g. von Willebrand Factor (vWF) and CD31, as well as Dil-Ac-LDL uptake assays are also carried out for each lot. Growth performance is tested through multiple passages up to 15 population doublings (PD) under culture conditions without antibiotics and antimycotics.
Mycoplasma contamination	All cells have been tested for the absence of HIV-1, HIV-2, HBV, HCV, HTLV-1, HTLV-2 and microbial contaminants (fungi, bacteria, and mycoplasma).
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	8–12-week-old female mice (eC57BL/6J, C57BL/6-Tg(CAG-EGFP)10sb/J; Jackson Laboratory, Bar Harbor, ME, http://www.jax.org) were housed in the Stanford University Veterinary Service Center in accordance with NIH and institution-approved animal care guidelines. Mice within one experiment were of the same strain, batch and birthday.
Wild animals	No wild animals were used in the study.
Field-collected samples	No field collected samples were used in the study.
Ethics oversight	All mouse procedures were approved by the Stanford Administrative Panel on Laboratory 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	On day 5, analysis of murine cells isolated from excisional wounds was performed according to published protocols for flow cytometry on murine tissue ⁷ . Briefly, tissue was explanted on day 5 from the parabiosis model, then micro-dissected and incubated in serum-free Dulbecco's Modified Eagle Medium (DMEM) with 240 U of collagenase IV per mL for 1h at 37°C in a rotating oven. Digested tissue was filtered, centrifuged and stained with PE/Cy7 rat anti-mouse CD11b antibody, PE rat anti-mouse CD163 antibody, and APC rat anti-mouse F4/80 antibody (Biolegend, San Diego, CA). 4',6-diamidino-2-phenylindole (DAPI) was used to stain dead cells. Flow cytometry was subsequently performed.
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Instrument	BD FACS Aria (Becton Dickinson, San Jose, CA)
Software	Flow cytometry data was analyzed using FlowJo (v. 10.5.3, Becton Dickinson, San Jose, CA).
Cell population abundance	The purity of cells were ensured by FACS sorting and the cell abundance was provided with details in Fig. S38.
Gating strategy	Detailed gate strategies were defined in Fig. S43. Briefly, all cells were first gated for single cells excluding duplets, followed by gating for live, DAPI-negative cells. Subsequently, live cells were gated for GFP and macrophages were identified among the GFP+ cells by gating for PE-Cy7-CD11b+ cells. Further, M2 macrophages were subset from all macrophage by gating for PE-CD163+ cells.

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