NOTE: Please save this file locally before filling in the table, DO NOT work on the file within your internet browser as changes will not be saved. Adobe Acrobat Reader (available free here) is recommended for completion.

The ARRIVE guidelines 2.0: author checklist

The ARRIVE Essential 10

These items are the basic minimum to include in a manuscript. Without this information, readers and reviewers cannot assess the reliability of the findings.

Item		Recommendation	Section/line number, or reason for not reporting
Study design	1	For each experiment, provide brief details of study design including: a. The groups being compared, including control groups. If no control group has been used, the rationale should be stated. b. The experimental unit (e.g. a single animal, litter, or cage of animals).	*GVH/PHH induction and Immunofluorescence in brain sections (lines 146-165): blood serum in right lateral ventricle, blood serum in both lateral ventricles, whole blood, collagenase, controls without injection, controls win saline In suplemental detailed methods in sections: Bone marrow-derived mesenchymal stem cell isolation and culture, Neural stem cell isolation and
Sample size	2	a. Specify the exact number of experimental units allocated to each group, and the total number in each experiment. Also indicate the total number of animals used. b. Explain how the sample size was decided. Provide details of any *a priori* sample size calculation, if done.	*GVH/PHH induction and Immunofluorescence in brain sections (lines 146-165): blood serum in right lateral ventricle (n=7), blood serum in both lateral In statistic section: To achieve 80% power with a 5% significance level, the required sample size was estimated using mean differences and pooled standard deviations
Inclusion and exclusion criteria	3	a. Describe any criteria used for including and excluding animals (or experimental units) during the experiment, and data points during the analysis. Specify if these criteria were established *a priori.* If no criteria were set, state this explicitly. b. For each experimental group, report any animals, experimental units or data points not included in the analysis and explain why. If there were no exclusions, state so. c. For each analysis, report the exact value of *n* in each experimental group.	Dead animals during the experimental procedures to induce the GMH/PHH were not included (in Experimental animals section). Results from all experimental animal were included in the results sections. *GVH/PHH induction and Immunofluorescence in brain sections (lines 146-165): 5 animals dead during injections. They were not included. *GVH/PHH induction and Immunofluorescence in brain sections (lines 146-165): blood serum in right lateral ventricle (n=7), blood serum in both lateral
Randomisation	4	a. State whether randomisation was used to allocate experimental units to control and treatment groups. If done, provide the method used to generate the randomisation sequence. b. Describe the strategy used to minimise potential confounders such as the order of treatments and measurements, or animal/cage location. If confounders were not controlled, state this explicitly.	No randomisation was used Every experimental group includes all littermates to avoid confusion. Also, all the cages were labelled, marked and with daily monitoring. In in vivo treatment experiments, each treatment was applied to complete litters. Cages were kept marked, labelled
Blinding	5	Describe who was aware of the group allocation at the different stages of the experiment (during the allocation, the conduct of the experiment, the outcome assessment, and the data analysis).	The correspondence authors were aware of the different experimental groups allocation in the different procedures. In supplemental detailed methods, section Image analysis and quantification
Outcome measures	6	a. Clearly define all outcome measures assessed (e.g. cell death, molecular markers, or behavioural changes). b. For hypothesis-testing studies, specify the primary outcome measure, i.e. the outcome measure that was used to determine the sample size.	In the different results sections and figures, including supplemental tables and figures NA
Statistical methods	7	a. Provide details of the statistical methods used for each analysis, including software used. b. Describe any methods used to assess whether the data met the assumptions of the statistical approach, and what was done if the assumptions were not met.	Statistic section Statistic section
Experimental animals	8	a. Provide species-appropriate details of the animals used, including species, strain and substrain, sex, age or developmental stage, and, if relevant, weight. b. Provide further relevant information on the provenance of animals, health/immune status, genetic modification status, genotype, and any previous procedures.	Provided in each methods subsection, including supplemental detailed methods Lines 168-169,179-180, 188-189, Sections: Bone marrow-derived mesenchymal stem cell isolation and culture; Neural stem cell isolation and culture in detailed
Experimental procedures	9	For each experimental group, including controls, describe the procedures in enough detail to allow others to replicate them, including: a. What was done, how it was done and what was used. b. When and how often. c. Where (including detail of any acclimatisation periods). d. Why (provide rationale for procedures).	Described in each methods subsection, including supplemental detailed methods. Some details described in each result subsection Described in each methods subsection, including supplemental detailed methods. Some details described in each result subsection Described in each methods subsection, including supplemental detailed methods. Some details described in each result subsection Described in each methods subsection, including supplemental detailed methods. Some details described in each result subsection
Results	10	For each experiment conducted, including independent replications, report: a. Summary/descriptive statistics for each experimental group, with a measure of variability where applicable (e.g. mean and SD, or median and range). b. If applicable, the effect size with a confidence interval.	Described in each result subsection, figures (figure legend) and in suplementary tables. NA

The Recommended Set

These items complement the Essential 10 and add important context to the study. Reporting the items in both sets represents best practice.

Item		Recommendation	Section/line number, or reason for not reporting
Abstract	11	Provide an accurate summary of the research objectives, animal species, strain and sex, key methods, principal findings, and study conclusions.	Lines 55-58, 59, Sexes and strain not reported
Background	12	a. Include sufficient scientific background to understand the rationale and context for the study, and explain the experimental approach. b. Explain how the animal species and model used address the scientific objectives and, where appropriate, the relevance to human biology.	Lines 103-118 Lines 551-555
Objectives	13	Clearly describe the research question, research objectives and, where appropriate, specific hypotheses being tested.	Lines 108-121
Ethical statement	14	Provide the name of the ethical review committee or equivalent that has approved the use of animals in this study, and any relevant licence or protocol numbers (if applicable). If ethical approval was not sought or granted, provide a justification.	Lines 134-138
Housing and husbandry	15	Provide details of housing and husbandry conditions, including any environmental enrichment.	Lines 141-142
Animal care and monitoring	16	a. Describe any interventions or steps taken in the experimental protocols to reduce pain, suffering and distress. b. Report any expected or unexpected adverse events. c. Describe the humane endpoints established for the study, the signs that were monitored and the frequency of monitoring. If the study did not have humane endpoints, state this.	Not reported. Local and government ethics committees have previously approved the detailed protocols that include this item Not reported. Local and government ethics committees have previously approved the detailed protocols that include this item. Not reported. Local and government ethics committees have previously approved the detailed protocols that include this item.
Interpretation/ scientific implications	17	a. Interpret the results, taking into account the study objectives and hypotheses, current theory and other relevant studies in the literature. b. Comment on the study limitations including potential sources of bias, limitations of the animal model, and imprecision associated with the results.	Lines 103-107 No reported. Limitations were not evident.
Generalisability/ translation	18	Comment on whether, and how, the findings of this study are likely to generalise to other species or experimental conditions, including any relevance to human biology (where appropriate).	Lines 551-555, 518-524
Protocol registration	19	Provide a statement indicating whether a protocol (including the research question, key design features, and analysis plan) was prepared before the study, and if and where this protocol was registered.	Lines 135-138
Data access	20	Provide a statement describing if and where study data are available.	Lines 126-127
Declaration of interests	21	a. Declare any potential conflicts of interest, including financial and non-financial. If none exist, this should be stated. b. List all funding sources (including grant identifier) and the role of the funder(s) in the design, analysis and reporting of the study.	Lines 581-582 Lines 568-576

SUPPLEMENTAL MATERIAL

Detailed methods

Experimental animals

The design of the experiments and animal housing, handling, care, and processing were conducted following European and Spanish laws (RD53/2013 and 2010/63UE) and ARRIVE guidelines. According to current legislation, experimental procedures (protocol 23/04/2019/069) were approved by the Institutional Animal Care and Use Committee of the University of Malaga (CEUMA, Spain) and the Regional Government Council (Junta de Andalucía, Spain).

Mice (C57/BL-6J strain) were originally obtained from Charles River Laboratory and bred in the Animal Experimentation Service of the University of Malaga at 22 °C with a 12:12 light/dark cycle and standard food and water available *ad libitum*. A total of 139 were used for all the experiments, excluding mice dead during PHH induction that were not used for the study.

GVH/PHH induction

Four-day-old male and female mice were anesthetized with 2% isoflurane in 0.5 l/minute oxygen anesthesia and injected with blood serum (9 µl in the right lateral ventricle or both right and left lateral ventricles), whole blood (4 µl in both right and left lateral ventricles), or 1 µl of sterile saline 0.9% NaCl containing 0.05 U/µl collagenase I (C2674-1G, Sigma–Aldrich, St Louis, MO, USA) in the subventricular germinal matrix of each hemisphere, to produce GMH/IVH conditions. The injected blood serum and whole blood were obtained from littermates after decapitation. Blood serum was obtained as the supernatant after centrifugation at 1,400 g for 10 minutes at 4 °C. Blood serum and whole blood injections were performed free-hand using a 26-gauge syringe (Hamilton Syringe 75N, Hamilton, Reno, NV, USA) at coordinates 1 mm posterior to the eye, 1 mm superior to the orbit, and 1 mm deep. Collagenase was injected free-hand using a 33-gauge syringe (Hamilton Neuros, HAMI65460-03) at coordinates 0.5 mm posterior to the eye, 1 mm superior to the orbit, and 2 mm deep. The coordinates were previously assayed with trypan blue injections. The aim of the collagenase injections in the subventricular GM was to mimic premature human GMH/IVH. Fourteen days after the injections, mice were sacrificed, and brains were processed to detect the main cytopathologies associated with PHH development. Normal littermates of the same age without any surgical procedure were used as controls. During PHH induction, mean mortality rate was about 30%.

Immunofluorescence in brain sections

Eighteen-day-old male and female mice (14 days after GVH/PHH induction) from the different experimental groups (blood serum in the right lateral ventricle; n = 7; blood serum in both lateral ventricles, n = 4; whole blood, n = 7; collagenase, n = 9; controls without any injection, n = 9; controls with saline serum injection, n = 6) were anesthetized with Dolethal (sodium pentobarbital; Vétoquinol, Lure, France; intraperitoneal administration, 0.2 mg/g body weight) and transcardially perfused with 4% paraformaldehyde diluted in 0.1 M, pH 7.2, phosphate buffer (PB). Fixed brains were dissected out and postfixed in the same solution for 24 hours at 4 °C. Then, brains were cryoprotected in 30% sucrose to obtain frozen sections (60 µm thick). Sections were processed with a free-floating section staining protocol for immunofluorescence using unconjugated primary antibodies (βIV-Tubulin, T7941, Sigma–Aldrich, dilution 1:400; GFAP, glial fibrillary acidic protein, G-A-5, Sigma–Aldrich, 1:1,000; and Iba1, 019-19741, Wako, Chuoku, Osaka, Japan, 1:500). Secondary antibodies conjugated with Alexa Fluor 488 or Alexa Fluor 568 (Thermo Fisher, Waltham, MA, USA) were used. The antibodies were diluted in PB saline (PBS) containing 0.05% Triton X-100, 0.01% sodium azide, 1% bovine albumin (05477, Sigma–Aldrich), and 5% appropriate normal sera. Primary antibody incubations were performed for 18 hours at 22 °C or 72 hours at 4 °C. Secondary antibody incubations were performed for 1 hour at 22 °C. Nuclei staining was performed with 4´,6 diamidino-2-phenylindole dihydrochloride (DAPI, Molecular Probes, Eugene, OR, USA) at 300 nM in PBS. For negative controls, the primary antibodies were omitted.

Magnetic resonance imaging

Magnetic resonance imaging (MRI) experiments were performed on a 9.4T Bruker Biospec small animal MRI system (Bruker Biospec, Bruker BioSpin, Ettlingen, Germany) equipped with a 40 mm quadrature bird-cage resonator and 440 mT/m gradients. Normal male and female mice (n = 5) and mice exhibiting modPHH (n = 3) and sevPHH (n = 2) were anesthetized with 1% isoflurane in 1 l/min oxygen, and body temperature and respiratory frequency were monitored throughout the experiment. The acquisition protocol consisted of a high-resolution T2-weighted RARE (Rapid Acquisition with Relaxation Enhancement) sequence with fat suppression and 3D FISP (Fast Imaging with Steady Precession). Sequence parameters were set as follows. T2-weighted: TR = 2.5 s; effective TE = 32 ms; echo train length = 6; 4 averages; matrix size = 512 × 512; FOV = 20 × 20 mm2; slice thickness = 0.75 mm. 3D FISP: TR = 8 ms, TE = 4 ms, matrix size = 256 × 256 × 128; resolution = 78 µm × 78 µm × 156 µm.

Lateral ventricle size was calculated from high-resolution T2-weighted images as the sum of the volumes (area x slice thickness) of contiguous slices using FIJI 1.53q software (NIH, USA).

UHPLC-HRMS analysis of protein expression

For ultrahigh-performance liquid chromatography high-resolution mass spectrometry (UHPLC-HRMS), the caudal cerebral wall was dissected from control mice (n = 10) and mice with modPHH (n = 7) and sevPHH (n = 6) at 18 days of age. Immediately after sacrifice by cervical dislocation, the tissue was frozen on dry ice and stored at -80 °C until further processing. The complete procedure took 2-5 minutes.

Proteins from the samples were purified by a modified trichloroacetic acid protein precipitation procedure (Clean-Up Kit; GE Healthcare, Munich, Germany), and gel-assisted proteolysis was carried out. Briefly, the protein solution was entrapped in a polyacrylamide gel matrix before reduction with dithiothreitol and cysteine residue carbamidomethylation with iodoacetamide. Then, the proteins were digested by trypsin (Promega, Madison, WI, USA), and peptides were extracted from the gel with an acetonitrile/formic acid solution. After extraction, the peptides were purified and concentrated using a C18 ZipTip (Merck Millipore) according to the manufacturer's instructions.

Samples were injected into an Easy nLC 1200 UHPLC system coupled to a Q Exactive™ HF-X Hybrid Quadrupole-Orbitrap mass spectrometer (Thermo Fisher). Data were acquired using Tune 2.9 and Xcalibur 4.1.31.9 (Thermo Fisher). Peptides from the samples were automatically loaded into a trap column (Acclaim PepMap 100, 75 µm Å~ 2 cm, C18, 3 µm, 100 A, Thermo Fisher) and eluted onto a 50 cm analytical column (PepMap RSLC C18, 2 µm, 100 A, 75 µm Å~ 50 cm, Thermo Fisher). The binary gradient mobile phase consisted of 0.1% formic acid in water (solvent A) and 0.1% formic acid in 80% acetonitrile (solvent B). Peptides were eluted from the analytical column with a 120-minute gradient from 2 to 20% solvent B, followed by a 30-minute gradient from 20 to 35% solvent B and finally 95% solvent B for 15 minutes before re-equilibration in 2% solvent B at a constant flow rate of 300 nL/minute. Data acquisition was performed in electrospray ionization positive mode. MS1 scans were acquired from m/z 300–1750 at a resolution of 120,000. With a data-dependent acquisition method, the 20 most intense precursor ions with + 2 to + 5 charges were isolated within a 1.2 m/z window and fragmented to obtain the corresponding MS/MS spectra. The fragment ions were generated in a higher-energy collisional dissociation cell with a fixed first mass at 110 m/z and detected by the Orbitrap mass analyzer at a resolution of 30,000.

The raw data were analyzed using Proteome Discoverer™ 2.4 (Thermo Fisher). For the identification of the MS2 spectra, Sequest HT was utilized as the search engine, and the Swiss-Prot part of UniProt for *Mus*

musculus was utilized as the database. Protein assignments were validated using the Percolator algorithm by imposing a strict 1% false discovery rate (FDR) cutoff.

Label-free quantitation was implemented using the Minora feature of Proteome Discoverer™ 2.4. Protein abundance ratios were directly calculated from the grouped protein abundances. ANOVA was based on the abundance of individual proteins or peptides.

The PANTHER Classification System (v.14.1) and GO Ontology database were used to identify the main biological processes related to the overexpressed/underexpressed proteins. Additionally, the STRING platform was used for functional enrichment analysis with the representation of protein–protein interaction networks.

Ventricle wall explant in vitro assays

Forty-eight hours after GMH/PHH induction with collagenase or blood serum, mice were sacrificed by decapitation, and the brain was dissected out and classified according to GMH extension and lateral ventricle size (in collagenase, blood serum and whole blood injections) in modGMH/PHH and sevGMH/PHH. Explants from the lateral wall of the lateral ventricle, the striatal wall, were carefully positioned on Millicell culture inserts (PICM0RG50, Sigma–Aldrich) into six-well culture plates (three explants/insert, Figure S1) containing 1 mL of sterile organotypic culture medium (26.6 mM HEPES, pH 7.1; 19.3 mM NaCl; 5 mM $NaHCO_3$; 511 µM ascorbic acid; 40 mM glucose; 2.7 mM $CaCl_2$; 2.5 mM $MgSO_4$; 0.033% v/v insulin, I6634, Sigma–Aldrich; and 0.5% v/v penicillin/streptomycin, P0781, Sigma–Aldrich) in ultrapure H_2O, sterile filtered, with 25% (v/v) heat-inactivated horse serum (H1138, Sigma–Aldrich). Explants were incubated at 37 °C, and the culture medium was partially replaced every 48 hours. Explants were maintained for a maximum of 7 days *in vitro* before harvesting.

The explants used to study the survival of transplanted stem cells and their progenies were fixed with 4% paraformaldehyde in PB 0.1 M, pH 7.2 at 4 °C for 24 hours and then immunostained using unconjugated primary antibodies followed by secondary antibodies conjugated with fluorochromes, as described above for brain sections. In addition to anti-GFAP and anti-βIVTubulin, antibodies against Foxj1 (HPA005714, Sigma–Aldrich, 1:150) and NG2 (neuron-glial antigen 2, AB5320, Merck Millipore, Burlington, MA, USA, 1:400) were used.

The explants used to study the stem cell therapy effect with the Evans Blue assay were processed as described below.

Bone marrow-derived mesenchymal stem cell isolation and culture

Bone marrow-derived MSCs were obtained from young male and female mice (20-24 days old) (n = 10) and characterized as previously described. Briefly, bone marrow-derived MSCs were selected according to their plastic adhesion *in vitro*, their positive expression of CD44, CD73 and CD90, their negative expression of CD34 and CD45, and their trilineage differentiation capacity. Dulbecco's modified Eagle's medium (DMEM, D5546, Sigma–Aldrich) containing 1% penicillin/streptomycin, 0.5% amphotericin B, 1.25% L-glutamine, and 10% fetal bovine serum (FBS, F7524, Sigma–Aldrich) was used as the culture medium. After approximately 80% confluence at passage one, the cells were detached with trypsin/ethylenediaminetetraacetic acid (EDTA; T3924, Sigma–Aldrich), centrifuged and resuspended in saline serum to be used to pretreat explants or primary cultures.

Neural stem cell isolation and culture

The subventricular zone (SVZ) of the rostral-dorsal striatal wall in newborn male and female mice (n = 5) was dissected out and mechanically dissociated in DMEM/F-12 containing 100 units/mL penicillin–streptomycin (P0781, Sigma–Aldrich) to obtain NSCs. After centrifugation for 2 minutes at 600 g, the pellet was resuspended and placed overnight in uncoated plastic tissue-culture dishes in N5 medium constituted by DMEM/F-12 (Gibco 21331020, Thermo Fisher) containing N2 supplements (Gibco 17502001, Thermo Fisher), 35 µg/mL bovine pituitary extract (Gibco 13028014, Thermo Fisher), 5% FBS (F7524, Sigma–Aldrich), 40 ng/mL EGF (epidermal growth factor, AF-100-15, PeproTech, Rocky Hill, New Jersey, USA) and 40 ng/mL bFGF (basic fibroblast growth factor, 130-093-564, Miltenyi Biotech, Bergisch Gladbach, Germany). New EGF and bFGF were added every 48 hours. For experimentation, cells were used at passage 2.

Ependymal progenitor cell collection

EpPs were obtained from newborn male and female mice (n = 37). In this case, the SVZ of the medial-dorsal striatal ventricle wall was dissected out and mechanically dissociated in DMEM-high glucose (glucose 4500 mg/L, D6546, Sigma–Aldrich) with 10% FBS (F7524, Sigma-Aldrich), 1% L-glutamine (Gibco 25030081, Thermo Fisher), and 1% penicillin/streptomycin. Cells were plated at 500,000 cells/mL using the same media on poly-D-lysine (P6407, Sigma–Aldrich)-coated round coverslips and incubated under standard cell culture conditions for 12 hours. The medium was switched entirely to fresh medium containing 2% FBS for

another 12 hours. Astrocytes do not attach to plates in these latter conditions; thus, these cells were eliminated when the medium was switched. Therefore, in this case, only EpPs were attached to the plates.

Stem cell transplantation in ventricular wall explants

Before application, NSCs, EpPs, and MSCs were labeled *in vitro* by adding green or red fluorescent cell tracker dyes (C2925, Thermo Fisher; and SCT107, Sigma–Aldrich) following the manufacturer´s instructions.

Fluorescently labeled NSCs, EpPs and MSCs were gently detached from plates using trypsin/EDTA, centrifuged and resuspended in their respective media (NSCs and EpPs, 10,000 cells/µl; MSCs 10,000 cells/µl). Then, the stem cells were transplanted by accommodating them on the surface of the lateral ventricle explants using a Hamilton syringe (26-gauge, 1 µl/per explant) to avoid any damage to the surface of the explant and thus any additional alteration of the tissue.

Experiments were performed with 3 explants per experimental condition and replicated five times (n = 5), with a total of 15 explants per experimental condition.

For the analysis of the results, each explant was initially independently studied. Pictures were taken, and cells and markers were quantified. For each explant, a mean marker was obtained. For each replicate, we calculated the mean of the three explants. For the different statistical tests represented in the figures, the mean and standard deviation of the mean were calculated using the final value of each replica (n = 5).

In vitro differentiation of ependymal progenitor cells under the effect of blood components

EpPs, obtained as described above, were plated at 500,000 cells/mL on poly-D-lysine-coated coverslips in 6-well culture plates (5 coverslips per well). Cells were incubated under standard cell culture conditions for 12 hours in high glucose DMEM with 10% FBS, 1% L-glutamine, and 1% penicillin/streptomycin. The medium was switched entirely to a new medium containing 2% FBS for another nine days. The medium was partially replaced every 48 hours.

Twenty-four hours after the medium was switched to 2% FBS, the EpP culture was treated and maintained with blood, blood serum, or TNFα. Blood and blood serum were obtained from newborn mice according to the above-described protocol and was applied to culture (50 μL per 500,000 cells/mL), and these treatments were applied once, 24 hours after the medium was switched to 2% FBS. TNFα (Genetex, Irvine, CA, USA) was

applied every two days at 50 ng/mL for a maximum of 9 days. In the different treatments, at 3, 6, and 9 days, the cells were fixed with 4% paraformaldehyde diluted in 0.1 M, pH 7.2 PB for 30 minutes at 4 °C and immunostained to detect Foxj1 protein and cilia (βIV-Tubulin) using unconjugated primary antibodies. Secondary fluorochrome-conjugated antibodies were used as described for brain sections. Nuclear staining was performed with DAPI. For negative controls, the primary antibodies were not added.

For analysis of the results, each well of the six-well plate was initially independently analyzed. Pictures were taken on each of the five coverslips, cells and markers were quantified, and an average was calculated per coverslip. Next, an average was calculated per well plate. Each condition was replicated 5 times. For the different statistical tests represented in the figures, the mean and standard deviation of the mean were calculated using the final value of each replicate (n = 5).

In vitro differentiation recovery of ependymal progenitor cells in the presence of blood components and bone marrow-derived mesenchymal stem cells

EpPs, obtained as described above, were plated at 500,000 cells/mL on poly-D-lysine-coated coverslips in 6-well culture plates (5 coverslips per well). MSCs (20,000 cells/mL) were added once to the EpP primary culture 24 hours after the medium was switched to fresh medium containing 2% FBS and then maintained with the different treatments for nine days. Additionally, blood, blood serum, and the inflammatory cytokine TNFα were applied as described above. Cell cultures were processed, immunostained, and quantified as described in the *Image analysis and quantification* section.

For the analysis of the results, we proceeded as in the previous section. Each condition was replicated 7 times. For the different statistical tests, the mean and standard deviation of the mean represented in the figures were calculated using the final value of each replicate (n = 7).

Evans Blue assay to test the brain parenchymal effect

Lateral ventricle wall explants from male and female mice with moderate GMH induced with collagenase (n = 9) were positioned on Millicell culture inserts in 6-well culture plates (3 explants/insert). After six hours *in vitro*, explants were transplanted with MSCs. Then, EpPs were transplanted 24 hours later. Transplantation was performed as described above. The medium was partially changed every 48 hours. After seven days of treatment, Evans Blue was applied. Then, tissue was fixed with 4% paraformaldehyde in 0.1 M PB, pH 7.2 at 4 °C for 24 hours.

Finally, explants were washed and analyzed under confocal microscopy at 650 nm based on the fluorescent properties of this compound. This colorant filled dead cells and edematous regions. Thus, the staining intensity indicated the grade of tissue damage and edematous status. Confocal images were transformed into greyscale, and every pixel obtained a value from 0 (black) to 255 (white). The highest intensity corresponds to a 255 value in the greyscale. The intensity of fluorescence in the grey scale was analyzed by ImageJ software. For each experimental condition, we used 6 explants.

Cytokine content in culture media from treated explants

From the Evans Blue assay experiments described above, culture media were collected at the end of the experiment to detect cytokines after different treatments: cell culture media without explants as the baseline for the cytokine kit array (empty wells), nontreated explants (9 explants), MSC-pretreated explants (9 explants), and sequential transplantation of MSCs and EpPs in explants (9 explants). A mouse cytokine kit array (Abcam, Cambridge, UK; AB133995) was used to detect the expression of 62 cytokines according to the manufacturer's instructions. Processed array membranes were scanned and analyzed using FIJI software 1.53q (NIH, USA). To obtain an accurate cytokine value for non-treated and treated explants, we subtracted the baseline expression of cytokines in the media with no explants for every case.

Image analysis and quantification

The correspondence authors were aware of the different experimental groups allocation in the different procedures. Confocal images were acquired with SP8 and Stellaris 8 confocal laser microscopes (Leica, Wetzlar, Germany). For each experiment, immunofluorescence images were obtained in batches with control and experimental samples imaged under identical instrument settings. The ependyma-denuded ventricle surface percentage was quantified from micrographs (3-6 brain sections per animal) scanned under fluorescence in an Olympus VS120 microscope (Olympus, Tokyo, Japan) with a 10x objective.

For ex vivo studies, experiments were performed with 15 explants per experimental condition. Pictures were taken with a 20x objective in a Leica laser confocal SP8 microscope, and quantification was manually and blindly performed using the confocal images.

For the *in vitro* primary EpP culture, the experiments were performed with 7-9 wells per condition. In each well, 4-5 coverslips and 9-15 pictures were taken per coverslip, depending on the needed magnification for the

experiment. Quantification was manually and blindly performed using confocal images. No randomization was used. Every experimental group includes all littermates to avoid confusion. Also, all the cages were labelled, marked and with daily monitoring. In *in vivo* treatment experiments, each treatment was applied to complete litters. Cages were kept marked, labelled and with daily monitoring. In explants and cells cultures, plates were photographed. Every experimental group was placed on the plate in such a way that unequivocal traceability can be made.

Statistics

Samples were analyzed using GraphPad 9.2.0 (GraphPad Software, San Diego, CA, USA) and Microsoft Excel 16.71. To achieve 80% power with a 5% significance level, the required sample size was estimated using mean differences and pooled standard deviations from preliminary quantifications. Normality was assessed with Shapiro–Wilk test. For Student's t test or the Wilcoxon-Mann Whitney test, two-tailed test was used. The ANOVA and Kruskal-Wallis tests were used to compare more than two groups with post-hoc Tukey's and Dunn's multiple comparisons tests, respectively. $P < 0.05$ was considered statistically significant.

Table S1. Enhanced cell processes comparing the mice with sevPHH with the controls

GO Process Reactome process (MMU)	Genes	Strength	False Discovery Rate
GO:0070495 Negative regulation of thrombin-activated receptor signaling pathway	Stmn1, Met	2.11	0.0072
GO:0006880 Intracellular sequestering of iron Ion	Fth1, Ftl1	1.99	0.0094
GO:0048012 Hepatocyte growth factor receptor signaling pathway	Nrp1, Stmn1, Met	1.81	0.0135
GO:0098903 Regulation of membrane repolarization during action potential	Cav1, Flna	1.74	0.0159
GO:0042730 Fibrinolysis	Anxa2, Fgb	1.41	0.0341
GO:0014002 Astrocyte development	Egfr, Vim, Gfap	1.33	0.0106
GO:0071526 Semaphorin-plexin signaling pathway	Nrp1, Flna, Met	1.33	0.0106
MMU-109581 Apoptosis	Vim, Dffa, Hmgb2, Casp3	0.92	0.0231

Results of GO processes and Reactome pathways (MMU). Strength represents log10 (observed/expected). This measure describes the size of the enrichment effect. It is the ratio between i) the number of proteins in the network annotated with a term and ii) the number of proteins that are expected to be annotated with this term in a random network of the same size. The false discovery rate describes how significant the enrichment is. The p values corrected for multiple testing within each category using the Benjamini–Hochberg procedure are shown.

Table S2. Enhanced cell processes comparing the mice with modPHH with the controls.

GO Process	Genes	Strength	False Discovery Rate
GO:0006880 Intracellular sequestering of iron ion	Fth1, Ftl1	2.08	0.0094
GO:0030193 Regulation of blood coagulation	Anxa2, Anxa5, Cav1	2.08	0.0122
GO:0060252 Positive regulation of glial cell proliferation	Gfap, Vim	1.48	0.0339
GO:0014002 Astrocyte development	Gfap, Vim	1.43	0.0122

See legend of Table S1.

Table S3. Decreased cell processes comparing the mice with sevPHH with the controls.

GO Process	Genes	Strength	False Discovery Rate
GO:0048709 Oligodendrocyte differentiation	Tspan2, Plp1, Cnp, Mag	1.69	0.0012
GO:1901215 Negative regulation of neuron death	Gfer, Prkci, Mag	1.05	0.0438
GO:0061564 Axon development	Tspan2, Plp1, Lamb2, Cnp	1.02	0.0227

See legend of Table S1.

Table S4. Decreased cell processes comparing the mice with modPHH with the controls.

GO Process	Genes	Strength	False Discovery Rate
GO:1900037 Regulation of cellular response to hypoxia	Chdchd2, Map2k1	1.9	0.0100
GO:2001171 Positive regulation of ATP biosynthetic process	Mif, Ma2pk1	1.7	0.0160
GO:0042552 Myelination	Mag, Mbp, Plp1, Sirt2, Tspan2, Ugt8a	1.58	3.11×10^{-5}
GO:0006101 Citrate metabolic process	Fh1, Suclg1	1.58	0.0198
GO:0010507 Negative regulation of autophagy	Htra2, Sirt2, Snca	1.45	0.0067
GO:0034599 Cellular response to oxidative stress	Dnm2, Htra2, Prkcd, Sirt2, Snca	1.14	0.0027

See legend of Table S1.

Table S5. Enhanced cell processes comparing the mice with sevPHH with those with modPHH.

GO Process **Reactome process (MMU)**	**Genes**	**Strength**	**False Discovery Rate**
MMU-109581 Apoptosis	Lgals1, Cp	1.39	0.0021
GO:0014002 Astrocyte development	Gfap, Vim	1.75	0.013
GO:0010977 Negative regulation of neuron projection development	Bcl11a, Vim, Flna, Cspg4, Gfap, Lgals1	1.46	1.78×10^{-5}
GO:0050768 Negative regulation of neurogenesis	Bcl11a, Vim, Flna, Cspg4, Gfap, Lgals1, Dynlt1c	1.23	2.74×10^{-5}
GO:0042063 Gliogenesis	Vim, Cspg4, Gfap, Dcx	1.15	0.0045

See the legend of Table S1.

Table S6. Decreased cell processes comparing the mice with sevPHH with those with modPHH.

GO Process	Genes	Strength	False Discovery Rate
GO:0019911 Structural constituent of myelin sheath	Plp1, Mobp	2.6	0.0012
GO:0017016 Ras GTPase binding	Mobp, Cdkl5, Rasgrp1	1.21	0.0283

See legend of Table S1.

Data Figure 3C Blood Serum (BS)

Shapiro-Wilk test Blood Serum	sevPHH NSC	sevPHH NSC+MSC	sevPHH EpP	sevPHH EpP+MSC	mdPHH NSC	modPHH NSC+MSC	modPHH EpP	modPHH EpP+MSC
W	0.9567	0.9572	0.9806	0.9421	0.9645	0.9515	0.9691	0.9343
P value	0.7939	0.7979	0.9545	0.6762	0.8534	0.7525	0.8861	0.6139
Passed normality test (alpha=0.05)?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

ANOVA summary Blood Serum	
F	57.55
P value	<0.0001
P value summary	****
Significant diff. among means (P < 0.05)?	Yes
R squared	0.9097

Tukey's multiple comparisons test Blood Serum	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
sev BS-NSC vs. sev BS-NSC+MSC	-4833	-14.17 to 4.500	No	ns	0.7146
sev BS-NSC vs. sev BS-EpP	-6467	-15.80 to 2.867	No	ns	0.3651
sev BS-NSC vs. sev BS-EpP+MSC	-9000	-18.33 to 0.3336	No	ns	0.0657
sev BS-NSC vs. mod BS-NSC	-26.17	-35.50 to -16.83	Yes	****	<0.0001
sev BS-NSC vs. mod BS-NSC+MSC	-27.73	-37.07 to -18.40	Yes	****	<0.0001
sev BS-NSC vs. mod BS-EpP	-29.67	-39.00 to -20.33	Yes	****	<0.0001
sev BS-NSC vs. mod BS-EpP+MSC	-44.67	-54.00 to -35.33	Yes	****	<0.0001
sev BS-NSC+MSC vs. sev BS-EpP	-1633	-10.97 to 7.700	No	ns	0.9992
sev BS-NSC+MSC vs. sev BS-EpP+MSC	-4167	-13.50 to 5.167	No	ns	0.8394
sev BS-NSC+MSC vs. mod BS-NSC	-21.33	-30.67 to -12.00	Yes	****	<0.0001
sev BS-NSC+MSC vs. mod BS-NSC+MSC	-22.9	-32.23 to -13.57	Yes	****	<0.0001
sev BS-NSC+MSC vs. mod BS-EpP	-24.83	-34.17 to -15.50	Yes	****	<0.0001
sev BS-NSC+MSC vs. mod BS-EpP+MSC	-39.83	-49.17 to -30.50	Yes	****	<0.0001
sev BS-EpP vs. sev BS-EpP+MSC	-2533	-11.87 to 6.800	No	ns	0.9874
sev BS-EpP vs. mod BS-NSC	-19.7	-29.03 to -10.37	Yes	****	<0.0001
sev BS-EpP vs. mod BS-NSC+MSC	-21.27	-30.60 to -11.93	Yes	****	<0.0001
sev BS-EpP vs. mod BS-EpP	-23.2	-32.53 to -13.87	Yes	****	<0.0001
sev BS-EpP vs. mod BS-EpP+MSC	-38.2	-47.53 to -28.87	Yes	****	<0.0001
sev BS-EpP+MSC vs. mod BS-NSC	-17.17	-26.50 to -7.833	Yes	****	<0.0001
sev BS-EpP+MSC vs. mod BS-NSC+MSC	-18.73	-28.07 to -9.400	Yes	****	<0.0001
sev BS-EpP+MSC vs. mod BS-EpP	-20.67	-30.00 to -11.33	Yes	****	<0.0001
sev BS-EpP+MSC vs. mod BS-EpP+MSC	-35.67	-45.00 to -26.33	Yes	****	<0.0001
mod BS-NSC vs. mod BS-NSC+MSC	-1567	-10.90 to 7.767	No	ns	0.9994
mod BS-NSC vs. mod BS-EpP	-3500	-12.83 to 5.834	No	ns	0.9276
mod BS-NSC vs. mod BS-EpP+MSC	-18.5	-27.83 to -9.166	Yes	****	<0.0001
mod BS-NSC+MSC vs. mod BS-EpP	-1933	-11.27 to 7.400	No	ns	0.9975
mod BS-NSC+MSC vs. mod BS-EpP+MSC	-16.93	-26.27 to -7.600	Yes	****	<0.0001
mod BS-EpP vs. mod BS-EpP+MSC	-15	-24.33 to -5.666	Yes	***	0.0002

Table S7. Statistical data corresponding to **Figure 3C**. Shapiro-Wilk, ANOVA, and Tukey's multiple comparison tests. (ns: no significant differences; *p < 0.05, ** p < 0.01, *** p < 0.001, ****p < 0.0001). It continues on the next page.

Data Figure 3C Collagenase (coll)

Shapiro-Wilk test Collagenase (coll)	sev coll-NSC	sev coll-NSC+MSC	sev coll-EpP	sev coll-EpP+MSC	mod coll-NSC	mod coll-NSC+MSC	mod coll-EpP	mod coll-EpP+MSC
W	0.9722	0.9309	0.9704	0,8830	0.9905	0.9537	0,9765	0.9878
P value	0.9067	0.5872	0.8953	0,2831	0.9904	0.7697	0,9331	0.9831
Passed normality test (alpha=0.05)?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

ANOVA summary Collagenase	
F	69.21
P value	<0.0001
P value summary	****
Significant diff. among means (P < 0.05)?	Yes
R squared	0.9237

Tukey's multiple comparisons test collagenase	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
sev coll-NSC vs. sev coll-NSC+MSC	-5867	-14.71 to 2.981	No	ns	0.4205
sev coll-NSC vs. sev coll-EpP	-11	-19.85 to -2.152	Yes	**	0.0064
sev coll-NSC vs. sev coll-EpP+MSC	-14.63	-23.48 to -5.785	Yes	***	0.0001
sev coll-NSC vs. mod coll-NSC	-33.3	-42.15 to -24.45	Yes	****	<0.0001
sev coll-NSC vs. mod coll-NSC+MSC	-30.87	-39.71 to -22.02	Yes	****	<0.0001
sev coll-NSC vs. mod coll-EpP	-28.07	-36.91 to -19.22	Yes	****	<0.0001
sev coll-NSC vs. mod coll-EpP+MSC	-48.37	-57.21 to -39.52	Yes	****	<0.0001
sev coll-NSC+MSC vs. sev coll-EpP	-5133	-13.98 to 3.715	No	ns	0.5884
sev coll-NSC+MSC vs. sev coll-EpP+MSC	-8767	-17.61 to 0.08132	No	ns	0.0537
sev coll-NSC+MSC vs. mod coll-NSC	-27.43	-36.28 to -18.59	Yes	****	<0.0001
sev coll-NSC+MSC vs. mod coll-NSC+MSC	-25	-33.85 to -16.15	Yes	****	<0.0001
sev coll-NSC+MSC vs. mod coll-EpP	-22.2	-31.05 to -13.35	Yes	****	<0.0001
sev coll-NSC+MSC vs. mod coll-EpP+MSC	-42.5	-51.35 to -33.65	Yes	****	<0.0001
sev coll-EpP vs. sev coll-EpP+MSC	-3633	-12.48 to 5.215	No	ns	0.8887
sev coll-EpP vs. mod coll-NSC	-22.3	-31.15 to -13.45	Yes	****	<0.0001
sev coll-EpP vs. mod coll-NSC+MSC	-19.87	-28.71 to -11.02	Yes	****	<0.0001
sev coll-EpP vs. mod coll-EpP	-17.07	-25.91 to -8.219	Yes	****	<0.0001
sev coll-EpP vs. mod coll-EpP+MSC	-37.37	-46.21 to -28.52	Yes	****	<0.0001
sev coll-EpP+MSC vs. mod coll-NSC	-18.67	-27.51 to -9.819	Yes	****	<0.0001
sev coll-EpP+MSC vs. mod coll-NSC+MSC	-16.23	-25.08 to -7.385	Yes	****	<0.0001
sev coll-EpP+MSC vs. mod coll-EpP	-13.43	-22.28 to -4.585	Yes	***	0.0005
sev coll-EpP+MSC vs. mod coll-EpP+MSC	-33.73	-42.58 to -24.89	Yes	****	<0.0001
mod coll-NSC vs. mod coll-NSC+MSC	2433	-6.415 to 11.28	No	ns	0.9863
mod coll-NSC vs. mod coll-EpP	5233	-3.615 to 14.08	No	ns	0.565
mod coll-NSC vs. mod coll-EpP+MSC	-15.07	-23.91 to -6.219	Yes	****	<0.0001
mod coll-NSC+MSC vs. mod coll-EpP	2800	-6.048 to 11.65	No	ns	0.97
mod coll-NSC+MSC vs. mod coll-EpP+MSC	-17.5	-26.35 to -8.652	Yes	****	<0.0001
mod coll-EpP vs. mod coll-EpP+MSC	-20.3	-29.15 to -11.45	Yes	****	<0.0001

Table S7. Statistical data corresponding to **Figure 3C**. Shapiro-Wilk, ANOVA, and Tukey's multiple comparison tests. (ns: no significant differences; *p < 0.05, ** p < 0.01, *** p < 0.001, ****p < 0.0001).

Data Figure 3E Blood Serum sevPHH

Shapiro-Wilk test	NSC neg	NSC+MSC neg	EpP neg	EpP+MSC neg	NSC Foxj1	NSC+MSC Foxj1	EpP Foxj1	EpP+MSC Foxj1	NSC GFAP	NSC+MSC GFAP	EpP neg GFAP	EpP+MSC GFAP	NSC NG2	NSC+MSC NG2
W	0.843	0.9676	0.954	0.9894	0.9167	0.999	0.9229	0.981	0.9809	0.8573	0.931	0.9582	0.9868	0.9283
P value	0.1734	0.8599	0.7656	0.9777	0.5088	0.9996	0.5487	0.94	0.9394	0.2187	0.6034	0.7951	0.9672	0.5846
Passed normality test (alpha=0.05)?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

ANOVA summary negative	
F	27.05
P value	<0.0001
P value summary	****
Significant diff. among means (P < 0.05)?	Yes
R squared	0.8353

Tukey's multiple comparisons test negative	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
NSC neg vs. NSC+MSC neg	20.8	8.105 to 33.50	Yes	**	0.0013
NSC neg vs. EpP neg	10.8	-1.895 to 23.50	No	ns	0.1104
NSC neg vs. EpP+MSC neg	38.4	25.70 to 51.10	Yes	****	<0.0001
NSC+MSC neg vs. EpP neg	-10	-22.70 to 2.695	No	ns	0.1511
NSC+MSC neg vs. EpP+MSC neg	17.6	4.905 to 30.30	Yes	**	0.0055
EpP neg vs. EpP+MSC neg	27.6	14.90 to 40.30	Yes	****	<0.0001

ANOVA summary Foxj1	
F	25.78
P value	<0.0001
P value summary	****
Significant diff. among means (P < 0.05)?	Yes
R squared	0.8286

Tukey's multiple comparisons test Foxj1	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
NSC Foxj1 vs. NSC+MSC Foxj1	-24.2	-37.87 to -10.53	Yes	***	0.0006
NSC Foxj1 vs. EpP Foxj1	-18.4	-32.07 to -4.733	Yes	**	0.0069
NSC Foxj1 vs. EpP+MSC Foxj1	-41.6	-55.27 to -27.93	Yes	****	<0.0001
NSC+MSC Foxj1 vs. EpP Foxj1	5.800	-7.867 to 19.47	No	ns	0.6272
NSC+MSC Foxj1 vs. EpP+MSC Foxj1	-17.4	-31.07 to -3.733	Yes	*	0.0106
EpP Foxj1 vs. EpP+MSC Foxj1	-23.2	-36.87 to -9.533	Yes	***	0.0009

ANOVA summary GFAP	
F	0.9816
P value	0.4261
P value summary	ns
Significant diff. among means (P < 0.05)?	No
R squared	0.1554

Tukey's multiple comparisons test GFAP	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
NSC GFAP vs. NSC+MSC GFAP	5.000	-6.558 to 16.56	No	ns	0.6131
NSC GFAP vs. EpP GFAP	4.800	-6.758 to 16.36	No	ns	0.6426
NSC GFAP vs. EpP+MSC GFAP	0	-11.56 to 11.56	No	ns	>0.9999
NSC+MSC GFAP vs. EpP GFAP	-0.2	-11.76 to 11.36	No	ns	>0.9999
NSC+MSC GFAP vs. EpP+MSC GFAP	-5.000	-16.56 to 6.558	No	ns	0.6131
EpP GFAP vs. EpP+MSC GFAP	-4.800	-16.36 to 6.758	No	ns	0.6426

ANOVA summary NG2	
F	11.83
P value	0.0002
P value summary	***
Significant diff. among means (P < 0.05)?	Yes
R squared	0.6893

Tukey's multiple comparisons test NG2	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
NSC NG2 vs. NSC+MSC NG2	-1.000	-4.028 to 2.028	No	ns	0.7815
NSC NG2 vs. EpP NG2	3.800	0.7722 to 6.828	Yes	*	0.0118
NSC NG2 vs. EpP+MSC NG2	4.000	0.9722 to 7.028	Yes	**	0.008
NSC+MSC NG2 vs. EpP NG2	4.800	1.772 to 7.828	Yes	**	0.0017
NSC+MSC NG2 vs. EpP+MSC NG2	5.000	1.972 to 8.028	Yes	**	0.0012
EpP NG2 vs. EpP+MSC NG2	0.2	-2.828 to 3.228	No	ns	0.9975

Table S8. Statistical data corresponding to **Figure 3E.** Shapiro-Wilk, ANOVA, and Tukey's multiple comparison tests (ns: no significant differences; *p < 0.05, ** p < 0.01, *** p < 0.001, ****p < 0.0001). It continues on the next pages.

Data Figure 3E Blood Serum modPHH

Shapiro-Wilk test	NSC neg	NSC+MSC neg	EpP neg	EpP+MSC neg	NSC Foxj1	NSC+MSC Foxj1	EpP Foxj1	EpP+MSC Foxj1	NSC GFAP	NSC+MSC GFAP	EpP neg GFAP	EpP+MSC GFAP	NSC NG2	NSC+MSC NG2
W	0.8136	0.953	0.9621	0.9449	0.8582	0.9427	0.9675	0.9017	0.9164	0.9564	0.9713	0.9621	0.9782	0.8668
P value	0.1041	0.7583	0.8225	0.7005	0.222	0.6853	0.8591	0.4195	0.5073	0.783	0.8838	0.8224	0.9249	0.2538
Passed normality test (alpha=0.05)?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

ANOVA summary negative	
F	2.614
P value	0.0869
P value summary	ns
Significant diff. among means (P < 0.05)?	No
R squared	0.3289

Tukey's multiple comparisons test negative	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
NSC neg vs. NSC+MSC neg	6.000	-5.354 to 17.35	No	ns	0.4537
NSC neg vs. EpP neg	-2.800	-14.15 to 8.554	No	ns	0.8934
NSC neg vs. EpP+MSC neg	6.400	-4.954 to 17.75	No	ns	0.3996
NSC+MSC neg vs. EpP neg	-8.800	-20.15 to 2.554	No	ns	0.1607
NSC+MSC neg vs. EpP+MSC neg	0.400	-10.95 to 11.75	No	ns	0.9996
EpP neg vs. EpP+MSC neg	9.200	-2.154 to 20.55	No	ns	0.1353

ANOVA summary Foxj1	
F	90.4
P value	<0.0001
P value summary	****
Significant diff. among means (P < 0.05)?	Yes
R squared	0.9443

Tukey's multiple comparisons test Foxj1	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
NSC Foxj1 vs. NSC+MSC Foxj1	-3.400	-9.388 to 2.588	No	ns	0.3934
NSC Foxj1 vs. EpP Foxj1	-17.8	-23.79 to -11.81	Yes	****	<0.0001
NSC Foxj1 vs. EpP+MSC Foxj1	-30.6	-36.59 to -24.61	Yes	****	<0.0001
NSC+MSC Foxj1 vs. EpP Foxj1	-14.4	-20.39 to -8.412	Yes	****	<0.0001
NSC+MSC Foxj1 vs. EpP+MSC Foxj1	-27.2	-33.19 to -21.21	Yes	****	<0.0001
EpP Foxj1 vs. EpP+MSC Foxj1	-12.8	-18.79 to -6.812	Yes	****	<0.0001

ANOVA summary GFAP	
F	18
P value	<0.0001
P value summary	****
Significant diff. among means (P < 0.05)?	Yes
R squared	0.7714

Tukey's multiple comparisons test GFAP	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
NSC GFAP vs. NSC+MSC GFAP	-5.600	-14.60 to 3.397	No	ns	0.3178
NSC GFAP vs. EpP neg GFAP	10.800	1.803 to 19.80	Yes	*	0.0161
NSC GFAP vs. EpP+MSC GFAP	14.800	5.803 to 23.80	Yes	**	0.0012
NSC+MSC GFAP vs. EpP GFAP	16.400	7.403 to 25.40	Yes	***	0.0004
NSC+MSC GFAP vs. EpP+MSC GFAP	20.400	11.40 to 29.40	Yes	****	<0.0001
EpP GFAP vs. EpP+MSC GFAP	4.000	-4.997 to 13.00	No	ns	0.5927

ANOVA summary NG2	
F	15.670
P value	<0.0001
P value summary	****
Significant diff. among means (P < 0.05)?	Yes
R squared	0.7461

Tukey's multiple comparisons test NG2	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
NSC NG2 vs. NSC+MSC NG2	-0.400	-4.476 to 3.676	No	ns	0.992
NSC NG2 vs. EpP NG2	6.600	2.524 to 10.68	Yes	**	0.0014
NSC NG2 vs. EpP+MSC NG2	6.800	2.724 to 10.88	Yes	**	0.0011
NSC+MSC NG2 vs. EpP NG2	7.000	2.924 to 11.08	Yes	***	0.0008
NSC+MSC NG2 vs. EpP+MSC NG2	7.200	3.124 to 11.28	Yes	***	0.0006
EpP NG2 vs. EpP+MSC NG2	0.200	-3.876 to 4.276	No	ns	0.999

Table S8. Statistical data corresponding to **Figure 3E.** Shapiro-Wilk, ANOVA, and Tukey's multiple comparison tests. (ns: no significant differences; *p < 0.05, ** p < 0.01, *** p < 0.001, ****p < 0.0001). It continues on the next pages.

Data Figure 3E Collagenase sevPHH

Shapiro-Wilk test	NSC neg	NSC+MSC neg	EpP neg	EpP+MSC neg	NSC Foxj1	NSC+MSC Foxj1	EpP Foxj1	EpP+MSC Foxj1	NSC GFAP	NSC+MSC GFAP	EpP neg GFAP	EpP+MSC GFAP	NSC NG2	NSC+MSC NG2
W	0.9193	0.9748	0.9517	0.9896	0.9128	0.942	0.9691	0.9786	0.9751	0.954	0.8887	0.9385	0.7787	0.9868
P value	0.5251	0.9052	0.7496	0.9784	0.4848	0.6799	0.8697	0.9268	0.9069	0.7656	0.3504	0.6553	0.0537	0.9672
Passed normality test (alpha=0.05)?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

ANOVA summary negative	
F	13.82
P value	0.0001
P value summary	***
Significant diff. among means (P < 0.05)?	Yes
R squared	0.7216

Tukey's multiple comparisons test negative	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
NSC neg vs. NSC+MSC neg	10.4	0.7063 to 20.09	Yes	*	0.0334
NSC neg vs. EpP neg	2.600	-7.094 to 12.29	No	ns	0.8679
NSC neg vs. EpP+MSC neg	19.8	10.11 to 29.49	Yes	***	0.0001
NSC+MSC neg vs. EpP neg	-7.700	-17.49 to 1.894	No	ns	0.1391
NSC+MSC neg vs. EpP+MSC neg	9.400	-0.2937 to 19.09	No	ns	0.059
EpP neg vs. EpP+MSC neg	17.2	7.506 to 26.89	Yes	***	0.0006

ANOVA summary Foxj1	
F	10.67
P value	0.0004
P value summary	***
Significant diff. among means (P < 0.05)?	Yes
R squared	0.6667

Tukey's multiple comparisons test Foxj1	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
NSC Foxj1 vs. NSC+MSC Foxj1	-12.2	-25.48 to 1.081	No	ns	0.0776
NSC Foxj1 vs. EpP Foxj1	-11.6	-24.88 to 1.681	No	ns	0.0983
NSC Foxj1 vs. EpP+MSC Foxj1	-26.2	-39.48 to -12.92	Yes	***	0.0002
NSC+MSC Foxj1 vs. EpP Foxj1	0.6	-12.68 to 13.88	No	ns	0.9992
NSC+MSC Foxj1 vs. EpP+MSC Foxj1	-14	-27.28 to -0.7186	Yes	*	0.0371
EpP Foxj1 vs. EpP+MSC Foxj1	-14.6	-27.88 to -1.319	Yes	*	0.0288

ANOVA summary GFAP	
F	0.5694
P value	0.6432
P value summary	ns
Significant diff. among means (P < 0.05)?	No
R squared	0.09646

Tukey's multiple comparisons test GFAP	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
NSC GFAP vs. NSC+MSC GFAP	1.800	-8.870 to 12.47	No	ns	0.9619
NSC GFAP vs. EpP GFAP	4.800	-5.870 to 15.47	No	ns	0.5837
NSC GFAP vs. EpP+MSC GFAP	2.600	-8.070 to 13.27	No	ns	0.8967
NSC+MSC GFAP vs. EpP GFAP	3.000	-7.670 to 13.67	No	ns	0.8514
NSC+MSC GFAP vs. EpP+MSC GFAP	0.800	-9.870 to 11.47	No	ns	0.9964
EpP GFAP vs. EpP+MSC GFAP	-2.200	-12.87 to 8.470	No	ns	0.9337

ANOVA summary NG2	
F	23.9
P value	<0.0001
P value summary	****
Significant diff. among means (P < 0.05)?	Yes
R squared	0.8176

Tukey's multiple comparisons test NG2	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
NSC NG2 vs. NSC+MSC NG2	1.200	-0.9410 to 3.341	No	ns	0.4043
NSC NG2 vs. EpP NG2	5.000	2.859 to 7.141	Yes	****	<0.0001
NSC NG2 vs. EpP+MSC NG2	5.000	2.859 to 7.141	Yes	****	<0.0001
NSC+MSC NG2 vs. EpP NG2	3.800	1.659 to 5.941	Yes	***	0.0006
NSC+MSC NG2 vs. EpP+MSC NG2	3.800	1.659 to 5.941	Yes	***	0.0006
EpP NG2 vs. EpP+MSC NG2	0.000	-2.141 to 2.141	No	ns	>0.9999

Table S8. Statistical data corresponding to **Figure 3E.** Shapiro-Wilk, ANOVA, and Tukey's multiple comparison tests. (ns: no significant differences; *p < 0.05, ** p < 0.01, *** p < 0.001, ****p < 0.0001). It continues on the next page.

Data Figure 3E Collagenase modPHH

Table 3E Collagenase modPHH	NSC neg	NSC+MSC neg	EpP neg	EpP+MSC neg	NSC Foxj1	NSC+MSC Foxj1	EpP Foxj1	EpP+MSC Foxj1	NSC GFAP	NSC+MSC GFAP	EpP neg GFAP	EpP+MSC GFAP	NSC NG2	NSC+MSC NG2
Shapiro-Wilk test														
W	0.9489	0.9866	0.9687	0.933	0.989	0.979	0.9255	0.9097	0.9522	0.9044	0.9001	0.9862	0.99	0.9636
P value	0.7296	0.9665	0.867	0.6169	0.9761	0.9293	0.5657	0.4657	0.7526	0.4348	0.4105	0.9648	0.9796	0.8325
Passed normality test (alpha=0.05)?	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes

ANOVA summary negative	
F	22.53
P value	<0.0001
P value summary	****
Significant diff. among means (P < 0.05)?	Yes
R squared	0.8086

Tukey's multiple comparisons test	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
NSC neg vs. NSC+MSC neg	27.800	17.78 to 37.82	Yes	****	<0.0001
NSC neg vs. EpP neg	11.800	1.778 to 21.82	Yes	*	0.0184
NSC neg vs. EpP+MSC neg	19.000	8.978 to 29.02	Yes	***	0.0003
NSC+MSC neg vs. EpP neg	-16.000	-26.02 to -5.978	Yes	**	0.0016
NSC+MSC neg vs. EpP+MSC neg	-8.800	-18.82 to 1.222	No	ns	0.0959
EpP neg vs. EpP+MSC neg	7.200	-2.822 to 17.22	No	ns	0.2096

ANOVA summary Foxj1	
F	29.37
P value	<0.0001
P value summary	****
Significant diff. among means (P < 0.05)?	Yes
R squared	0.8463

Tukey's multiple comparisons test Foxj1	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
NSC Foxj1 vs. NSC+MSC Foxj1	-16	-28.81 to -3.192	Yes	*	0.0122
NSC Foxj1 vs. EpP Foxj1	-31.4	-44.21 to -18.59	Yes	****	<0.0001
NSC Foxj1 vs. EpP+MSC Foxj1	-38.6	-51.41 to -25.79	Yes	****	<0.0001
NSC+MSC Foxj1 vs. EpP Foxj1	-15.4	-28.21 to -2.592	Yes	*	0.016
NSC+MSC Foxj1 vs. EpP+MSC Foxj1	-22.6	-35.41 to -9.792	Yes	***	0.0006
EpP Foxj1 vs. EpP+MSC Foxj1	-7.200	-20.01 to 5.608	No	ns	0.4018

ANOVA summary GFAP	
F	11.01
P value	0.0004
P value summary	***
Significant diff. among means (P < 0.05)?	Yes
R squared	0.6737

Tukey's multiple comparisons test GFAP	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
NSC GFAP vs. NSC+MSC GFAP	-10.000	-21.49 to 1.494	No	ns	0.1
NSC GFAP vs. EpP GFAP	10.200	-1.294 to 21.69	No	ns	0.0914
NSC GFAP vs. EpP+MSC GFAP	9.200	-2.294 to 20.69	No	ns	0.142
NSC+MSC GFAP vs. EpP GFAP	20.200	8.706 to 31.69	Yes	***	0.0006
NSC+MSC GFAP vs. EpP+MSC GFAP	19.200	7.706 to 30.69	Yes	**	0.0011
EpP GFAP vs. EpP+MSC GFAP	-1.000	-12.49 to 10.49	No	ns	0.9944

ANOVA summary NG2	
F	32.29
P value	<0.0001
P value summary	****
Significant diff. among means (P < 0.05)?	Yes
R squared	0.8582

Tukey's multiple comparisons test NG2	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
NSC NG2 vs. NSC+MSC NG2	-1.600	-6.106 to 2.906	No	ns	0.7427
NSC NG2 vs. EpP NG2	10	5.494 to 14.51	Yes	****	<0.0001
NSC NG2 vs. EpP+MSC NG2	10.2	5.694 to 14.71	Yes	****	<0.0001
NSC+MSC NG2 vs. EpP NG2	11.6	7.094 to 16.11	Yes	****	<0.0001
NSC+MSC NG2 vs. EpP+MSC NG2	11.8	7.294 to 16.31	Yes	****	<0.0001
EpP NG2 vs. EpP+MSC NG2	0.2	-4.306 to 4.706	No	ns	0.9992

Table S8. Statistical data corresponding to **Figure 3E.** Shapiro-Wilk, ANOVA, and Tukey's multiple comparison tests. (ns: no significant differences; *p < 0.05, ** p < 0.01, *** p < 0.001, ****p < 0.0001).

Data Figure 4A Blood Serum (BS)

Shapiro-Wilk test sevPHH	sev BS NSC	sev BS NSC+MSC	sev BS EP	sev BS EP+MSC
W	0.953	0.95	0.9279	0.9738
P value	0.7583	0.7371	0.5819	0.8989
Passed normality test (alpha=0.05)?	Yes	Yes	Yes	Yes

ANOVA summary sevPHH	
F	56.95
P value	<0.0001
P value summary	****
Significant diff. among means (P < 0.05)?	Yes
R squared	0.9144

Tukey's multiple comparisons test sevPHH	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
sev BS NSC vs. sev BS NSC+MSC	11.8	1.019 to 22.58	Yes	*	0.0295
sev BS NSC vs. sev BS EP	-27.2	-37.98 to -16.42	Yes	****	<0.0001
sev BS NSC vs. sev BS EP+MSC	-28.6	-39.38 to -17.82	Yes	****	<0.0001
sev BS NSC+MSC vs. sev BS EP	-39.0	-49.78 to -28.22	Yes	****	<0.0001
sev BS NSC+MSC vs. sev BS EP+MSC	-40.4	-51.18 to -29.62	Yes	****	<0.0001
sev BS EP vs. sev BS EP+MSC	-1.4	-12.18 to 9.381	No	ns	0.9819

Shapiro-Wilk test modPHH	mod BS NSC	mod BS NSC+MSC	mod BS EP	mod BS EP+MSC
W	0.9956	0.9501	0.9623	0.9564
P value	0.9952	0.7377	0.8239	0.7827
Passed normality test (alpha=0.05)?	Yes	Yes	Yes	Yes

ANOVA summary modPHH	
F	36.64
P value	<0.0001
P value summary	****
Significant diff. among means (P < 0.05)?	Yes
R squared	0.8729

Tukey's multiple comparisons test modPHH	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
mod BS NSC vs. mod BS NSC+MSC	3.6	-5.798 to 13.00	No	ns	0.697
mod BS NSC vs. mod BS EP	-20.6	-30.00 to -11.20	Yes	****	<0.0001
mod BS NSC vs. mod BS EP+MSC	-24.0	-33.40 to -14.60	Yes	****	<0.0001
mod BS NSC+MSC vs. mod BS EP	-24.2	-33.60 to -14.80	Yes	****	<0.0001
mod BS NSC+MSC vs. mod BS EP+MSC	-27.6	-37.00 to -18.20	Yes	****	<0.0001
mod BS EP vs. mod BS EP+MSC	-3.4	-12.80 to 5.998	No	ns	0.7319

Table S9. Statistical data corresponding to **Figure 4A**. Shapiro-Wilk, ANOVA, and Tukey's multiple comparison tests. (ns: no significant differences; *p < 0.05, ** p < 0.01, *** p < 0.001, ****p < 0.0001). It continues on the next page.

Data Figure 4A Collagenase (Coll)

Shapiro-Wilk test sevPHH	sev Coll NSC	sev Coll NSC+MSC	sev Coll Ep	sev Coll Ep+MSC
W	0.982	0.9569	0.9937	0.8954
P value	0.9453	0.7866	0.9909	0.3852
Passed normality test (alpha=0.05)?	Yes	Yes	Yes	Yes

ANOVA summary sevPHH	
F	106.4
P value	<0.0001
P value summary	****
Significant diff. among means (P < 0.05)?	Yes
R squared	0.9523

Tukey's multiple comparisons test sevPHH	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
sev Coll NSC vs. sev Coll NSC+MSC	10.2	1.703 to 18.70	Yes	*	0.0161
sev Coll NSC vs. sev Coll Ep	-32.4	-40.90 to -23.90	Yes	****	<0.0001
sev Coll NSC vs. sev Coll Ep+MSC	-31.0	-39.50 to -22.50	Yes	****	<0.0001
sev Coll NSC+MSC vs. sev Coll Ep	-42.6	-51.10 to -34.10	Yes	****	<0.0001
sev Coll NSC+MSC vs. sev Coll Ep+MSC	-41.2	-49.70 to -32.70	Yes	****	<0.0001
sev Coll Ep vs. sev Coll Ep+MSC	1.4	-7.097 to 9.897	No	ns	0.9643

Shapiro-Wilk test modPHH	mod Coll NSC	mod Coll NSC+MSC	mod Coll Ep	mod Coll Ep+MSC
W	0.9943	0.9417	0.9896	0.9675
P value	0.9924	0.6779	0.9784	0.8591
Passed normality test (alpha=0.05)?	Yes	Yes	Yes	Yes

ANOVA summary modPHH	
F	14.16
P value	<0.0001
P value summary	****
Significant diff. among means (P < 0.05)?	Yes
R squared	0.7264

Tukey's multiple comparisons test modPHH	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
mod Coll NSC vs. mod Coll NSC+MSC	12.6	1.891 to 23.31	Yes	*	0.0185
mod Coll NSC vs. mod Coll Ep	-6.2	-16.91 to 4.509	No	ns	0.3772
mod Coll NSC vs. mod Coll Ep+MSC	-10.2	-20.91 to 0.5088	No	ns	0.0647
mod Coll NSC+MSC vs. mod Coll Ep	-18.8	-29.51 to -8.091	Yes	***	0.0007
mod Coll NSC+MSC vs. mod Coll Ep+MSC	-22.8	-33.51 to -12.09	Yes	****	<0.0001
mod Coll Ep vs. mod Coll Ep+MSC	-4.0	-14.71 to 6.709	No	ns	0.7127

Table S9. Statistical data corresponding to **Figure 4A**. Shapiro-Wilk, ANOVA, and Tukey's multiple comparison tests. (ns: no significant differences; *p < 0.05, ** p < 0.01, *** p < 0.001, ****p < 0.0001).

Shapiro-Wilk test 3d	3d control	3d MSC	3d Blood	3d Blood Serum	3d TNF
W	0.9957	0.9329	0.8561	0.9938	0.7972
P value	0.9954	0.6164	0.2147	0.9911	0.0769
Passed normality test (alpha=0.05)?	Yes	Yes	Yes	Yes	Yes
ANOVA summary 3d					
F	21.16				
P value	<0.0001				
P value summary	****				
Significant diff. among means (P < 0.05)?	Yes				
R squared	0.8089				
Tukey's multiple comparisons test 3d	**Mean Diff.**	**95.00% CI of diff.**	**Below threshold?**	**Summary**	**Adjusted P Value**
3d control vs. 3d MSC	-1.6130	-5.416 to 2.189	No	ns	0.7119
3d control vs. 3d Blood	7.1670	3.364 to 10.97	Yes	***	0.0001
3d control vs. 3d BS	5.6800	1.878 to 9.482	Yes	**	0.002
3d control vs. 3d TNF	6.9400	3.138 to 10.74	Yes	***	0.0002
3d MSC vs. 3d Blood	8.7800	4.978 to 12.58	Yes	****	<0.0001
3d MSC vs. 3d BS	7.2930	3.491 to 11.10	Yes	***	0.0001
3d MSC vs. 3d TNF	8.5530	4.751 to 12.36	Yes	****	<0.0001
3d Blood vs. 3d BS	-1.4870	-5.289 to 2.316	No	ns	0.7678
3d Blood vs. 3d TNF	-0.2267	-4.029 to 3.576	No	ns	0.9998
3d BS vs. 3d TNF	1.2600	-2.542 to 5.062	No	ns	0.856

Shapiro-Wilk test 6d	6d control	6d MSC	6d Blood	6d BS	6d TNF
W	0.9525	0.9738	0.9112	0.9464	0.8465
P value	0.7548	0.8989	0.4751	0.7111	0.1838
Passed normality test (alpha=0.05)?	Yes	Yes	Yes	Yes	Yes
ANOVA summary 6d					
F	318.4				
P value	<0.0001				
P value summary	****				
Significant diff. among means (P < 0.05)?	Yes				
R squared	0.9845				
Tukey's multiple comparisons test 6d	**Mean Diff.**	**95.00% CI of diff.**	**Below threshold?**	**Summary**	**Adjusted P Value**
6d control vs. 6d MSC	-7.5600	-10.00 to -5.120	Yes	****	<0.0001
6d control vs. 6d Blood	15.5800	13.14 to 18.02	Yes	****	<0.0001
6d control vs. 6d BS	12.1500	9.707 to 14.59	Yes	****	<0.0001
6d control vs. 6d TNF	14.8900	12.45 to 17.33	Yes	****	<0.0001
6d MSC vs. 6d Blood	23.1400	20.70 to 25.58	Yes	****	<0.0001
6d MSC vs. 6d BS	19.7100	17.27 to 22.15	Yes	****	<0.0001
6d MSC vs. 6d TNF	22.4500	20.01 to 24.89	Yes	****	<0.0001
6d Blood vs. 6d BS	-3.4330	-5.873 to -0.9933	Yes	**	0.0035
6d Blood vs. 6d TNF	-0.6867	-3.127 to 1.753	No	ns	0.9141
6d BS vs. 6d TNF	2.7470	0.3067 to 5.187	Yes	*	0.0227

Shapiro-Wilk test 9d	9d control	9d MSC	9d Blood	9d BS	9d TNF
W	0.9902	0.9816	0.9738	0.9331	0.8838
P value	0.9804	0.9429	0.8989	0.6173	0.3267
Passed normality test (alpha=0.05)?	Yes	Yes	Yes	Yes	Yes
ANOVA summary 9d					
F	230.4				
P value	<0.0001				
P value summary	****				
Significant diff. among means (P < 0.05)?	Yes				
R squared	0.9788				
Tukey's multiple comparisons test 9d	**Mean Diff.**	**95.00% CI of diff.**	**Below threshold?**	**Summary**	**Adjusted P Value**
9d control vs. 9d MSC	1.1400	-2.538 to 4.818	No	ns	0.8829
9d control vs. 9d Blood	26.4000	22.72 to 30.08	Yes	****	<0.0001
9d control vs. 9d BS	20.7900	17.11 to 24.47	Yes	****	<0.0001
9d control vs. 9d TNF	25.7600	22.08 to 29.44	Yes	****	<0.0001
9d MSC vs. 9d Blood	25.2600	21.58 to 28.94	Yes	****	<0.0001
9d MSC vs. 9d BS	19.6500	15.97 to 23.33	Yes	****	<0.0001
9d MSC vs. 9d TNF	24.6200	20.94 to 28.30	Yes	****	<0.0001
9d Blood vs. 9d BS	-5.6130	-9.292 to -1.935	Yes	**	0.0016
9d Blood vs. 9d TNF	-0.6400	-4.318 to 3.038	No	ns	0.9842
9d BS vs. 9d TNF	4.9730	1.295 to 8.652	Yes	**	0.0051

Table S10. Statistical data corresponding to **Figure 4C**. Shapiro-Wilk, ANOVA, and Tukey's multiple comparison tests. (ns: no significant differences; *p < 0.05, ** p < 0.01, *** p < 0.001, ****p < 0.0001).

Data Figure 4E Blood, Blood+MSC

Shapiro-Wilk test Blood, Blood+MSC	Blood 3d	Blood+MSC 3d	Blood 6d	Blood+MSC 6d	Blood 9d	Blood+MSC 9d
W	0.8604	0.963	0.9634	0.9446	0.9076	0.9329
P value	0.1527	0.844	0.8476	0.6802	0.3794	0.5755
Passed normality test (alpha=0.05)?	Yes	Yes	Yes	Yes	Yes	Yes

ANOVA summary Blood, Blood+MSC	
F	12.09
P value	<0.0001
P value summary	****
Significant diff. among means (P < 0.05)?	Yes
R squared	0.6268

Tukey's multiple comparisons test, Blood, Blood+MSC	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
Blood 3d vs. Blood+MSC 3d	6.641	-5.079 to 18.36	No	ns	0.5377
Blood 3d vs. Blood 6d	17.860	6.141 to 29.58	Yes	***	0.0007
Blood 3d vs. Blood+MSC 6d	15.150	3.425 to 26.87	Yes	**	0.0052
Blood 3d vs. Blood 9d	24.720	13.00 to 36.44	Yes	****	<0.0001
Blood 3d vs. Blood+MSC 9d	22.900	11.18 to 34.62	Yes	****	<0.0001
Blood+MSC 3d vs. Blood 6d	11.220	-0.5005 to 22.94	No	ns	0.0673
Blood+MSC 3d vs. Blood+MSC 6d	8.504	-3.217 to 20.22	No	ns	0.2705
Blood+MSC 3d vs. Blood 9d	18.080	6.361 to 29.80	Yes	***	0.0006
Blood+MSC 3d vs. Blood+MSC 9d	16.260	4.536 to 27.98	Yes	**	0.0023
Blood 6d vs. Blood+MSC 6d	-2.716	-14.44 to 9.004	No	ns	0.9811
Blood 6d vs. Blood 9d	6.862	-4.859 to 18.58	No	ns	0.5023
Blood 6d vs. Blood+MSC 9d	5.037	-6.684 to 16.76	No	ns	0.7869
Blood+MSC 6d vs. Blood 9d	9.578	-2.143 to 21.30	No	ns	0.1638
Blood+MSC 6d vs. Blood+MSC 9d	7.753	-3.967 to 19.47	No	ns	0.3676
Blood 9d vs. Blood+MSC 9d	-1.825	-13.55 to 9.896	No	ns	0.997

Table S11. Statistical data corresponding to **Figure 4E**. Shapiro-Wilk, ANOVA, and Tukey's multiple comparison tests. (ns: no significant differences; *p < 0.05, ** p < 0.01, *** p < 0.001, ****p < 0.0001). It continues on the next pages.

Data Figure 4E Blood Serum (BS), BS+MSC

Shapiro-Wilk test BS, BS+MSC	Blood 3d	Blood+MSC 3d	Blood 6d	Blood+MSC 6d	Blood 9d	Blood+MSC 9d
W	0.8604	0.963	0.9634	0.9446	0.9076	0.9329
P value	0.1527	0.844	0.8476	0.6802	0.3794	0.5755
Passed normality test (alpha=0.05)?	Yes	Yes	Yes	Yes	Yes	Yes

ANOVA summary BS, BS+MSC	
F	12.09
P value	<0.0001
P value summary	****
Significant diff. among means (P < 0.05)?	Yes
R squared	0.6268

Tukey's multiple comparisons test BS, BS+MSC	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
BS 3d vs. BS+MSC 3d	-30.530	-43.99 to -17.07	Yes	****	<0.0001
BS 3d vs. BS 6d	8.605	-4.856 to 22.07	No	ns	0.4052
BS 3d vs. BS+MSC 6d	-19.660	-33.12 to -6.196	Yes	**	0.0012
BS 3d vs. BS 9d	16.220	2.762 to 29.68	Yes	*	0.0106
BS 3d vs. BS+MSC 9d	-12.960	-26.42 to 0.5026	No	ns	0.0648
BS+MSC 3d vs. BS 6d	39.140	25.68 to 52.60	Yes	****	<0.0001
BS+MSC 3d vs. BS+MSC 6d	10.880	-2.585 to 24.34	No	ns	0.1728
BS+MSC 3d vs. BS 9d	46.760	33.30 to 60.22	Yes	****	<0.0001
BS+MSC 3d vs. BS+MSC 9d	17.580	4.114 to 31.04	Yes	**	0.0046
BS 6d vs. BS+MSC 6d	-28.260	-41.72 to -14.80	Yes	****	<0.0001
BS 6d vs. BS 9d	7.618	-5.843 to 21.08	No	ns	0.539
BS 6d vs. BS+MSC 9d	-21.560	-35.02 to -8.102	Yes	***	0.0004
BS+MSC 6d vs. BS 9d	35.880	22.42 to 49.34	Yes	****	<0.0001
BS+MSC 6d vs. BS+MSC 9d	6.699	-6.762 to 20.16	No	ns	0.6681
BS 9d vs. BS+MSC 9d	-29.180	-42.64 to -15.72	Yes	****	<0.0001

Table S11. Statistical data corresponding to **Figure 4E**. Shapiro-Wilk, ANOVA, and Tukey's multiple comparison tests. (ns: no significant differences; *p < 0.05, ** p < 0.01, *** p < 0.001, ****p < 0.0001). It continues on the next page.

Data Figure 4E TNF, TNF+MSC

Shapiro-Wilk test TNF, TNF+MSC	TNF 3d	TNF+MSC 3d	TNF 6d	TNF+MSC 6d	TNF 9d	TNF+MSC 9d
W	0.9583	0.9254	0.9783	0.9328	0.9648	0.9499
P value	0.8038	0.5128	0.9511	0.5750	0.8588	0.7285
Passed normality test (alpha=0.05)?	Yes	Yes	Yes	Yes	Yes	Yes

ANOVA summary TNF, TNF+MSC	
F	32.51
P value	<0.0001
P value summary	****
Significant diff. among means (P < 0.05)?	Yes
R squared	0.8187

Tukey's multiple comparisons test TNF, TNF+MSC	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
TNF 3d vs. TNF+MSC 3d	-31.140	-42.84 to -19.44	Yes	****	<0.0001
TNF 3d vs. TNF 6d	-10.990	-22.70 to 0.7054	No	ns	0.0758
TNF 3d vs. TNF+MSC 6d	-27.430	-39.13 to -15.73	Yes	****	<0.0001
TNF 3d vs. TNF 9d	9.811	-1.889 to 21.51	No	ns	0.1443
TNF 3d vs. TNF+MSC 9d	-9.756	-21.46 to 1.944	No	ns	0.1485
TNF+MSC 3d vs. TNF 6d	20.150	8.450 to 31.85	Yes	***	0.0001
TNF+MSC 3d vs. TNF+MSC 6d	3.714	-7.986 to 15.41	No	ns	0.9289
TNF+MSC 3d vs. TNF 9d	40.960	29.26 to 52.66	Yes	****	<0.0001
TNF+MSC 3d vs. TNF+MSC 9d	21.390	9.688 to 33.09	Yes	****	<0.0001
TNF 6d vs. TNF+MSC 6d	-16.440	-28.14 to -4.735	Yes	**	0.002
TNF 6d vs. TNF 9d	20.810	9.106 to 32.51	Yes	****	<0.0001
TNF 6d vs. TNF+MSC 9d	1.239	-10.46 to 12.94	No	ns	0.9995
TNF+MSC 6d vs. TNF 9d	37.240	25.54 to 48.94	Yes	****	<0.0001
TNF+MSC 6d vs. TNF+MSC 9d	17.670	5.974 to 29.37	Yes	***	0.0008
TNF 9d vs. TNF+MSC 9d	-19.570	-31.27 to -7.867	Yes	***	0.0002

Table S11. Statistical data corresponding to **Figure 4E**. Shapiro-Wilk, ANOVA, and Tukey's multiple comparison tests. (ns: no significant differences; *p < 0.05, ** p < 0.01, *** p < 0.001, ****p < 0.0001).

Shapiro-Wilk test light	Non-treated	MSC	MSC+EpP
W	0.6928	0.9777	0.8715
P value	0.0052	0.922	0.2321
Passed normality test (alpha=0.05)?	No	Yes	Yes
P value summary	**	ns	ns

Kruskal-Wallis test light	
P value	0.0002
Exact or approximate P value?	Exact
P value summary	***
Do the medians vary signif. (P < 0.05)?	Yes
Number of groups	3
Kruskal-Wallis statistic	11.49

Dunn's multiple comparisons test light	Mean rank diff.	Significant?	Summary	Adjusted P Value
Non-treated vs. MSC	-7.400	Yes	*	0.0458
Non-treated vs. MSC+EpP	-9.417	Yes	**	0.0036
MSC vs. MSC+EpP	-2.017	No	ns	>0.9999

Shapiro-Wilk test moderate	Non-treated	MSC	MSC+EpP
W	0.8586	0.8472	0.8924
P value	0.1843	0.1858	0.331
Passed normality test (alpha=0.05)?	Yes	Yes	Yes
P value summary	ns	ns	ns

ANOVA summary moderate	
F	264.5
P value	<0.0001
P value summary	****
Significant diff. among means (P < 0.05)?	Yes
R squared	0.9742

Tukey's multiple comparisons test moderate	Mean Diff.	95.00% CI of diff.	Below threshold?	Summary	Adjusted P Value
Non-treated vs. MSC	52.730	44.96 to 60.50	Yes	****	<0.0001
Non-treated vs. MSC+EpP	60.330	52.92 to 67.74	Yes	****	<0.0001
MSC vs. MSC+EpP	7.600	-0.1703 to 15.37	No	ns	0.0556

Shapiro-Wilk test severe	Non-treated	MSC	MSC+EpP
W	0.7431	0.881	0.7013
P value	0.017	0.314	0.0064
Passed normality test (alpha=0.05)?	No	Yes	No
P value summary	*	ns	**

Kruskal-Wallis test severe	
P value	<0.0001
Exact or approximate P value?	Exact
P value summary	****
Do the medians vary signif. (P < 0.05)?	Yes
Number of groups	3
Kruskal-Wallis statistic	13.08

Dunn's multiple comparisons test severe	Mean rank diff.	Significant?	Summary	Adjusted P Value
Non-treated vs. MSC	6.300	No	ns	0.1106
Non-treated vs. MSC+EpP	10.330	Yes	***	0.001
MSC vs. MSC+EpP	4.033	No	ns	0.5443

Table S12. Statistical data corresponding to **Figure 5A**. Shapiro-Wilk, Kruskal-Wallis, Dunn's multiple comparisons, ANOVA, and Tukey's multiple comparison tests. (ns: no significant differences; ****$p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, ****$p < 0.0001$).

Anti-inflammatory cytokines

	G_1	G_2	n_1	Mean_1	StanDev_1	Median_1	Sum of Ranks_1	n_2	Mean_2	StanDev_2	Median_2	Sum of Ranks_2	Difference	p	Significance
Axl	Trauma	Trauma + MSC	4	-3.254	0.965	-3.254	10	4	6.429	0.459	6.429	26	9.683	0.0286	*
Axl	Trauma	Trauma + MSC + EpP	4	-3.254	0.965	-3.254	10	4	2.962	0.785	2.962	26	6.216	0.0286	*
CD30 T	Trauma	Trauma + MSC	4	-4.147	0.327	-4.147	10	4	5.594	0.432	5.594	26	9.740	0.0286	*
CD30 T	Trauma	Trauma + MSC + EpP	4	-4.147	0.327	-4.147	10	4	1.518	0.743	1.518	26	5.665	0.0286	*
Fas Ligand	Trauma	Trauma + MSC	4	-3.498	0.319	-3.498	10	4	6.480	0.635	6.480	26	9.978	0.0286	*
Fas Ligand	Trauma	Trauma + MSC + EpP	4	-3.498	0.319	-3.498	10	4	1.361	0.403	1.361	26	4.859	0.0286	*
IGFBP-3	Trauma	Trauma + MSC	4	15.250	3.000	15.250	26	4	-8.329	0.319	-8.329	10	-23.580	0.0286	*
IGFBP-3	Trauma	Trauma + MSC + EpP	4	15.250	3.000	15.250	10	4	20.040	1.485	20.040	26	4.788	0.0286	*
IL-10	Trauma	Trauma + MSC	4	-5.919	0.685	-5.919	10	4	4.131	0.796	4.131	26	10.050	0.0286	*
IL-10	Trauma	Trauma + MSC + EpP	4	-5.919	0.685	-5.919	10	4	0.021	0.157	0.021	26	5.940	0.0286	*
M-CSF	Trauma	Trauma + MSC	4	6.384	1.282	6.384	26	4	-7.098	3.041	-7.098	10	-13.480	0.0286	*
M-CSF	Trauma	Trauma + MSC + EpP	4	6.384	1.282	6.384	14	4	9.385	4.349	9.385	22	3.001	0.4000	NS
sTNF RII	Trauma	Trauma + MSC	4	4.850	0.020	4.850	10	4	10.020	1.457	10.020	26	5.171	0.0286	*
sTNF RII	Trauma	Trauma + MSC + EpP	4	4.850	0.020	4.850	10	4	17.740	2.271	17.740	26	12.890	0.0286	*
TIMP-1	Trauma	Trauma + MSC	4	-3.342	0.489	-3.342	10	4	7.232	0.710	7.232	26	10.570	0.0286	*
TIMP-1	Trauma	Trauma + MSC + EpP	4	-3.342	0.489	-3.342	10	4	2.026	0.172	2.026	26	5.367	0.0286	*

Homeostasis and Cell survival cytokines

	G_1	G_2	n_1	Mean_1	StanDev_1	Median_1	Sum of Ranks_1	n_2	Mean_2	StanDev_2	Median_2	Sum of Ranks_2	Difference	P	Significance
IGFBP-6	Trauma	Trauma + MSC	4	-1.087	0.1853	-1.087	10	4	2.137	0.5196	2.137	26	3.224	0.0286	*
IGFBP-6	Trauma	Trauma + MSC + EpP	4	-1.087	0.1853	-1.087	10	4	6.686	0.9497	6.686	26	7.772	0.0286	*
IL-17	Trauma	Trauma + MSC	4	1.864	0.4555	1.864	10	4	7.241	0.2257	7.241	26	5.377	0.0286	*
IL-17	Trauma	Trauma + MSC + EpP	4	1.864	0.4555	1.864	10	4	12.38	0.8031	12.38	26	10.52	0.0286	*

Pro-inflammatory cytokines

	G_1	G_2	n_1	Mean_1	StanDev_1	Median_1	Sum of Ranks_1	n_2	Mean_2	StanDev_2	Median_2	Difference	P	Significance
CD40	Trauma	Trauma + MSC	4	-3.422	0.272	-3.422	10	4	7.343	0.270	7.343	10.760	0.0286	*
CD40	Trauma	Trauma + MSC + EpP	4	-3.422	0.272	-3.422	10	4	1.127	0.217	1.127	4.548	0.0286	*
GM-CSF	Trauma	Trauma + MSC	4	8.658	1.609	8.658	26	4	-2.211	1.084	-2.211	-10.870	0.0286	*
GM-CSF	Trauma	Trauma + MSC + EpP	4	8.658	1.609	8.658	22	4	6.999	0.424	6.999	-1.659	0.4000	NS
IL-1alpha	Trauma	Trauma + MSC	4	7.672	0.166	7.672	26	4	-5.010	1.881	-5.010	-12.680	0.0286	*
IL-1alpha	Trauma	Trauma + MSC + EpP	4	7.672	0.166	7.672	10	4	12.170	0.057	12.170	4.495	0.0286	*
IL-1 beta	Trauma	Trauma + MSC	4	-3.098	0.120	-3.098	10	4	6.279	0.046	6.279	9.377	0.0286	*
IL-1 beta	Trauma	Trauma + MSC + EpP	4	-3.098	0.120	-3.098	10	4	1.538	0.211	1.538	4.636	0.0286	*
IL-2	Trauma	Trauma + MSC	4	-4.608	0.032	-4.608	10	4	2.242	0.107	2.242	6.850	0.0286	*
IL-2	Trauma	Trauma + MSC + EpP	4	-4.608	0.032	-4.608	10	4	3.409	0.648	3.409	8.017	0.0286	*
IL-3	Trauma	Trauma + MSC	4	-4.491	0.249	-4.491	10	4	4.771	0.212	4.771	9.261	0.0286	*
IL-3	Trauma	Trauma + MSC + EpP	4	-4.491	0.249	-4.491	10	4	-0.069	0.166	-0.069	4.422	0.0286	*
IL-6	Trauma	Trauma + MSC	4	-2.714	0.156	-2.714	10	4	7.315	0.085	7.315	10.030	0.0286	*
IL-6	Trauma	Trauma + MSC + EpP	4	-2.714	0.156	-2.714	10	4	1.899	0.289	1.899	4.613	0.0286	*
IL-9	Trauma	Trauma + MSC	4	-1.042	0.760	-1.042	22	4	-1.893	0.379	-1.893	-0.851	0.4000	NS
IL-9	Trauma	Trauma + MSC + EpP	4	-1.042	0.760	-1.042	10	4	4.662	0.678	4.662	5.704	0.0286	*
MCP-1	Trauma	Trauma + MSC	4	42.360	3.137	42.360	26	4	9.565	0.708	9.565	-32.790	0.0286	*
MCP-1	Trauma	Trauma + MSC + EpP	4	42.360	3.137	42.360	18	4	43.220	8.272	43.220	0.860	>0.9999	NS
MCP-5	Trauma	Trauma + MSC	4	22.170	6.380	22.170	26	4	13.010	2.361	13.010	-9.158	0.0286	*
MCP-5	Trauma	Trauma + MSC + EpP	4	22.170	6.380	22.170	26	4	15.290	0.193	15.290	-6.881	0.0286	*
TNFalpha	Trauma	Trauma + MSC	4	-4.497	0.538	-4.497	10	4	6.706	0.788	6.706	11.200	0.0286	*
TNFalpha	Trauma	Trauma + MSC + EpP	4	-4.497	0.538	-4.497	10	4	8.724	1.818	8.724	13.220	0.0286	*
TPO	Trauma	Trauma + MSC	4	9.618	0.573	9.618	26	4	4.967	1.649	4.967	-4.651	0.0286	*
TPO	Trauma	Trauma + MSC + EpP	4	9.618	0.573	9.618	10	4	20.650	0.273	20.650	11.030	0.0286	*
VCAM-1	Trauma	Trauma + MSC	4	112.200	8.627	112.200	26	4	41.470	5.133	41.470	-70.750	0.0286	*
VCAM-1	Trauma	Trauma + MSC + EpP	4	112.200	8.627	112.200	26	4	70.600	3.884	70.600	-41.620	0.0286	*

Table S13. Statistical data corresponding to **Figure 5C**. Wilcoxon-Mann-Whitney test was performed to study the existence of significant differences in the cytokine content between different treatments: MSC-treated explant medium versus nontreated explant medium and MSC+EpP-treated explant medium versus nontreated explant medium. G1: experimental group 1; G2: experimental group 2; Mean_1: mean of experimental group_1; Mean_2: mean of experimental group_2; StandDev_1: standard deviation of the mean of experimental group_1; StandDev_2: standard deviation of the mean of experimental group_2; p: p value; NS: no significant differences; *$p < 0.05$.

Shapiro-Wilk test	Control MSC light	MSC light	Control MSC mod	MSC mod	Control MSC sev	MSC sev
W	0.728	0.8178	0.8268	0.8966	0.8893	0.7709
P value	0.0184	0.1124	0.1317	0.3912	0.3535	0.046
Passed normality test (alpha=0.05)?	No	Yes	Yes	Yes	Yes	No

Mann-Whitney test	P value	Exact or approximate P value?	P value summary	Significantly different (P < 0.05)?	One- or two-tailed P value?	Sum of ranks	Mann-Whitney U
Control MSC light vs. MSC light	0.0079	Exact	**	Yes	Two-tailed	15 , 40	0
Control MSC mod vs. MSC mod	0.8413	Exact	ns	No	Two-tailed	26 , 29	11
Control MSC sev vs. MSC sev	0.0079	Exact	**	Yes	Two-tailed	40 , 15	0

Shapiro-Wilk test	Control MSC+EpP light	MSC+EpP light	Control MSC+EpP mod	MSC+EpP mod	Control MSC+EpP sev	MSC+EpP sev
W	0.8282	0.9635	0.8844	0.981	0.9965	0.5522
P value	0.1348	0.8318	0.3295	0.9401	0.9968	0.0001
Passed normality test (alpha=0.05)?	Yes	Yes	Yes	Yes	Yes	No

Mann-Whitney test	P value	Exact or approximate P value?	P value summary	Significantly different (P < 0.05)?	One- or two-tailed P value?	Sum of ranks	Mann-Whitney U
Control MSC+EpP light vs. MSC+EpP light	0.0079	Exact	**	Yes	Two-tailed	15 , 40	0
Control MSC+EpP mod vs. MSC+EpP mod	0.0079	Exact	**	Yes	Two-tailed	40 , 15	0
Control MSC+EpP sev vs. MSC+EpP sev	0.0079	Exact	**	Yes	Two-tailed	40 , 15	0

Table S14. Statistical data corresponding to **Figure 6B, D**. Shapiro-Wilk and Mann-Whitney tests. (ns: no significant differences; ** $p < 0.01$).

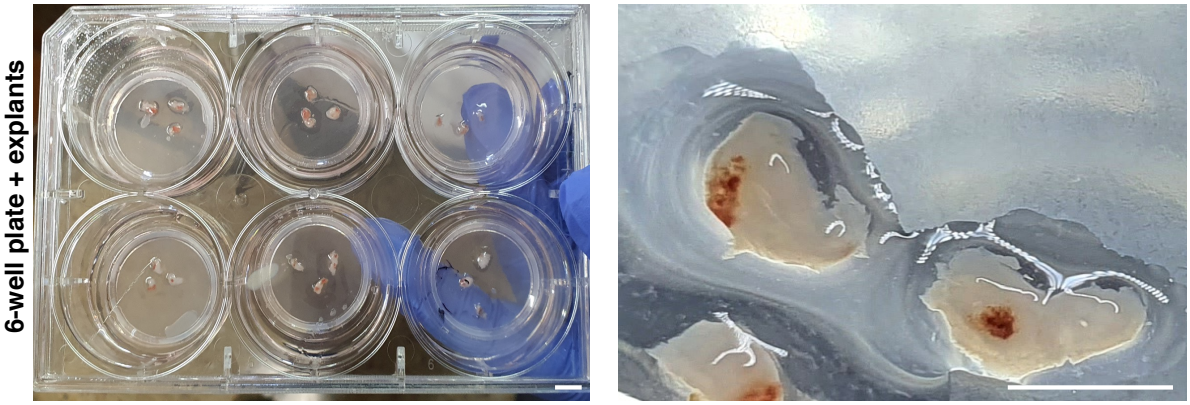


Figure S1. Lateral ventricle wall explants distribution in the 6-well plate. Details of the explants with moderate hemorrhage are shown in the picture on the **right**. Bars: 8 mm.

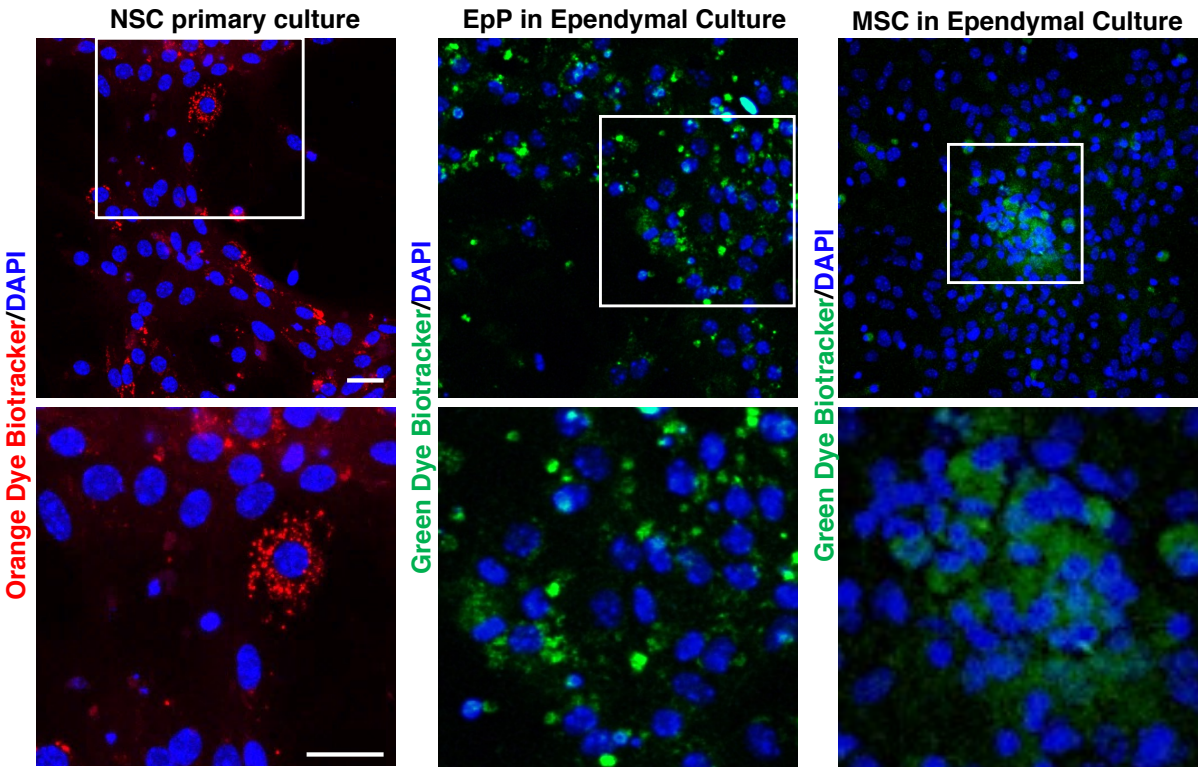


Figure S2. Primary cell cultures. **Left**: NSCs were labeled with an orange dye biotracker in passage 3 and fixed on day 21 of passage 5, showing the persistence of the tracker. **Center**: EpPs were labeled with a green dye biotracker before plating and fixed 11 days after plating. **Right**: EpPs cocultured with mouse MSCs; MSCs were labeled with a green dye biotracker and fixed 11 days after coculture, showing persistence of the dye and survival of MSCs in EpP culture media. Bars: 20 μm.

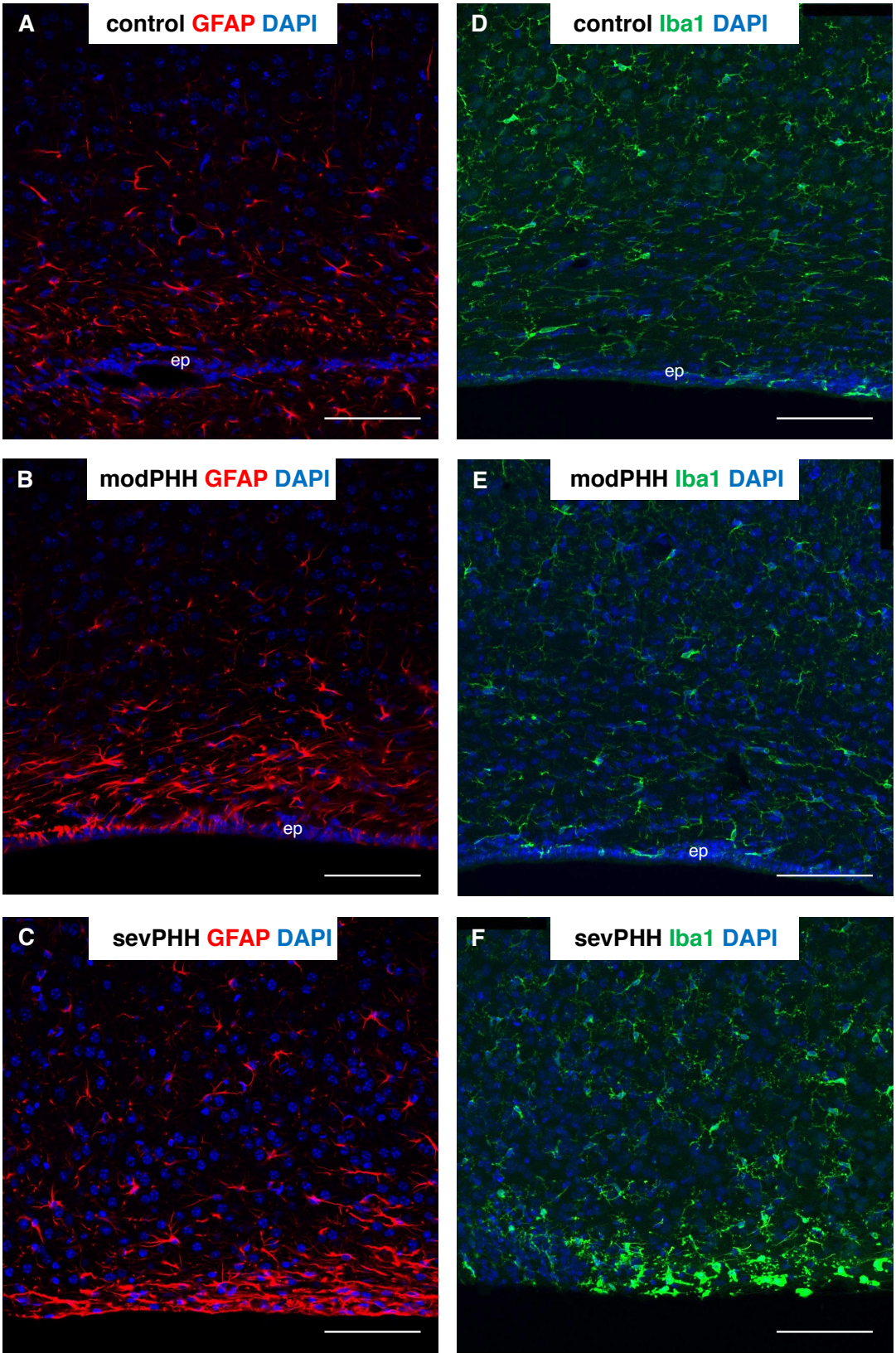


Figure S3. Reactions of astroglia (*GFAP* labeling) and microglia (*Iba1* labeling), compared with a normal (*control*) mouse **(A, D),** in mice with modPHH **(B, E)** and sevPHH **(C, F)**. The presence of ependyma is indicated when present (*ep*). Cell nuclei stained with DAPI (*blue*). Scale bars: 77 µm. The results corresponding to mice with PHH correspond to GMH induction by collagenase injection.

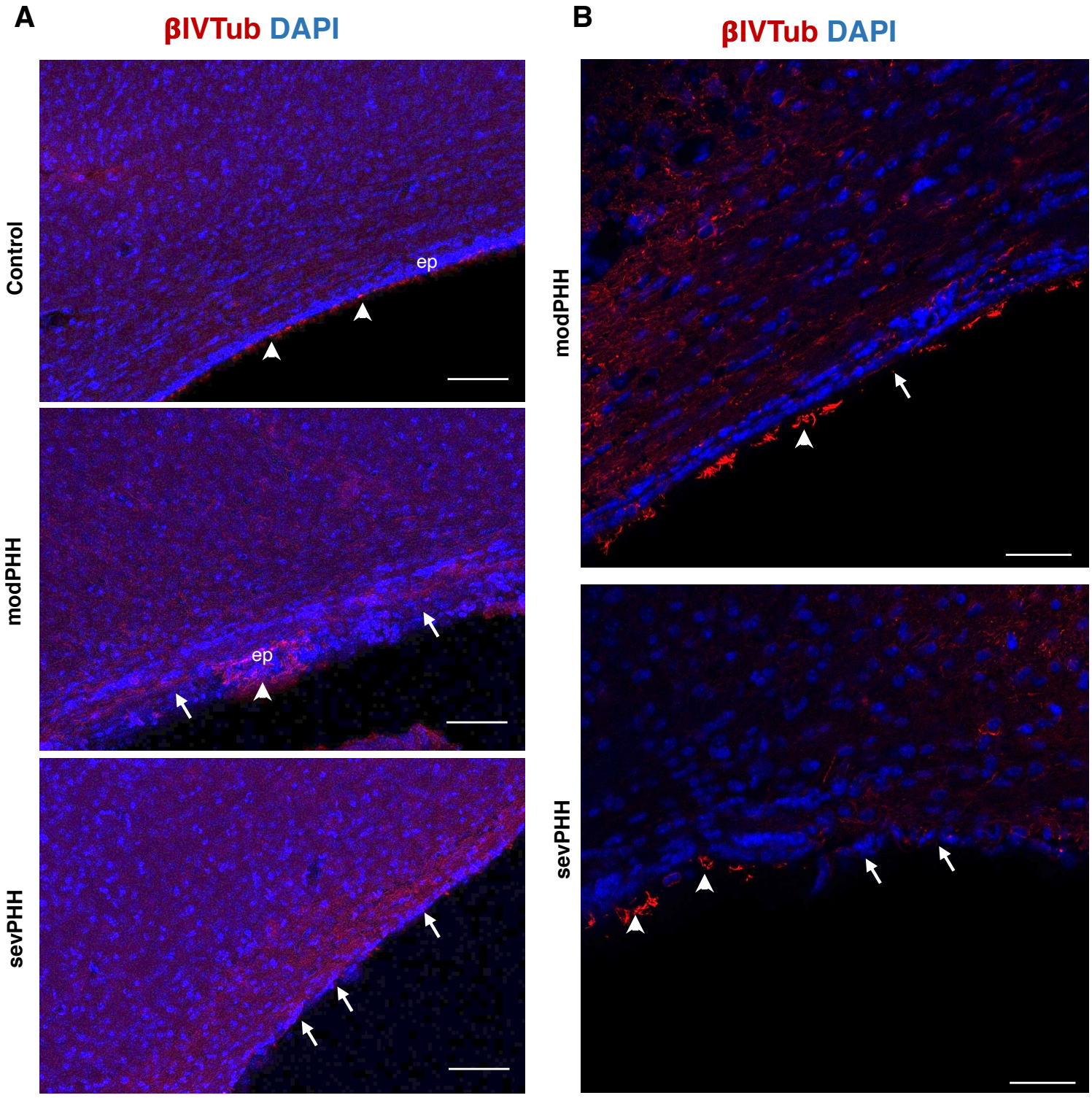


Figure S4. A, Control mouse (**top**) and mice injected with whole blood into both lateral ventricles presenting modPHH (**center**) and sevPHH (**bottom**). Cilia labeling (*arrowheads*) with βIV-tubulin. Areas with ependyma (*ep*) and denuded ependyma (*arrows*) are shown. **B,** Mice injected with blood serum into both lateral ventricles. **Top,** Mouse with modPHH. **Bottom,** Mouse with sevPHH. Areas with ependyma (*arrowheads*) and denuded ependyma (*arrows*) are present. βIV-Tubulin immunofluorescence. DAPI nuclear staining. Scale bar: 75 *μ*m.

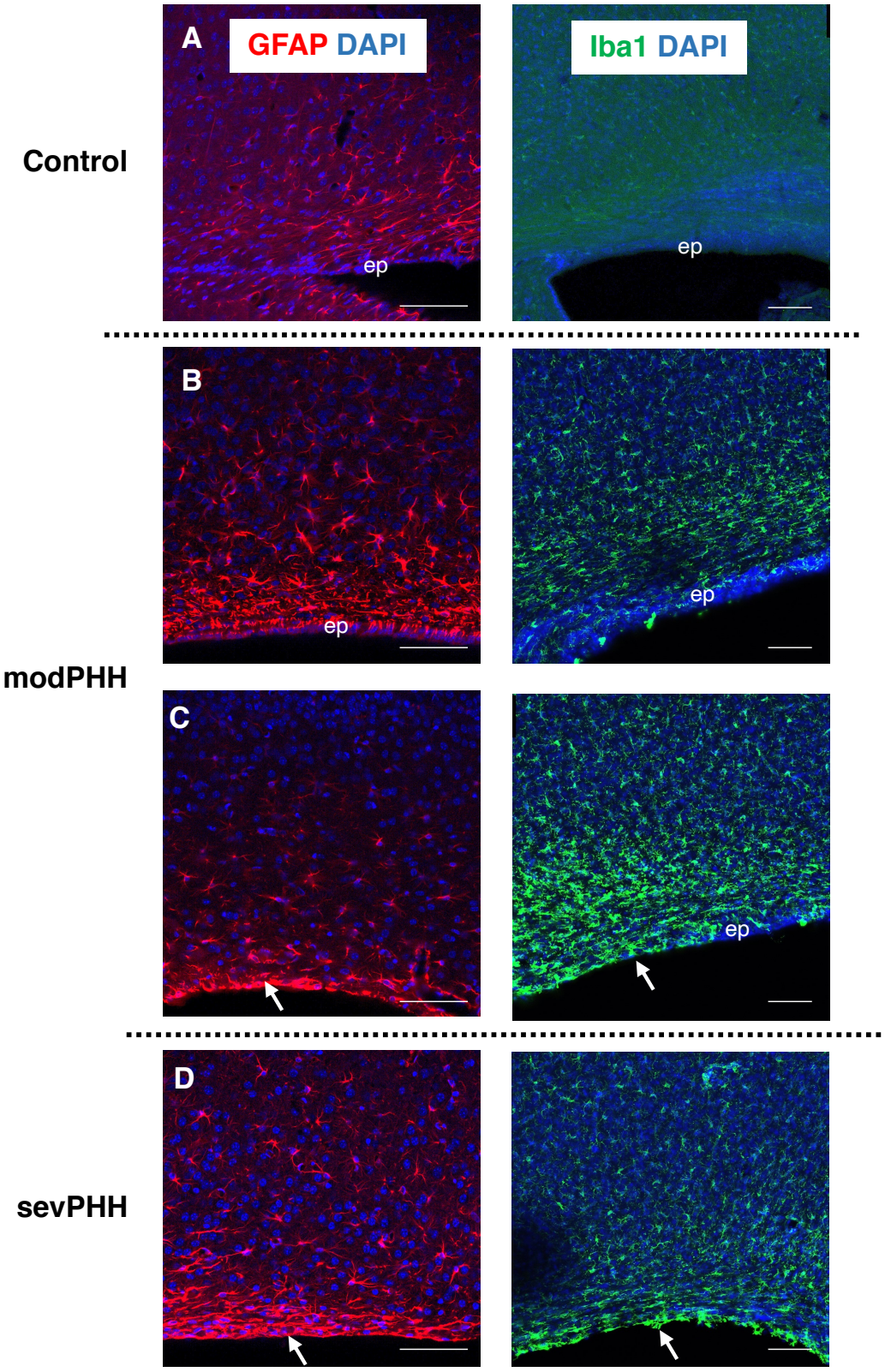


Figure S5. Mice injected with whole blood into both lateral ventricles. GFAP and Iba1 immunofluorescence; DAPI nuclear staining. **A,** Control mice. **B, C** Mice with modPHH, presenting ependyma (B) and denuded surface without ependyma (C). **D,** Mice with sevPHH. Areas with ependyma (*ep*) and denuded ependyma (*arrows*) are shown. Scale bars: 75 μm.

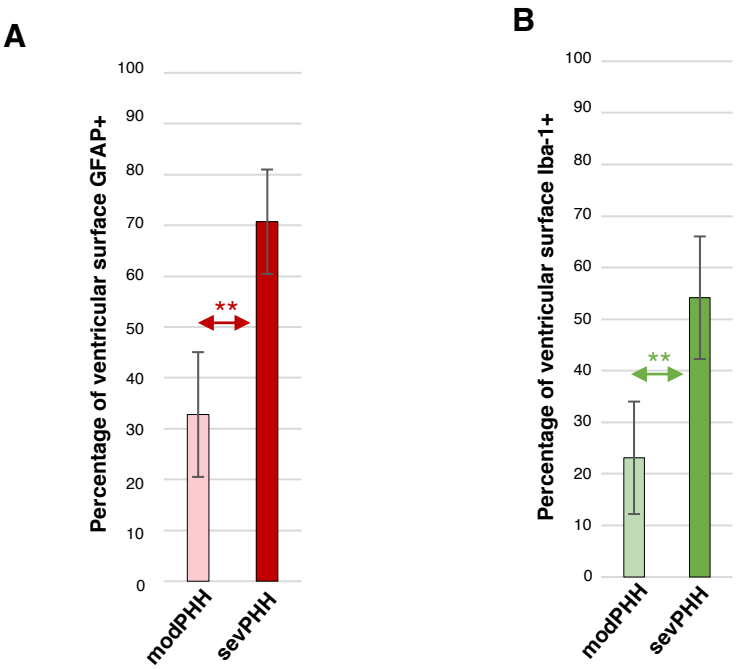
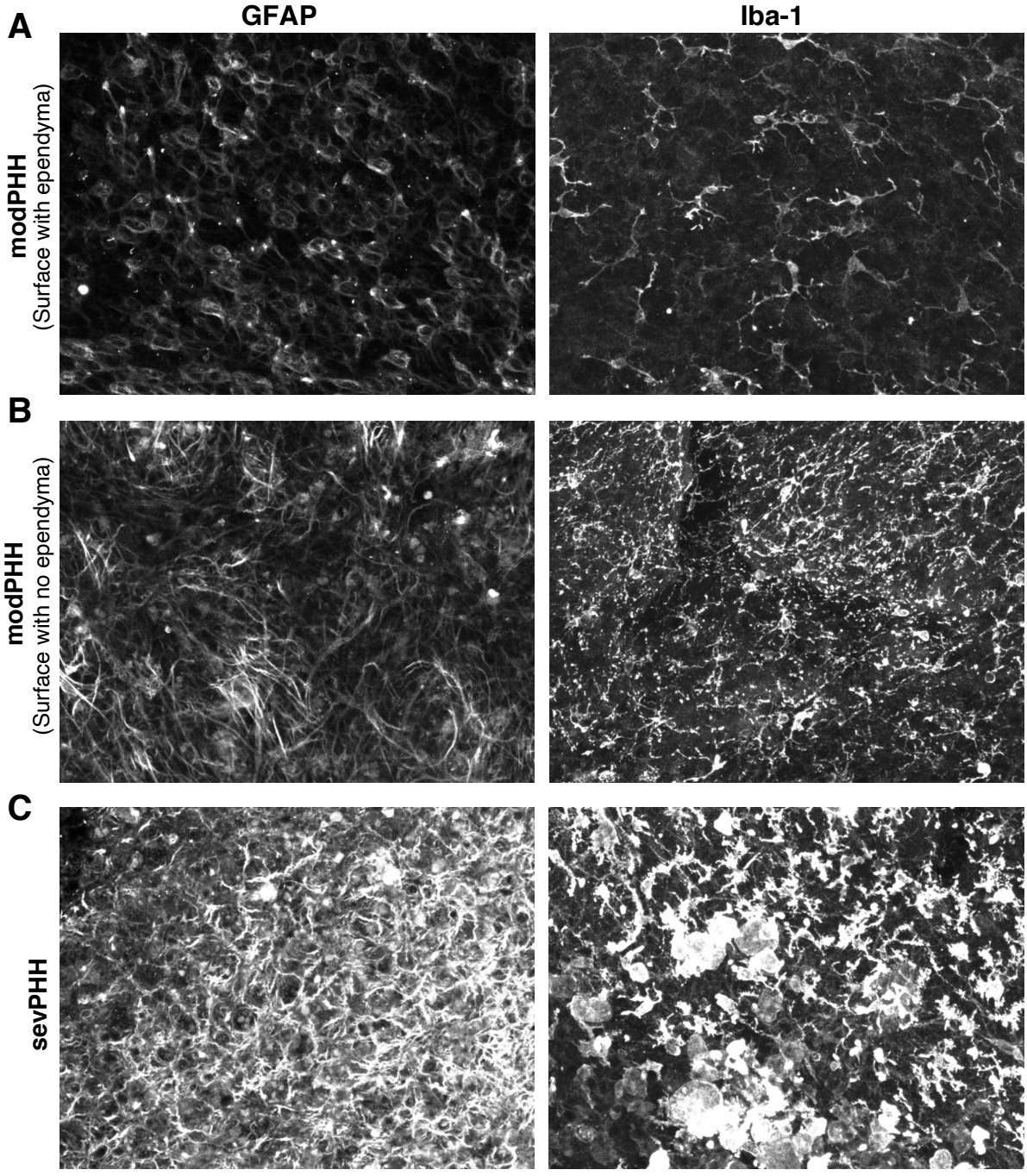


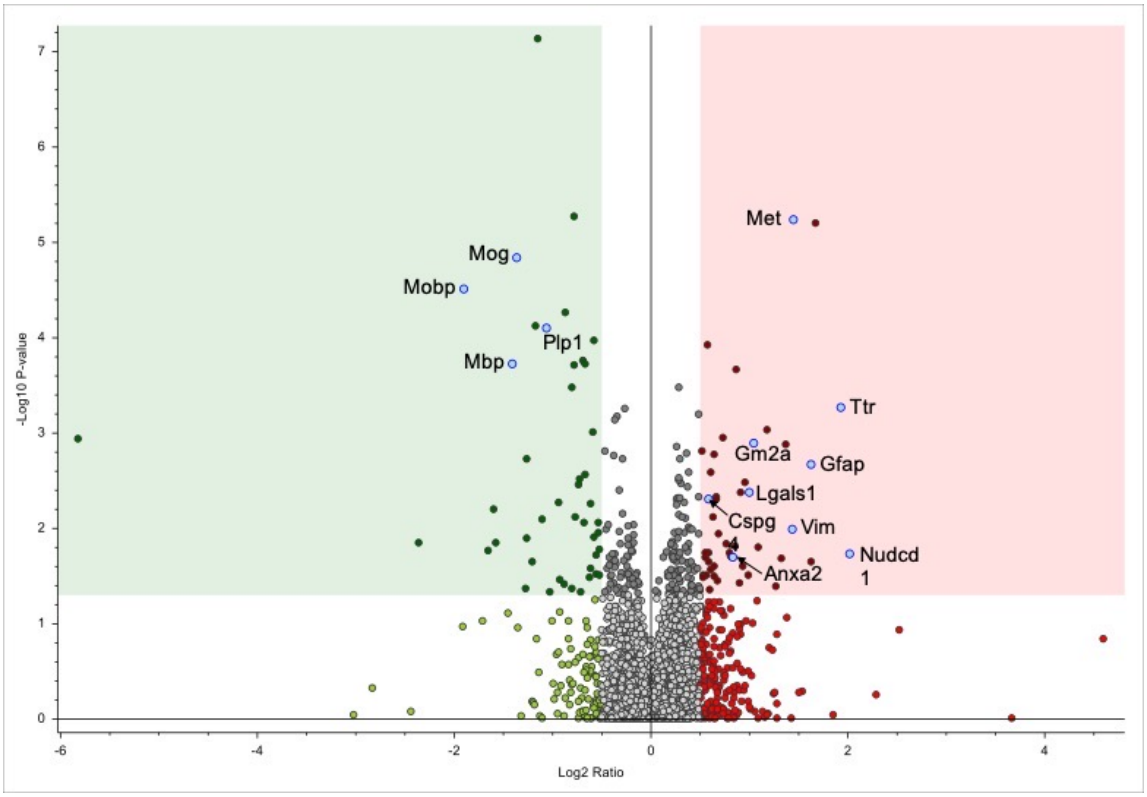
Figure S6. Percentage of GFAP-possitive ventricular surface (**A**) or Iba-1-possitive ventricular surface (**B**) in modPHH and sevPHH mice (mean ± SEM). **p < 0.01; Wilcoxon-Mann-Whitney test.



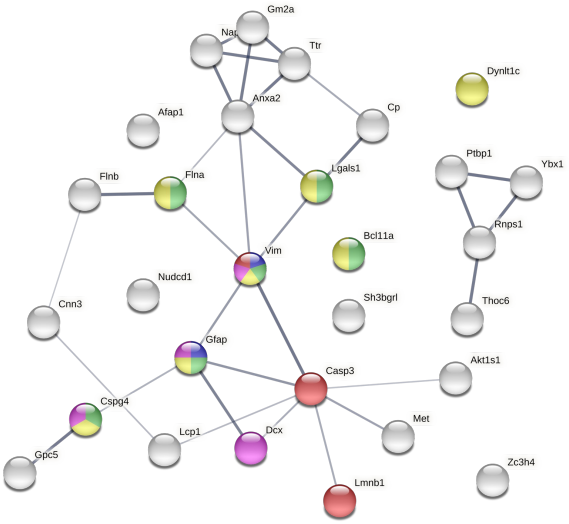
D

	G_1	G_2	Mean_1	StanDev_1	Mean_2	StanDev_2	Significance	
GFAP	sevPHH	modPHH	70	8	30	1.3	P < 0.01	**
Iba-1	sevPHH	modPHH	54	23	23	20	P < 0.01	**

Figure S7. A, Expression of GFAP (**left**) and Iba-1 (**right**) in the ventricular surface of modPHH in the area presenting ependyma. **B,** Expression of GFAP (**left**) and Iba-1 (**right**) in the ventricular surface of modPHH in the area where ependyma is lost. **C,** Expression of GFAP (**left**) and Iba-1 (**right**) in the ventricular surface of sevPHH. The surface covered by positive cells to anti-GFAP or anti-Iba-1 was higher in mice with sevPHH **(C)** than in modPHH **(A, B)**. In modPHH, the surface covered by positive cells to anti-GFAP or anti-Iba-1 was higher in areas with no ependyma than in areas with ependyma. **(D)** Statistical data corresponding to graphics contained in Figure 1E and Figure 1F**.** Wilcoxon-Mann-Whitney test. **Top,** Statistics corresponding to the comparison between the surface covered by GFAP positive cells in mice with modPHH versus sevPHH. **Bottom,** Iba-1 possitive cells in mice with modPHH versus sevPHH. G1: experimental group1; G2: experimental group2; Mean_1: mean of experimental group_1; Mean_2: mean of experimental group_2; StandDev_1: standard deviation of the mean of experimental group_1; StandDev_2: standard deviation of the mean of experimental group_2; p: p value; **$0.005 \leq p < 0.01$.



Overexpressed



MMU-109581 Apoptosis
(Lgals1,Cp)
Strength: 1.39; False discovery rate: 0.0021

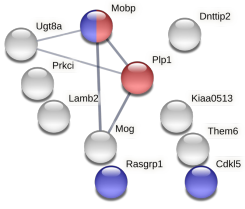
GO:0014002 Astrocyte development
(Gfap,Vim)
Strength: 1.75; False discovery rate: 0.013

GO:0010977 Negative regulation of neuron projection development
(Bcl11a,Vim,Flna,Cspg4,Gfap,Lgals1)
Strength: 1.46; False discovery rate: 1.78×10^{-5}

GO:0050768 Negative regulation of neurogenesis
(Bcl11a,Vim,Flna,Cspg4,Gfap,Lgals1,Dynlt1c)
Strength: 1.23; False discovery rate: 2.74×10^{-5}

GO:0042063 Gliogenesis
(Vim,Cspg4,Gfap,Dcx)
Strength: 1.15; False discovery rate: 0.0045

Underexpressed



GO:0019911 Structural constituent of myelin sheath
(Plp1,Mobp)
Strength: 2.6; False discovery rate: 0.0012

GO:0017016 Ras GTPase binding
(Mobp,Cdkl5,Rasgrp1)
Strength: 1.21; False discovery rate: 0.0283

Figure S8. Overexpressed and underexpressed proteins comparing sevPHH with modPHH. Upper: volcano plot. Bottom: protein-protein interaction networks and functional enrichment analysis with STRING.

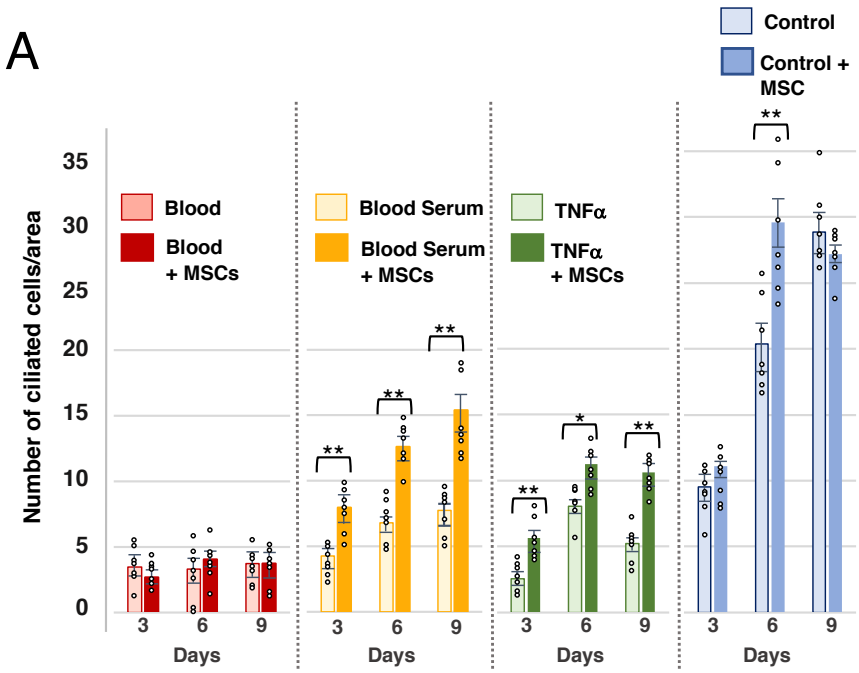


Figure S9. Number of EpPs developing cilia per area at different times in primary cultures under treatment with blood, blood serum, and TNFα. The effect of MSC coculture is shown for each condition. T-Student significance: *$p < 0.01$; **$p < 0.005$. Bars represent the standard error of the mean.