

Major Resources Table

In order to allow validation and replication of experiments, all essential research materials listed in the Methods should be included in the Major Resources Table below. Authors are encouraged to use public repositories for protocols, data, code, and other materials and provide persistent identifiers and/or links to repositories when available. Authors may add or delete rows as needed.

Animals (in vivo studies)

Species	Vendor or Source	Background Strain	Sex	Persistent ID / URL
Mouse	Jackson Laboratory	C57BL/6	Male	https://www.jax.org/strain/000664

Genetically Modified Animals

	Species	Vendor or Source	Background Strain	Other Information	Persistent ID / URL
Parent - Male	Mouse	Jackson Laboratory	C57BL/6	<i>ApoE</i> ^{-/-}	https://www.jax.org/strain/002052
Parent - Female	Mouse	Jackson Laboratory	C57BL/6	<i>ApoE</i> ^{-/-}	https://www.jax.org/strain/002052
Parent - Male	Mouse	Dr. Holger Eltzschig, University of Texas Houston Medical School, USA	C57BL/6	<i>Tram</i> ^{-/-}	
Parent - Female	Mouse	Dr. Holger Eltzschig, University of Texas Houston Medical School, USA	C57BL/6	<i>Tram</i> ^{-/-}	
Parent - Male	Mouse	Dr. Jürg Tschopp, University of Lausanne, Switzerland	C57BL/6	<i>Tollip</i> ^{-/-}	
Parent - Female	Mouse	Dr. Jürg Tschopp, University of Lausanne, Switzerland	C57BL/6	<i>Tollip</i> ^{-/-}	
Parent - Male	Mouse	Dr. Yang Liu, University of Maryland, USA	C57BL/6	<i>Cd24</i> ^{-/-}	
Parent - Female	Mouse	Dr. Yang Liu, University of Maryland, USA	C57BL/6	<i>Cd24</i> ^{-/-}	

Antibodies

Target antigen	Vendor or Source	Catalog #	Working concentration	Lot # (preferred but not required)	Persistent ID / URL
CD16/CD32	BD Biosciences	553141	1:100		https://wwwbdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/purified-rat-anti-mouse-cd16-cd32-mouse-bd-fc-block.553141
CD11b	BioLegend	101226	1:200		https://www.biolegend.com/en-us/products/apc-cyanine7-anti-mouse-human-cd11b-antibody-3930

CD11b	BioLegend	101212	1:200		https://www.biolegend.com/en-us/products/apc-anti-mouse-human-cd11b-antibody-345
CD11b	BioLegend	101208	1:200		https://www.biolegend.com/en-us/products/pe-anti-mouse-human-cd11b-antibody-349
Ly6C	BioLegend	128018	1:200		https://www.biolegend.com/en-us/products/pe-cyanine7-anti-mouse-ly-6c-antibody-6063
Ly6C	BioLegend	128026	1:200		https://www.biolegend.com/en-us/products/apc-cyanine7-anti-mouse-ly-6c-antibody-6758
Ly6C	BioLegend	128016	1:200		https://www.biolegend.com/en-us/products/apc-anti-mouse-ly-6c-antibody-6047
Ly6G	BioLegend	127616	1:200		https://www.biolegend.com/en-us/products/percp-cyanine5-5-anti-mouse-ly-6g-antibody-6116
Ly6G	BioLegend	127608	1:200		https://www.biolegend.com/en-us/products/pe-anti-mouse-ly-6g-antibody-4777
Ly6G	BioLegend	127624	1:200		https://www.biolegend.com/en-us/products/apc-cyanine7-anti-mouse-ly-6g-antibody-6755
ICAM-1	BioLegend	116120	1:200		https://www.biolegend.com/en-us/products/apc-anti-mouse-cd54-antibody-6673
ICAM-1	BioLegend	116108	1:200		https://www.biolegend.com/en-us/products/pe-anti-mouse-cd54-antibody-1680
CD24	BioLegend	101806	1:200		https://www.biolegend.com/en-us/products/fitc-anti-mouse-cd24-antibody-341
CD24	BioLegend	101808	1:200		https://www.biolegend.com/en-us/products/pe-anti-mouse-cd24-antibody-343
c-kit	BioLegend	105806	1:200		https://www.biolegend.com/en-us/products/fitc-anti-mouse-cd117-c-kit-antibody-74
CD93	BioLegend	136509	1:200		https://www.biolegend.com/en-us/products/apc-anti-mouse-cd93-aa4-1-early-b-lineage-antibody-6621
CD105	BioLegend	120413	1:200		https://www.biolegend.com/en-us/products/apc-anti-mouse-cd105-antibody-6519
CD11c	BioLegend	117310	1:200		https://www.biolegend.com/en-us/products/apc-anti-mouse-cd11c-antibody-1813
MHCII	BioLegend	107606	1:200		https://www.biolegend.com/en-us/products/fitc-anti-mouse-i-a-i-e-antibody-366

CD200R	BioLegend	123916	1:200		https://www.biolegend.com/en-us/products/apc-anti-mouse-cd200r-ox2r-antibody-17940
CD19	BioLegend	115520	1:200		https://www.biolegend.com/en-us/products/pe-cyanine7-anti-mouse-cd19-antibody-1907
CD3	BioLegend	100205	1:200		https://www.biolegend.com/en-us/products/pe-anti-mouse-cd3-antibody-47
CD8	BioLegend	100705	1:200		https://www.biolegend.com/en-us/products/fitc-anti-mouse-cd8a-antibody-153
CD122	BioLegend	123214	1:200		https://www.biolegend.com/en-us/products/apc-anti-mouse-cd122-il-2rbeta-antibody-8908
SYK	Cell Signaling Technology	2712S	1:1000		https://www.cellsignal.com/products/primary-antibodies/syk-antibody/2712
p-p38	Cell Signaling Technology	4511S	1:1000		https://www.cellsignal.com/products/primary-antibodies/phospho-p38-mapk-thr180-tyr182-d3f9-xp-rabbit-mab/4511
IRF5	Cell Signaling Technology	4950S	1:1000		https://www.cellsignal.com/products/primary-antibodies/irf-5-antibody/4950
β-Actin	Cell Signaling Technology	5125S	1:1000		https://www.cellsignal.com/products/antibody-conjugates/b-actin-13e5-rabbit-mab-hrp-conjugate/5125
Rabbit IgG	Cell Signaling Technology	7074S	1:1000		https://www.cellsignal.com/products/secondary-antibodies/anti-rabbit-igg-hrp-linked-antibody/7074
mTOR	Cell Signaling Technology	5043S	1:200		https://www.cellsignal.com/products/antibody-conjugates/mTOR-7c10-rabbit-mab-alexa-fluor-174-488-conjugate/5043
mTOR	Proteintech,	CL594-66888	1:300		https://www.ptglab.com/products/mTOR-Antibody-CL594-66888.htm
SYK	BioLegend	646004	1:500		https://www.biolegend.com/en-us/products/pe-anti-syk-antibody-11650
TRAM	Biorbyt	orb452158	1:500		https://www.biorbyt.com/ticam2-conjugated-antibody-orb1621486.html
Tollip	NOVUS	H00054472-M01	20 µg		https://www.novusbio.com/products/tollip-antibody-1a5-2a3_h00054472-m01
NEDD8	Thermo Fisher Scientific	MA5-32552	50 µg		https://www.thermofisher.com/antibody/product/NEDD8-Antibody-clone-JF69-09-Recombinant-Monoclonal/MA5-32552
PPARγ	Thermo Fisher Scientific	PA3-821A	1:1000		https://www.thermofisher.com/antibody/product/PPAR-gamma-Antibody-Polyclonal/PA3-821A
CD45.1	BioLegend	110730	1:200		https://www.biolegend.com/en-us/products/pe-cyanine7-anti-mouse-cd45-1-antibody-4917
CD14	BioLegend	325618	1:50		https://www.biolegend.com/en-us/products/pe-cyanine7-anti-human-cd14-antibody-3958

CD16	BioLegend	360710	1:50		https://www.biolegend.com/en-us/products/apc-cyanine7-anti-human-cd16-antibody-9134
ICAM-1	BioLegend	353114	1:50		https://www.biolegend.com/en-us/products/alexa-fluor-647-anti-human-cd54-antibody-14743
CD24	BioLegend	311106	1:50		https://www.biolegend.com/en-us/products/pe-anti-human-cd24-antibody-1805

DNA/cDNA Clones

Clone Name	Sequence	Source / Repository	Persistent ID / URL

Cultured Cells

Name	Vendor or Source	Sex (F, M, or unknown)	Persistent ID / URL
Mouse bone marrow derived monocytes	Isolated from C57BL/6, B6 SJL, <i>Tram</i> ^{-/-} , <i>Tollip</i> ^{-/-} , <i>Cd24</i> ^{-/-} mice	female and male	
Human peripheral blood mononuclear cells	Isolated from peripheral blood of healthy individuals purchased from Research Blood Components, LLC	unknown	https://www.researchbloodcomponents.com/

Data & Code Availability

Description	Source / Repository	Persistent ID / URL
Single cell RNA-seq data	NCBI Gene Expression Omnibus	accession # GSE160450
Methylation profiling data	NCBI Gene Expression Omnibus	accession # GSE243358

Other (key reagents & kits)

Description	Source / Repository	Catalog #	Persistent ID / URL
Murine M-CSF	Peprtech	315-02	https://www.peprtech.com/en/recombinant-murine-m-csf
4-PBA	MilliporeSigma	SML0309	https://www.sigmaaldrich.com/US/en/product/sigma/sml0309
oxLDL	Kalen Biomedical	770202	https://kalenbiomed.com/products/moxldl
Cholesterol	MilliporeSigma	C4951	https://www.sigmaaldrich.com/US/en/product/sigma/c4951
Propidium iodide	MilliporeSigma	P4170	https://www.sigmaaldrich.com/US/en/product/sigma/p4170
Murine GM-CSF	Peprtech	315-03	https://www.peprtech.com/en/recombinant-murine-gm-csf
AAV8-mPCSK9-D377Y vectors	Center for Cardiovascular Diseases and Sciences of		https://www.lsuhs.edu/centers/cardiovascular-diseases-and-sciences

	Louisiana State University		
ACK buffer	Quality Biological	118-156-721	https://www.qualitybiological.com/product/ack-lysing-buffer-4/
Collagenase, Type 1	Worthington	LS004196	https://www.worthington-biochem.com/products/collagenase?v=705
Collagenase, Type XI	MilliporeSigma	C7657	https://www.sigmaaldrich.com/US/en/product/sigma/c7657
Hyaluronidase	MilliporeSigma	H6254	https://www.sigmaaldrich.com/US/en/product/sigma/h6254
DNase	MilliporeSigma	DN25	https://www.sigmaaldrich.com/US/en/product/sigma/dn25
HEPES solution	MilliporeSigma	H0887	https://www.sigmaaldrich.com/US/en/product/sigma/h0887
CFSE	Thermo Fisher Scientific	C34570	https://www.thermofisher.com/order/catalog/product/C34554
CellTrace™ Far Red	Thermo Fisher Scientific	C34572	https://www.thermofisher.com/order/catalog/product/C34572?SID=srch-hj-c34572
RIPA buffer	Thermo Fisher Scientific	89900	https://www.thermofisher.com/order/catalog/product/89900?SID=srch-srp-89900
Protease Inhibitor Cocktail	MilliporeSigma	P8340	https://www.sigmaaldrich.com/US/en/product/sigma/p8340
Phosphatase Inhibitor Cocktail 2	MilliporeSigma	P5726	https://www.sigmaaldrich.com/US/en/product/sigma/p5726
Blotting-Grade Blocker	Bio-Rad	1706404	https://www.bio-rad.com/en-us/sku/1706404-blotting-grade-blocker?ID=1706404
ECL Western Blotting Substrate	Thermo Fisher Scientific	32106	https://www.thermofisher.com/order/catalog/product/32106?SID=srch-srp-32106
ProLong™ Gold Antifade Mountant	Thermo Fisher Scientific	P36930	https://www.thermofisher.com/order/catalog/product/P36930?SID=srch-hj-P36930
Alexa Fluor™ 488 conjugated streptavidin	Thermo Fisher Scientific	S32354	https://www.thermofisher.com/order/catalog/product/S32354?SID=srch-hj-S32354
Rabbit IgG Isotype Control	Thermo Fisher Scientific	31235	https://www.thermofisher.com/antibody/product/Rabbit-IgG-Polyclonal/31235
PE Mouse IgG1 Isotype Control	BioLegend	400112	https://www.biolegend.com/en-us/products/pe-mouse-igg1-kappa-isotype-ctrl-1408
CoraLite®594 Mouse IgG2a Isotype Control	Proteintech	CL594-65208	https://www.ptglab.com/products/IgG2a-Isotype-Control-Antibody-CL594-65208.htm
Biotin Rabbit IgG Isotype Control	Abcam	ab200208	https://www.abcam.com/en-us/products/primary-antibodies/biotin-rabbit-igg-isotype-control-ab200208
Ficoll®-Paque	MilliporeSigma	GE17-5442-02	https://www.sigmaaldrich.com/US/en/product/sigma/ge17544202
Human M-CSF	Peptotech	300-25	https://www.peptotech.com/en/recombinant-human-m-csf
Human TruStain FcX™	BioLegend	422302	https://www.biolegend.com/en-us/products/human-trustain-fcx-fc-receptor-blocking-solution-6462
Cyto-Fast™ Fix/Perm Buffer Set	BioLegend	426803	https://www.biolegend.com/en-us/products/cyto-fast-fix-perm-buffer-set-16765
oxLDL Uptake Assay Kit	Cayman Chemical	601180	https://www.caymanchem.com/product/601180/oxidized-ldl-uptake-assay-kit
Fat, Oil Red O, Propylene Glycol Stain Kit	Newcomer Supply	9119A	https://www.newcomersupply.com/product/fat-oil-red-o-propylene-glycol-stain-kit/

Picosirius Red Stain Kit	Polysciences	24901	https://www.polysciences.com/german/picosirius-red-stain-kit-40771
Cholesterol Quantitation Kit	MilliporeSigma	MAK043	https://www.sigmaaldrich.com/US/en/product/sigma/mak043
Triglyceride Assay Kit	BioVision	K622	https://www.abcam.com/en-us/products/assay-kits/triglyceride-assay-kit-quantification-ab65336
SelectFX™ Alexa Fluor™ 488 Peroxisome Labeling Kit	Thermo Fisher Scientific	S34201	https://www.thermofisher.com/order/catalog/product/S34201
Pierce™ Co-Immunoprecipitation Kit	Thermo Fisher Scientific	26149	https://www.thermofisher.com/order/catalog/product/26149?SID=srch-srp-26149
CCL5 ELISA Kit	R&D Systems	MMR00	https://www.rndsystems.com/products/mouse-rat-ccl5-rantes-quantikine-elisa-kit_mmr00
Vybrant™ Cell Adhesion Assay Kit	Thermo Fisher Scientific	V13181	https://www.thermofisher.com/order/catalog/product/V13181?SID=srch-hj-V13181
In Vivo EdU Flow Cytometry 50 Kit	MilliporeSigma	BCK488-IV-FC-S	https://www.sigmaaldrich.com/US/en/product/sigma/bck488ivfcs
Seahorse XF Cell Mito Stress Test Kit	Agilent	103015-100	https://www.agilent.com/en/product/cell-analysis/real-time-cell-metabolic-analysis/xf-assay-kits-reagents-cell-assay-media/seahorse-xf-cell-mito-stress-test-kit-740885
DNeasy Blood & Tissue Kits	QIAGEN	69504	https://www.qiagen.com/us/products/discovery-and-translational-research/dna-rna-purification/dna-purification/genomic-dna/dneasy-blood-and-tissue-kit
EpiTect Bisulfite Kit	QIAGEN	59104	https://www.qiagen.com/us/products/discovery-and-translational-research/epigenetics/dna-methylation/bisulfite-conversion-assays/epitect-bisulfite-kits?catno=59104
PyroMark PCR Kit	QIAGEN	978705	https://www.qiagen.com/us/products/discovery-and-translational-research/pyrosequencing/pyromark-q24-and-advanced?catno=978705

ARRIVE GUIDELINES

The ARRIVE guidelines (<https://arriveguidelines.org/>) are a checklist of recommendations to improve the reporting of research involving animals. Key elements of the study design should be included below to better enable readers to scrutinize the research adequately, evaluate its methodological rigor, and reproduce the methods or findings.

Study Design

Groups	Sex	Age	Number (prior to experiment)	Number (after termination)	Littermates (Yes/No)	Other description
Group 1 (Control) PBS	Male	8 weeks	10	10	No	Figure 2
Group 2 4-PBA	Male	8 weeks	10	10	No	Figure 2
Group 1 (Control) PBS-primed monocytes	Male	8 weeks	12	12	No	Figure 7A-D
Group 2 4-PBA-primed monocytes	Male	8 weeks	11	11	No	Figure 7A-D
Group 1 (Control) PBS-primed monocytes	Male	9 weeks	3	3	No	Figure 7E-F
Group 2 4-PBA-primed monocytes	Male	9 weeks	4	4	No	Figure 7E-F
Group 1 PBS-primed WT monocytes	Male	8 weeks	10	10	No	Figure 8
Group 2 4-PBA-primed WT monocytes	Male	8 weeks	10	10	No	Figure 8
Group 3 PBS-primed <i>Cd24</i> ^{-/-} monocytes	Male	8 weeks	10	10	No	Figure 8
Group 4 4-PBA-primed <i>Cd24</i> ^{-/-} monocytes	Male	8 weeks	10	10	No	Figure 8
Group 1 (Control) PBS	Male	9 weeks	6	5	No	Figure S4
Group 2 4-PBA	Male	9 weeks	6	6	No	Figure S4
Group 1 (Control) PBS	Male	8 weeks	10	10	No	Figure S5
Group 2 4-PBA	Male	8 weeks	10	10	No	Figure S5
Group 1 (Control) PBS-primed monocytes	Female	8 weeks	5	5	No	Figure S9
Group 2 4-PBA-primed monocytes	Female	8 weeks	5	5	No	Figure S9

Group 1 (Control) PBS-primed monocytes	Male	9 weeks	7	7	No	Figure S10A upper panels
Group 2 4-PBA-primed monocytes	Male	9 weeks	5	5	No	Figure S10A upper panels
Group 1 (Control) PBS-primed monocytes	Male	8 weeks	6	6	No	Figure S10A lower panels
Group 2 4-PBA-primed monocytes	Male	8 weeks	5	5	No	Figure S10A lower panels
Group 1 (Control) PBS-primed monocytes	Male	8 weeks	4	4	No	Figure S10B
Group 2 4-PBA-primed monocytes	Male	8 weeks	5	5	No	Figure S10B
Group 1 (Control) PBS-primed monocytes	Male	9 weeks	5	5	No	Figure S10C
Group 2 4-PBA-primed monocytes	Male	9 weeks	5	5	No	Figure S10C
Group 1 (Control) PBS-primed monocytes	Male	8 weeks	5	5	Yes	Figure S11
Group 2 4-PBA-primed monocytes	Male	8 weeks	4	4	Yes	Figure S11

Sample Size: Please explain how the sample size was decided Please provide details of any a *prior* sample size calculation, if done.

The sample sizes were determined based on our previous publications and the power analyses performed by others following the principle of 3Rs (Replacement, Reduction, Refinement). We determined that a sample size of at least 5 mice per group was sufficient to achieve 80% power to detect a 50% change in atherosclerotic burden at a significance level of 0.05. For ex vivo measurement of biochemical markers on harvested cells, at least 3 animals were used in each group based on publications cited in the supplemental materials.

Inclusion Criteria

Genotype, age and sex matched mice were included.

Exclusion Criteria

Mice that showed health concerns unrelated to the experimental conditions (for example, fight wounds and dermatitis) were excluded.

Randomization

Mice were randomly assigned to different treatment groups.

Blinding

DOI [to be added]

For all the in vivo animal studies (Figures 2, 7, 8, S4, S5, S9, S10, and S11), the samples were collected and analyzed by different investigators, ensuring that investigators who analyzed the data were blinded to the treatment groups.