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
Mice	LASEC/CUHK	C57BL/6	M&F	NA

Genetically Modified Animals

	Species	Strains	Vendor or Source	Background Strain	Other Information	Persistent ID / URL
Parent-Male	Mice	*Ucp2* floxed mice (B6;129S-Ucp2tm2.1Lowl/J)	Jackson Laboratory	C57BL/6J		https://www.jax.org/strain/022394
Parent-Female	Mice	*Cdh5*^{Cre} mice (B6;129-Tg (Cdh5-cre)1Spe/J)	Jackson Laboratory	C57BL/6J		https://www.jax.org/strain/017968
	Mice	*ApoE*$^{-/-}$	LASEC/CUHK			

Antibodies

Target antigen	Vendor or Source	Catalog #	Working concentration	Lot # (preferred but not required)	Persistent ID / URL
Myc-tag	Abcam	ab9132	ChIP (1:100)		https://www.abcam.com/myc-tag-antibody-chip-grade-ab9132.html
VCAM-1	Abcam	ab134047	WB (1:1000) IF (1:100)		https://www.abcam.com/vcam1-antibody-epr5047-ab134047.html
MCP-1	Abcam	ab25124	WB (1:1000)		https://www.abcam.com/mcp1-antibody-ab25124.html
CD68	Abcam	ab237968	IF (1:100)		https://www.abcam.com/cd68-antibody-fa-11-bsa-and-azide-free-ab237968.html
H3	Abcam	ab1791	WB (1:5000)		https://www.abcam.com/histone-h3-antibody-nuclear-marker-and-chip-grade-ab1791.html
eNOS	BD Bioscience	610297	WB (1:1000)		https://www.bdbiosciences.com/eu/reagents/research/antibodies-buffers/cell-biology-reagents/cell-biology-antibodies/purified-mouse-anti-enosnos-type-iii-3enosnos-type-iii/p/610297
p-eNOS S1177	BD Bioscience	612392	WB (1:1000)		https://www.bdbiosciences.com/en-ca/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/purified-mouse-anti-enos-ps1177.612392
FoxO1	Cell Signaling Technology	2880	WB (1:1000)		https://www.cellsignal.com/products/primary-antibodies/foxo1-c29h4-rabbit-mab/2880
p-FoxO1 S256	Cell Signaling Technology	9461	WB (1:1000)		https://www.cellsignal.com/product/productDetail.jsp?productId=9461

DOI [to be added]

AMPKα	Cell Signaling Technology	2532	WB (1:1000)		https://www.cellsignal.com/product/productDetail.jsp?productId=2532
p-AMPK T172	Cell Signaling Technology	2535	WB (1:1000)		https://www.cellsignal.com/product/productDetail.jsp?productId=2535
AKT	Cell Signaling Technology	9272	WB (1:1000)		https://www.cellsignal.com/product/productDetail.jsp?productId=9272
p-AKT S473	Cell Signaling Technology	4060	WB (1:1000)		https://www.cellsignal.com/product/productDetail.jsp?productId=4060
p-AKT T308	Cell Signaling Technology	4056	WB (1:1000)		https://www.cellsignal.com/product/productDetail.jsp?productId=4056
UCP2	Cell Signaling Technology	89326	WB (1:1000)		https://www.cellsignal.com/product/productDetail.jsp?productId=89326
IκBα	Cell Signaling Technology	4814	WB (1:1000)		https://www.cellsignal.com/product/productDetail.jsp?productId=4814
GAPDH	Cell Signaling Technology	2118	WB (1:1000)		https://www.cellsignal.com/products/primary-antibodies/gapdh-14c10-rabbit-mab/2118
LDLR	Invitrogen	PA5-22976	WB (1:1000)		https://www.thermofisher.com/antibody/product/LDLR-Antibody-Polyclonal/PA5-22976
KLF2	Millipore	09-820	WB (1:3000) ChIP (1:100)		https://www.emdmillipore.com/US/en/product/Anti-Klf2-Antibody,MM_NF-09-820?ReferrerURL=https%3A%2F%2Fwww.google.com.hk%2F&bd=1
UCP2	R&D Systems	AF4739	WB (1:500)		https://www.rndsystems.com/cn/products/human-mouse-ucp2-antibody_af4739
UCP2	Santa Cruz Biotechnology	sc-6526	IHC (1:100)		https://www.scbt.com/p/ucp2-antibody-n-19
IL-6	Santa Cruz Biotechnology	sc-57315	WB (1:400)		https://www.scbt.com/p/il-6-antibody-10e5
Donkey anti-Rabbit IgG (H+L) Highly Cross-Adsorbed Secondary Antibody, Alexa Fluor 546	Thermo Fisher	A10040	IF (1:500)		https://www.thermofisher.com/antibody/product/Donkey-anti-Rabbit-IgG-H-L-Highly-Cross-Adsorbed-Secondary-Antibody-Polyclonal/A10040
Rabbit IgG Isotype control	Invitrogen	10500C	IF (1:100)		https://www.thermofisher.com/antibody/product/Rabbit-IgG-Isotype-Control/10500C
Rat IgG Isotype control	Invitrogen	10700	IF (1:100)		https://www.thermofisher.com/antibody/product/Rat-IgG-Isotype-Control/10700

DNA/cDNA Clones

DOI [to be added]

Clone Name	Sequence	Source / Repository	Persistent ID / URL
Human KLF2		NM_016270.4	
Mouse Klf2		NM_008452.2	
pAdtrack-CMV	https://www.addgene.org/16405/sequences/	Addgene/ Bert Vogelstein	https://www.addgene.org/16405/
pAdEasy-1	https://www.addgene.org/16400/sequences/	Addgene/ Bert Vogelstein	https://www.addgene.org/16400/
Ad-KLF2		Generated in Yu Huang lab/CUHK	
Ad-shKLF2		Vector Biolabs; Cat. No: shADV-213187	https://www.vectorbiolabs.com/product/shadv-213187-human-klf2-shrna-silencing-adenovirus/
Ad-GFP		Generated in Yu Huang lab	
Ad-SCR		Generated in Yu Huang lab	
psPAX2	https://www.addgene.org/12260/sequences/	Addgene/ Didier Trono	https://www.addgene.org/12260/
pMD2.G	https://www.addgene.org/12259/sequences/	Addgene/ Didier Trono	https://www.addgene.org/12259/
LV-SCR		Genechem	CON077
LV-shFOXO1		Genechem	http://www.taogene.com/emkt.htm#/PcMerchandises?id=367f4d07-e482-408a-8ac1-0582436bf35e&categoryId=12
LV-shSMAD4		Genechem	http://www.taogene.com/emkt.htm#/PcMerchandises?id=6f567ccf-4e7f-4e23-906d-c0c817c36fc0&categoryId=12
LV-shPPARGC1A		Genechem	http://www.taogene.com/emkt.htm#/PcMerchandises?id=b30c0b84-69ac-4b13-89c9-97d3e1e191c7&categoryId=12
Cdh5 promoter		PCR cloned from genomic DNA isolated from mouse liver	https://pubmed.ncbi.nlm.nih.gov/9864160/
pAAV-MCS	https://www.addgene.org/browse/sequence_vdb/1642/	Stratagene	https://www.addgene.org/vector-database/1642/
pAAV-DJ	VPK-420-DJ	Cell Biolabs	https://www.cellbiolabs.com/sites/default/files/VPK-420-DJ-aav-dj-vector.pdf
RGDLRVS-AAV9-cap		Dr. O.J. Müller	https://pubmed.ncbi.nlm.nih.gov/21956692/
pAAV/D377Y-mPCSK9	58376	Addgene/Jacob Bentzon	https://www.addgene.org/58376/
AAV-*Cdh5*-Vector	CMV promoter in pAAV-MCS was replaced by *Cdh5* promoter	Generated in Yu Huang lab	
AAV-*Cdh5*-Ucp2	CMV promoter in pAAV-MCS was replaced by *Cdh5* promoter	Generated in Yu Huang lab	
Ad-*Cdh5*-Klf2	Mouse Klf2 cDNA was inserted into pAd-*Cdh5* vector	Generated in Yu Huang lab	
pGL3-Basic Luciferase	E1751	Promega	https://worldwide.promega.com/products/luciferase-assays/genetic-reporter-vectors-and-cell-lines/pgl3-luciferase-reporter-vectors/?catNum=E1751
pLX313-Renilla luciferase	https://www.addgene.org/118016/sequences/	Addgene/ William Hahn, David Root	https://www.addgene.org/118016/

DOI [to be added]

Cultured Cells

Name	Vendor or Source	Sex (F, M, or unknown)	Persistent ID / URL
HUVECs	Lonza	Unknown	CC-2519
HAEC	Invitrogen	Unknown	C0065C
HEK239	ATCC	Unknown	CRL-1573
HEK293T	ATCC	Unknown	CRL-3216

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)	M/F	8-10 wks	7	7	NA	*Ucp2*$^{f/f}$ mice fed on western diet
Group 2	M/F	8-10 wks	9	9	NA	*Ucp2*$^{\Delta EC}$ mice fed on western diet
Group 3 (Control)	M/F	8-10 wks	7	6	NA	*Ucp2*$^{f/f}$ mice fed on western diet and subjected to partial ligation of carotid artery
Group 4	M/F	8-10 wks	7	7	NA	*Ucp2*$^{\Delta EC}$ mice fed on western diet and subjected to partial ligation of carotid artery
Group 5 (Control)	M	10-12 wks	8	8	NA	*ApoE*$^{-/-}$ mice receiving AAV-vector, subjected to partial ligation of carotid artery
Group 6	M	10-12 wks	8	8	NA	*ApoE*$^{-/-}$ mice receiving AAV-Cdh5-Ucp2, subjected to partial ligation of carotid artery
Group 7 (Control)	M/F	8-10 wks	7	7	NA	*Ucp2*$^{f/f}$ mice subjected to partial ligation of carotid artery, and treated with vehicle
Group 8	M/F	8-10 wks	7	7	NA	*Ucp2*$^{\Delta EC}$ mice subjected to partial ligation of

						carotid artery, and treated with vehicle
Group 9	M/F	8-10 wks	7	7	NA	*Ucp2*$^{f/f}$ mice subjected to partial ligation of carotid artery, and treated with AS1842856
Group 10	M/F	8-10 wks	7	7	NA	*Ucp2*$^{\Delta EC}$ mice subjected to partial ligation of carotid artery, and treated with AS1842856

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

We did not use G*power software to determine the animal group sizes. Sample size were determined according to our previous experience with mouse model of atherosclerosis. To account for potential loss of mice due to illness or sudden death, group size of 7-10 mice were chosen.

Inclusion Criteria

All the mice and samples were included for analysis unless unsuccessful surgical operation or sample processing happens.

Exclusion Criteria

Partial ligation of carotid artery was not successful in one mouse of the *Ucp2*$^{f/f}$ group and the data from this mouse was excluded. In all other cases, no animals were excluded from analysis.

Randomization

Animals with same date of birth were randomly assigned to each experimental group.

Blinding

Analyses of animal experiments were blinded whenever possible by numerical coding of samples.

DOI [to be added]