

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
SPHK2 KO : B6N.129S6- <i>Sphk2</i> ^{tm1Rlp} /J	The Jackson Laboratory	C57BL/6NJ	M	https://www.jax.org/strain/019140
C57BL/6NJ	The Jackson Laboratory	C57BL/6NJ	M	https://www.jax.org/strain/005304

Genetically Modified Animals

	Species	Vendor or Source	Background Strain	Other Information	Persistent ID / URL
Parent - Male	SPHK2 KO: B6N.129S6- <i>Sphk2</i> ^{tm1Rlp} /J	The Jackson Laboratory	C57BL/6NJ		https://www.jax.org/strain/019140
Parent - Female	SPHK2 KO: B6N.129S6- <i>Sphk2</i> ^{tm1Rlp} /J	The Jackson Laboratory	C57BL/6NJ		

Antibodies

Target antigen	Vendor or Source	Catalog #	Working concentration	Lot # (preferred but not required)	Persistent ID / URL
Ac-H3K9	Cell Signaling Technology	9649T	1:1000		https://www.cellsignal.com/products/primary-antibodies/acetyl-histone-h3-lys9-c5b11-rabbit-mab/9649
Total H3	Cell Signaling Technology	9715S	1:1000		https://www.cellsignal.com/products/primary-antibodies/histone-h3-antibody/9715?site-search-type=Products&N=4294956287&Ntt=9715s&fromPage=plp&_requestid=1844484
SPHK2	Cell Signaling Technology	32346	1:1000		https://www.cellsignal.com/products/primary-antibodies/sphk2-d2v3g-rabbit-mab/32346
SPHK2	Proteintech	17096-1-AP	1:1000		https://www.ptglab.com/products/SPHK2-Antibody-17096-1-AP.htm
phosphoSPHK2 (Thr614)	Thermo Fischer Scientific	PA5-39812	1:50		https://www.fishersci.com/shop/products/phosphosphk2-thr614-polyclonal-antibody-invitrogen/PIPA539812
phosphoSPHK2 (Thr614)	Abcam	Ab212750	1:1000		https://www.abcam.com/products/primary-antibodies/sphk2-phospho-t614-antibody-ab111948.html

α -tubulin	Cell Signaling Technology	3873T	1:1000		https://www.cellsignal.com/products/primary-antibodies/a-tubulin-dm1a-mouse-mab/3873
Lamin B	Santa Cruz	sc-6217	1:800		https://www.scbt.com/p/lamin-b-antibody-m-20
KLF4	Cell Signaling Technology	4038S	1:1000		https://www.cellsignal.com/products/primary-antibodies/klf4-antibody/4038?gclid=Cj0KCQjw756lBhDMARIsAEi0AglKGHRiZiXmLSxFSP23Rcehvrac1_oBXOnjHZr4xllzWoXaupQzcywaAiyMEALw_wcB&gclsrc=aw.ds
Alexa Fluor 488 Phalloidin	Thermo Fischer Scientific	A12379	1:500		https://www.thermofisher.com/order/catalog/product/A12379
HRP-conjugated rabbit secondary antibody	Cell Signaling Technology	7074S	1:4000		https://www.cellsignal.com/products/secondary-antibodies/anti-rabbit-igg-hrp-linked-antibody/7074
HRP-conjugated mouse secondary antibody	Cell Signaling Technology	7076S	1:4000		https://www.cellsignal.com/products/secondary-antibodies/anti-mouse-igg-hrp-linked-antibody/7076
AIMP1	Bethyl Laboratories	A304-896a	1:1000		https://www.thermofisher.com/antibody/product/AIMP1-EMAPII-SCYE1-Antibody-Polyclonal/A304-896A
EMAP II (546-2)	Santa Cruz	Sc-32723	1:100		https://www.scbt.com/p/emap-ii-antibody-546-2
Vinculin	Cell Signaling Technology	13901T	1:1000		https://www.cellsignal.com/products/secondary-antibodies/anti-mouse-igg-hrp-linked-antibody/7076
HDAC1	Cell Signaling Technology	65816T	1:1000		https://www.cellsignal.com/products/primary-antibodies/class-i-hdac-antibody-sampler-kit/65816
HDAC2	Bethyl Laboratories	A300-705A-T	1:1000		https://www.cellsignal.com/products/primary-antibodies/class-i-hdac-antibody-sampler-kit/65816
OCT4A	Cell Signaling Technology	2840T	1:1000		https://www.cellsignal.com/products/primary-antibodies/oct-4a-c30a3-rabbit-mab/2840
SOX2	Cell Signaling Technology	4195	1:1000		https://www.cellsignal.com/products/primary-antibodies/sox2-l73b4-mouse-mab/4195
Actin	Sigma-Aldrich	A5228-25ul	1:1000		https://www.sigmaaldrich.com/US/en/substance/antiactinasmoothmuscleantibodymousemonooclonal1234598765?gclid=Cj0KCQjw756lBhDMARIsAEi0AgnCBX5AOrbQp1i6L-Nx1gRdDOVXjrZYxFEXYVvkqZeLIV6is2LLc0kAaAnp6EALw_wcB&gclsrc=aw.ds
Ac-H4K5	Cell Signaling Technology	8647S	1:1000		https://www.cellsignal.com/products/primary-antibodies/acetyl-histone-h4-lys5-d12b3-rabbit-mab/8647

Prolong Gold Antifade Reagent with DAPI	Cell Signaling Technology	89615			https://www.cellsignal.com/products/buffers-dyes/prolong-gold-antifade-reagent-with-dapi/8961
TripleStain IHC Kit: R&R&M on human	Abcam	Ab183290			https://www.abcam.com/products/ihc-kits/triplestain-ihc-kit-mrg-on-human-tissue-dab-apred--hrpgreen-ab183290.html
CAS Block™ Histochemical reagent	Life Technologies	00-8120			https://www.thermofisher.com/order/catalog/product/008120
Citrate 6.0 retrieval	Life Technologies	00-5000			https://www.thermofisher.com/order/catalog/product/005000

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
Human PASMCMC	Lonza	Male and Female donors	https://bioscience.lonza.com/lonza_bs/US/en/Primary-and-Stem-Cells/p/000000000000185155/PASMC---Human-Pulmonary-Artery-Smooth-Muscle-Cells
Human Lung MVEC	Lonza	Male and Female donors	https://bioscience.lonza.com/lonza_bs/US/en/Primary-and-Stem-Cells/p/000000000000184961/HMVEC-L-%E2%80%93-Human-Lung-Microvascular-Endothelial-Cells

Data & Code Availability

Description	Source / Repository	Persistent ID / URL

Other

Description	Source / Repository	Persistent ID / URL
ON-TARGETplus Human SPHK2 siRNA (SMART pool)	Dharmacon L-004831-00-0005 (56848)	https://horizondiscovery.com/en/gene-modulation/knockdown/sirna/products/on-targetplus-sirna-reagents?nodeid=entrezgene-56848
ON-TARGETplus Non-targeting Control Pool	Dharmacon D-001810-10-20	https://horizondiscovery.com/en/gene-modulation/knockdown/controls/products/on-targetplus-non-targeting-control-pool

DOI [to be added]

S1P Elisa Kit: General Sphingosine-1-Phosphate (ELISA kit)	MyBioSource MB2700637	https://www.mybiosource.com/general-elisa-kits/sphingosine-1-phosphate-s1p/2700637
Histone Deacetylase (HDAC) Activity Assay Kit	Abcam Ab156064	https://www.abcam.com/products/chip-kits/histone-deacetylase-hdac-activity-assay-kit-fluorometric-ab156064.html

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)	Male	12-14 weeks			yes	
Group 2	Male	12-14 weeks			yes	
Add more if needed						

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

Based on data from similar studies by colleagues and from related published studies, sample size necessary to achieve significance identified the mean change for multiple parameters. Using these mean differences, 5-8 samples for human tissue and 6-10 mice/ group, to achieve a power=0.8-0.9 and alpha=0.01. Using these sample sizes, we calculate that we will have sufficient power to achieve an alpha of 0.05. The level of significance was defined with a cutoff of $p < 0.05$.

Inclusion Criteria

Male and 12-14 weeks of age and littermates.

Exclusion Criteria

none

Randomization

Randomization on littermate cohorts was performed by using a coin flip methodology and distribution of littermates across all experimental groups.

Blinding

Samples were randomized by an individual not involved in the study and analyzed by a different student not involved in the collection of the data. Results were then unblinded and analyzed.

DOI [to be added]