

## 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
Mus musculus	In house, Originally from The Jackson Laboratory	C57BL/6J	M	<a href="https://www.jax.org/strain/000664">https://www.jax.org/strain/000664</a>

### Genetically Modified Animals

	Species	Vendor or Source	Background Strain	Sex	Persistent ID / URL
Adipoq-Cre mice	Mus musculus	The Jackson Laboratory	C57BL/6J	M	<a href="https://www.jax.org/strain/010803">https://www.jax.org/strain/010803</a>
Gsk3 $\beta$ -flox mice	Mus musculus	Originally from Dr. James R. Woodgett	C57BL/6	Both	N/A
Gsk3 $\alpha$ -flox mice	Mus musculus	Originally from Dr. James R. Woodgett	C57BL/6	Both	N/A
Gsk3 $\beta$ <sup>ADKO</sup>	Mus musculus	In house	C57BL/6	Both	N/A
Gsk3 $\alpha$ <sup>ADKO</sup>	Mus musculus	In house	C57BL/6	M	N/A

### Antibodies

Target antigen	Vendor or Source	Catalog #	Working concentration	Persistent ID / URL
Rat anti-F4/80 antibody	eBioscience	14-4801-85	5 $\mu$ g/ml for IF	<a href="https://www.thermofisher.com/order/genome-database/generatePdf?productName=F4/80&amp;assayType=PRANT&amp;detailed=true&amp;productId=14-4801-85">https://www.thermofisher.com/order/genome-database/generatePdf?productName=F4/80&amp;assayType=PRANT&amp;detailed=true&amp;productId=14-4801-85</a>
Rat Anti-Mouse CD31 antibody	BD Biosciences	553370	1:100 or IF	<a href="https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/purified-rat-anti-mouse-cd31.553370">https://www.bdbiosciences.com/en-us/products/reagents/flow-cytometry-reagents/research-reagents/single-color-antibodies-ruo/purified-rat-anti-mouse-cd31.553370</a>
Rabbit Anti-HIF-1 $\alpha$	Abcam	ab179483	2 $\mu$ g for IP; 1:100 for IF, and 1:1000 for WB	<a href="https://www.abcam.com/en-us/products/primary-antibodies/hif-1-alpha-antibody-epr16897-ab179483">https://www.abcam.com/en-us/products/primary-antibodies/hif-1-alpha-antibody-epr16897-ab179483</a>
Rabbit Anti-HIF-2 $\alpha$	Cell Signaling Technology	57921	2 $\mu$ g for IP; 1:100 for IF, and 1:1000 for WB	<a href="https://www.cellsignal.cn/products/primary-antibodies/hif-2a-e2n9w-rabbit-mab/57921">https://www.cellsignal.cn/products/primary-antibodies/hif-2a-e2n9w-rabbit-mab/57921</a>
Mouse Anti-SOD1	Santa Cruz Biotechnology	sc-101523	1:1000 for WB	<a href="https://www.scbt.com/p/sod-1-antibody-24">https://www.scbt.com/p/sod-1-antibody-24</a>
Mouse Anti-ITGA5	Santa Cruz Biotechnology	sc-376199	1:1000 for WB	<a href="https://www.scbt.com/p/integrin-alpha5-antibody-c-9">https://www.scbt.com/p/integrin-alpha5-antibody-c-9</a>
Mouse Anti- $\beta$ -actin	Santa Cruz Biotechnology	sc-1615	1:1000 for WB	<a href="https://www.scbt.com/p/actin-antibody-c-11">https://www.scbt.com/p/actin-antibody-c-11</a>

anti-CHOP	Cell Signaling Technology	5554	1:1000 for WB	<a href="https://www.cellsignal.cn/products/primary-antibodies/chop-d46f1-rabbit-mab/5554">https://www.cellsignal.cn/products/primary-antibodies/chop-d46f1-rabbit-mab/5554</a>
anti-calnexin	Cell Signaling Technology	2679	1:1000 for WB	<a href="https://www.cellsignal.cn/products/primary-antibodies/calnexin-c5c9-rabbit-mab/2679">https://www.cellsignal.cn/products/primary-antibodies/calnexin-c5c9-rabbit-mab/2679</a>
anti-phospho (p)-AKT Serine 473	Cell Signaling Technology	9271	1:1000 for WB	<a href="https://www.cellsignal.cn/products/primary-antibodies/phospho-akt-ser473-antibody/9271">https://www.cellsignal.cn/products/primary-antibodies/phospho-akt-ser473-antibody/9271</a>
total (t)-AKT	Cell Signaling Technology	9272	1:1000 for WB	<a href="https://www.cellsignal.cn/products/primary-antibodies/akt-antibody/9272">https://www.cellsignal.cn/products/primary-antibodies/akt-antibody/9272</a>
anti-phospho (p)-AMPK	Cell Signaling Technology	2535	1:1000 for WB	<a href="https://www.cellsignal.cn/products/primary-antibodies/phospho-ampka-thr172-40h9-rabbit-mab/2535">https://www.cellsignal.cn/products/primary-antibodies/phospho-ampka-thr172-40h9-rabbit-mab/2535</a>
total (t)-AMPK	Cell Signaling Technology	5831	1:1000 for WB	<a href="https://www.cellsignal.cn/products/primary-antibodies/ampka-d5a2-rabbit-mab/5831">https://www.cellsignal.cn/products/primary-antibodies/ampka-d5a2-rabbit-mab/5831</a>
total (t)-GSK3 $\beta$	Cell Signaling Technology	9315	1:1000 for WB	<a href="https://www.cellsignal.cn/products/primary-antibodies/gsk-3b-27c10-rabbit-mab/9315">https://www.cellsignal.cn/products/primary-antibodies/gsk-3b-27c10-rabbit-mab/9315</a>
Mouse Anti-VEGF	Santa Cruz Biotechnology	sc-7269	1:1000 for WB	<a href="https://www.scbt.com/p/vegf-antibody-c-1">https://www.scbt.com/p/vegf-antibody-c-1</a>
Mouse Anti-VEGFB	Santa Cruz Biotechnology	sc-80442	1:1000 for WB	<a href="https://www.scbt.com/p/vegf-b-antibody-j-14i">https://www.scbt.com/p/vegf-b-antibody-j-14i</a>
Goat Anti-VEGFR1	R&D systems	AF471	1:1000 for WB	<a href="https://www.rndsystems.com/products/mouse-vegfr1-flt-1-antibody_af4711-rabbit-mab/5554">https://www.rndsystems.com/products/mouse-vegfr1-flt-1-antibody_af4711-rabbit-mab/5554</a>
Mouse Anti-VEGFR2	R&D systems	AF644	1:1000 for WB	<a href="https://www.rndsystems.com/products/mouse-vegfr2-kdr-flk-1-antibody_af644">https://www.rndsystems.com/products/mouse-vegfr2-kdr-flk-1-antibody_af644</a>
Rabbit Anti-UCP1	Cell Signaling Technology	72298	1:100 for IF	<a href="https://www.cellsignal.cn/products/primary-antibodies/ucp1-e9z2v-xp-rabbit-mab/72298">https://www.cellsignal.cn/products/primary-antibodies/ucp1-e9z2v-xp-rabbit-mab/72298</a>
Donkey anti-Rat Secondary Antibody, Alexa Fluor™ 594	Thermo Fisher Scientific	A-21209	1:200 for IF	<a href="https://www.thermofisher.com/antibody/product/Donkey-anti-Rat-IgG-H-L-Highly-Cross-Adsorbed-Secondary-Antibody-Polyclonal/A-21209v-xp-rabbit-mab/72298">https://www.thermofisher.com/antibody/product/Donkey-anti-Rat-IgG-H-L-Highly-Cross-Adsorbed-Secondary-Antibody-Polyclonal/A-21209v-xp-rabbit-mab/72298</a>
Lycopersicon Esculentum (Tomato) Lectin (LEL, TL), DyLight 594	Vectorlab	DL-1177-1	50 $\mu$ g/100 $\mu$ l/mouse	<a href="https://vectorlabs.com/products/dyLight-594-lycopersicon-esculentum-tomato?srltid=AfmBOoqUvmbNtAe7y3C1JLPKEnuVjvqEFLNvj75WohS65h6M-AoX5Q9f">https://vectorlabs.com/products/dyLight-594-lycopersicon-esculentum-tomato?srltid=AfmBOoqUvmbNtAe7y3C1JLPKEnuVjvqEFLNvj75WohS65h6M-AoX5Q9f</a>
Goat anti-Rat IgG (H+L) Cross-Adsorbed Secondary Antibody, Alexa Fluor™ 488	Thermo Fisher Scientific	A-11006	1:200 for IF	<a href="https://www.thermofisher.com/antibody/product/Goat-anti-Rat-IgG-H-L-Cross-Adsorbed-Secondary-Antibody-Polyclonal/A-11006">https://www.thermofisher.com/antibody/product/Goat-anti-Rat-IgG-H-L-Cross-Adsorbed-Secondary-Antibody-Polyclonal/A-11006</a>

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### DNA/cDNA Clones

Clone Name	Sequence	Source / Repository	Persistent ID / URL
Primer-Mouse-16srRNA	Forward: ctggagcctgttttgcctctg Reverse: tgagatggactgtcggatgg	product length =100bp	<a href="https://www.ncbi.nlm.nih.gov/nucleotide/NM_013647.2">https://www.ncbi.nlm.nih.gov/nucleotide/NM_013647.2</a>
Primer-Mouse-Col1A1	Forward: gacttctctggctcctctgt Reverse: cacggaaactccagctgat	product length =113bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_007742.4">https://www.ncbi.nlm.nih.gov/nucore/NM_007742.4</a>
Primer-Mouse-Col3A1	Forward: tggcattctgggagaa Reverse: ttctcccactccagactg	product length =158bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_009930.2">https://www.ncbi.nlm.nih.gov/nucore/NM_009930.2</a>
Primer-Mouse-Fn1	Forward: gaccggacattttaccaga Reverse: ctgggggtctccgtgataat	product length =168bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_001276413.1">https://www.ncbi.nlm.nih.gov/nucore/NM_001276413.1</a>
Primer-Mouse-Itga4	Forward: ttttacatgaagagcga Reverse: attccagcttgacatgatgc	product length =153bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_010576.4">https://www.ncbi.nlm.nih.gov/nucore/NM_010576.4</a>
Primer-Mouse-Itga5	Forward: tgggggcttcaacctagac Reverse: tagacagcaccacctgcag	product length =174bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_010577.4">https://www.ncbi.nlm.nih.gov/nucore/NM_010577.4</a>
Primer-Mouse-ItgaX	Forward: gacgtgaatggggacagtct Reverse: cactcagtgactgcccaaaa	product length =181bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_021334.3">https://www.ncbi.nlm.nih.gov/nucore/NM_021334.3</a>
Primer-Mouse-ItgaM	Forward: tggcttcaatctggacactg	product length =175bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_001082960.1">https://www.ncbi.nlm.nih.gov/nucore/NM_001082960.1</a>

	Reverse: acaccggcttgctgt agt		
Primer- Mouse- Itgb2	Forward: agctggcacacaaactt tcc Reverse: tgatgagctgcaccacg tt	product length =153bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_008404.5">https://www.ncbi.nlm.nih.gov/nucore/NM_008404.5</a>
Primer- Mouse- Ucp3	Forward: ccggtggatgtggtaaa gac Reverse: ttaaggcccttctcagtt gc	product length =196bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_009464.3">https://www.ncbi.nlm.nih.gov/nucore/NM_009464.3</a>
Primer- Mouse- Catalas e	Forward: ggcttttgaccaagca ata Reverse: ccatcacgctgtagtt gg	product length =174bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_009804.2">https://www.ncbi.nlm.nih.gov/nucore/NM_009804.2</a>
Primer- Mouse- Sod1	Forward: gtgcagggaaccatcc act Reverse: ccatactgatggacgtg gaa	product length =110bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_011434.2">https://www.ncbi.nlm.nih.gov/nucore/NM_011434.2</a>
Primer- Mouse- Sod2	Forward: tcaatggtgggggacat att Reverse: gaacctggactcccac aga	product length =166bp	<a href="https://www.ncbi.nlm.nih.gov/nucleotide/76253932">https://www.ncbi.nlm.nih.gov/nucleotide/76253932</a>
Primer- Mouse- Sod3	Forward: ctgctcgctcacataac agc Reverse: ggcaagcctgtctgct agg	product length =249bp	<a href="https://www.ncbi.nlm.nih.gov/nucleotide/86439990">https://www.ncbi.nlm.nih.gov/nucleotide/86439990</a>
Primer- Mouse- Grp78	Forward: tcagcatcaagcaagg attg Reverse: gctccttgccattgaag aac	product length =248bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_001163434.1">https://www.ncbi.nlm.nih.gov/nucore/NM_001163434.1</a>
Primer- Mouse- Grp94	Forward: cagcacatctgggaatc aga Reverse: ctccacacgtagatggg aaag	product length =191bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_011631.1">https://www.ncbi.nlm.nih.gov/nucore/NM_011631.1</a>
Primer- Mouse- Atf4	Forward: gaaacctcatgggttct cca	product length =203bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_001287180.1">https://www.ncbi.nlm.nih.gov/nucore/NM_001287180.1</a>

	Reverse: agagctcatctggcatg gtt		
Primer- Mouse- Atf6	Forward: cttctccagttgctcca tc Reverse: caggaccagtgcagg cttc	product length =183bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_001081304.1">https://www.ncbi.nlm.nih.gov/nucore/NM_001081304.1</a>
Primer- Mouse- HIF2 $\alpha$	Forward: agtagcctctgtggctc caa Reverse: tccagggcatgtaga actc	product length =230bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_010137.3">https://www.ncbi.nlm.nih.gov/nucore/NM_010137.3</a>
Primer- Mouse- HIF1 $\alpha$	Forward: cacgggccatattcatg tct Reverse: tatcgaggctgtgtcga ctg	product length =167bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_001313919.2">https://www.ncbi.nlm.nih.gov/nucore/NM_001313919.2</a>
Primer- Mouse- LPL	Forward: ttcaaccacagcagcaa gac Reverse: aatctggccacatcatt cc	product length = 210bp	<a href="https://www.ncbi.nlm.nih.gov/nucleotide/AH001996.2">https://www.ncbi.nlm.nih.gov/nucleotide/AH001996.2</a>
Primer- Mouse- CD68	Forward: cttcccacaggcagca cag Reverse: aatgatgagaggcagc aagagg	product length =235bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_001291058.1">https://www.ncbi.nlm.nih.gov/nucore/NM_001291058.1</a>
Primer- Mouse- F4/80	Forward: ctttggctatgggcttc agtc Reverse: gcaaggaggacagagt ttatcgtg	product length =165bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_001355722.2">https://www.ncbi.nlm.nih.gov/nucore/NM_001355722.2</a>
Primer- Mouse- CD11c	Forward: ctggatagcctttctctg ctg Reverse: gcacactgtgtccgaac tc	product length =113bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_001363984.1">https://www.ncbi.nlm.nih.gov/nucore/NM_001363984.1</a>
Primer- Mouse- IL-1 $\beta$	Forward: ctccatgagctttgtaca agg Reverse: tgctgatgtaccagttgg gg	product length =245bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_008361.4">https://www.ncbi.nlm.nih.gov/nucore/NM_008361.4</a>
Primer- Mouse- TNF $\alpha$	Forward: catcttctcaaaattcga gtga	product length =175bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_013693.3">https://www.ncbi.nlm.nih.gov/nucore/NM_013693.3</a>

	Reverse: tgggagtagacaaggt acaaccc		
Primer-Mouse-Ccl2	Forward: cccaatgagtaggctg gaga Reverse: gaactgcctttgccttctt g	product length = 200bp	<a href="https://www.ncbi.nlm.nih.gov/nucleotide/BC055070.1">https://www.ncbi.nlm.nih.gov/nucleotide/BC055070.1</a>
Primer-Mouse-Prdm16	Forward: cagcacggtgaagccattc Reverse: gcgtgcatccgcttgtg	product length =87bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_001177995.2">https://www.ncbi.nlm.nih.gov/nucore/NM_001177995.2</a>
Primer-Mouse-Ucp1	Forward: ggccttgtaacaaca aaatac Reverse: ggcaacaagagctgac agtaaat	product length =67bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_009463.3">https://www.ncbi.nlm.nih.gov/nucore/NM_009463.3</a>
Primer-Mouse-PGC1 $\alpha$	Forward: acagctttctgggtggat tg Reverse: aatgagggcaatccgt ctt	product length =181bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_001402987.1">https://www.ncbi.nlm.nih.gov/nucore/NM_001402987.1</a>
Primer-Mouse-PGC1 $\beta$	Forward: ctggaactgaggctggt ct Reverse: ttccagaactggatga agg	product length =225bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_001364996.1">https://www.ncbi.nlm.nih.gov/nucore/NM_001364996.1</a>
Primer-Mouse-VEGFa	Forward: cacgacagaaggagagcaga Reverse: ctccagggttcatcgta ac	product length =193bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_001025250.3">https://www.ncbi.nlm.nih.gov/nucore/NM_001025250.3</a>
Primer-Mouse-VEGFb	Forward: ggcttagactcaacc aga Reverse: gtcctggggcagtgac ct	product length =163bp	<a href="https://www.ncbi.nlm.nih.gov/nucleotide/297632417">https://www.ncbi.nlm.nih.gov/nucleotide/297632417</a>
Primer-Mouse-VEGFc	Forward: ccaggacaggggacagtgtgta Reverse: tgctgaggtaacctgtg ctg	product length =246bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_009506.2">https://www.ncbi.nlm.nih.gov/nucore/NM_009506.2</a>
Primer-Mouse-Flt1 (VEGFR1)	Forward: caggaggacaaaagg ctgag	product length =248bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_001363135.1">https://www.ncbi.nlm.nih.gov/nucore/NM_001363135.1</a>

	Reverse: tccgtcatgtgcacaag ttt		
Primer- Mouse- Kdr (VEGF R2)	Forward: ttctggactctccctgcc ta Reverse: ctggttctccaatggg ata	product length =176bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_001403141.1">https://www.ncbi.nlm.nih.gov/nucore/NM_001403141.1</a>
Primer- Mouse- CD31	Forward: atgaccagcaacattc aca Reverse: cacagagcaccgaagt acca	product length =200bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_001032378.2">https://www.ncbi.nlm.nih.gov/nucore/NM_001032378.2</a>
Primer- Mouse- Cxcr4	Forward: aaaccccaaacacatt cac Reverse: tggtaacccatgaccag gat	product length =238bp	<a href="https://www.ncbi.nlm.nih.gov/nucleotide/2496538637">https://www.ncbi.nlm.nih.gov/nucleotide/2496538637</a>
Primer- Mouse- Mif	Forward: gtgccagaaccgcaa ctac Reverse: ggcagcgttcattgctg aat	product length =107bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_010798.3">https://www.ncbi.nlm.nih.gov/nucore/NM_010798.3</a>
Primer- Mouse- HK1	Forward: aagatgctccaacctt gt Reverse: gatgttctctgggtgct gt	product length =171bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_001146100.2">https://www.ncbi.nlm.nih.gov/nucore/NM_001146100.2</a>
Primer- Mouse- ANGP T4	Forward: cagcaggacacaatcc agaa Reverse: gctgttggtggacagt gag	product length = 172bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_009641.2">https://www.ncbi.nlm.nih.gov/nucore/NM_009641.2</a>
Primer- Mouse- Bnip3	Forward: gaactgcaactcagcaa tgg Reverse: gctgtggctgtctatttc agc	product length =195bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_009760.4">https://www.ncbi.nlm.nih.gov/nucore/NM_009760.4</a>
Primer- Mouse- Ndr1	Forward: cctacatggctccctgc at Reverse: acatggcagacagcaa aatg	product length =165bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_008681.2">https://www.ncbi.nlm.nih.gov/nucore/NM_008681.2</a>
Primer- Mouse- Prkca	Forward: agaaggacgtggtgat ccag	product length =153bp	<a href="https://www.ncbi.nlm.nih.gov/nucore/NM_011101.3">https://www.ncbi.nlm.nih.gov/nucore/NM_011101.3</a>

	Reverse: cgttgacgtattccatgacg		
Primer-Mouse-Pycard	Forward: acatgggcttacaggagctg Reverse: cgaactgcctggtactgtcc	product length =210bp	<a href="https://ncbi.nlm.nih.gov/nuccore/NC_000073.7?report=genbank&amp;from=127590545&amp;to=127593039&amp;strand=true">https://ncbi.nlm.nih.gov/nuccore/NC_000073.7?report=genbank&amp;from=127590545&amp;to=127593039&amp;strand=true</a>
Primer-Mouse-Aim2	Forward: cctgattcaaaagtgcaggtg Reverse: gaggcagcagagcagtttc	product length =170bp	<a href="https://ncbi.nlm.nih.gov/nuccore/NC_000067.7?report=genbank&amp;from=173177105&amp;to=173293606">https://ncbi.nlm.nih.gov/nuccore/NC_000067.7?report=genbank&amp;from=173177105&amp;to=173293606</a>
Primer-Mouse-Casp1	Forward: tgctacagaagattctaaaggagga Reverse: cctctgaaggattttcttccat	product length =152bp	<a href="https://ncbi.nlm.nih.gov/nuccore/NC_000075.7?report=genbank&amp;from=5298517&amp;to=5307281">https://ncbi.nlm.nih.gov/nuccore/NC_000075.7?report=genbank&amp;from=5298517&amp;to=5307281</a>
Primer-Mouse-Bcl2	Forward: gaggattgtggccttcttg Reverse: catgctggggccatatagtt	product length =180bp	<a href="https://ncbi.nlm.nih.gov/nuccore/NC_000067.7?report=genbank&amp;from=106465906&amp;to=106642020&amp;strand=true">https://ncbi.nlm.nih.gov/nuccore/NC_000067.7?report=genbank&amp;from=106465906&amp;to=106642020&amp;strand=true</a>
Primer-Mouse-Bax	Forward: gatgattgctgacgtggaca Reverse: gatcagctcgggcacttag	product length =160bp	<a href="https://ncbi.nlm.nih.gov/nuccore/NC_000073.7?report=genbank&amp;from=4511124&amp;to=45116332&amp;strand=true">https://ncbi.nlm.nih.gov/nuccore/NC_000073.7?report=genbank&amp;from=4511124&amp;to=45116332&amp;strand=true</a>
Primer-Mouse-Bak1	Forward: aggtgggctgcatgagt Reverse: aggggcaagttgtccatctc	product length =162bp	<a href="https://ncbi.nlm.nih.gov/nuccore/NC_000083.7?report=genbank&amp;from=27238786&amp;to=27247601&amp;strand=true">https://ncbi.nlm.nih.gov/nuccore/NC_000083.7?report=genbank&amp;from=27238786&amp;to=27247601&amp;strand=true</a>
Primer-Mouse-Casp3	Forward: caaaacctcagtgattcaaaa Reverse: gcatatgccatttcagat	product length =130bp	<a href="https://ncbi.nlm.nih.gov/nuccore/NC_000074.7?report=genbank&amp;from=47070326&amp;to=47092733">https://ncbi.nlm.nih.gov/nuccore/NC_000074.7?report=genbank&amp;from=47070326&amp;to=47092733</a>
Primer-Mouse-Casp8	Forward: ttggaggaaggcaatctgtc Reverse: tctcaattccaactcgctca	product length =190bp	<a href="https://ncbi.nlm.nih.gov/nuccore/NC_000067.7?report=genbank&amp;from=58834553&amp;to=58886663">https://ncbi.nlm.nih.gov/nuccore/NC_000067.7?report=genbank&amp;from=58834553&amp;to=58886663</a>
Primer-Mouse-Casp9	Forward: gccagaggttctcagaccag	product length =210bp	<a href="https://ncbi.nlm.nih.gov/nuccore/NC_000070.7?report=genbank&amp;from=141520923&amp;to=141543289">https://ncbi.nlm.nih.gov/nuccore/NC_000070.7?report=genbank&amp;from=141520923&amp;to=141543289</a>



	Reverse: tcaagttgtcacggtcc aa		
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### Cultured Cells

Name	Vendor or Source	Sex (F, M, or unknown)	Persistent ID / URL
3B-11	ATCC, CRL-2160	M	<a href="https://www.atcc.org/products/crl-2160#detailed-product-information">https://www.atcc.org/products/crl-2160#detailed-product-information</a>
3T3-L1	ATCC, CL-173	unknown	<a href="https://www.atcc.org/products/cl-173">https://www.atcc.org/products/cl-173</a>
EOMA	ATCC, CRL-2586	unknown	<a href="https://www.atcc.org/products/crl-2586">https://www.atcc.org/products/crl-2586</a>

### Data & Code Availability

Description	Source / Repository	Persistent ID / URL
RNA-SEQ	NGDC	OMIX007374

### Other

Name	Vendor or Source	Catalog #	Persistent ID / URL
Pierce™ IP Lysis Buffer	Thermo Fisher Scientific	87787	<a href="https://www.thermofisher.com/order/catalog/product/87787?SID=srch-srp-87787">https://www.thermofisher.com/order/catalog/product/87787?SID=srch-srp-87787</a>
PT2385	Selleck Chemicals,	S8352	<a href="https://www.selleckchem.com/products/pt2385.html">https://www.selleckchem.com/products/pt2385.html</a>
Protein A/G beads	Thermo Fisher Scientific	26161	
Compound C	Selleck Chemicals	S7840	<a href="https://www.selleckchem.com/products/dorsomorphin.html">https://www.selleckchem.com/products/dorsomorphin.html</a>
CHIR99021	Sigma-Aldrich	SML1046	<a href="https://www.sigmaaldrich.com/MO/en/product/sigma/sml1046">https://www.sigmaaldrich.com/MO/en/product/sigma/sml1046</a>
SB216763	Selleck Chemicals	S1075	<a href="https://www.selleckchem.com/products/SB-216763.html">https://www.selleckchem.com/products/SB-216763.html</a>
Triciribine	Sigma-Aldrich	T3830	<a href="https://www.sigmaaldrich.com/MO/en/product/sigma/t3830">https://www.sigmaaldrich.com/MO/en/product/sigma/t3830</a>
SCH772984	Selleck Chemicals	S7101	<a href="https://www.selleckchem.com/products/sch772984.html">https://www.selleckchem.com/products/sch772984.html</a>
3-Isobutyl-1-methylxanthine	Sigma-Aldrich	I5879	<a href="https://www.sigmaaldrich.com/MO/en/product/sigma/i5879">https://www.sigmaaldrich.com/MO/en/product/sigma/i5879</a>
Dexamethasone	Sigma-Aldrich	265005	<a href="https://www.sigmaaldrich.com/MO/en/product/mm/265005">https://www.sigmaaldrich.com/MO/en/product/mm/265005</a>
Mouse Insulin ELISA	ALPCO	80-INSMS-E01	<a href="https://www.alpco.com/mouse-insulin-elisa.html">https://www.alpco.com/mouse-insulin-elisa.html</a>
Mouse Adiponectin ELISA	R&D system	MRP300	<a href="https://www.rndsystems.com/products/mouse-adiponectin-acrp30-quantikine-elisa-kit_mrp300">https://www.rndsystems.com/products/mouse-adiponectin-acrp30-quantikine-elisa-kit_mrp300</a>
Triglyceride assay kit	Sigma-Aldrich	mak264	<a href="https://www.sigmaaldrich.com/MO/en/product/sigma/mak264">https://www.sigmaaldrich.com/MO/en/product/sigma/mak264</a>
Oil Red O	Sigma-Aldrich	O0625	<a href="https://www.sigmaaldrich.com/MO/en/product/sial/o0625?srltid=AfmBOorDri0kOZfQO-fFj_2iJAxDtxW_923pPICIiImJCxxyCAEu4vKH">https://www.sigmaaldrich.com/MO/en/product/sial/o0625?srltid=AfmBOorDri0kOZfQO-fFj_2iJAxDtxW_923pPICIiImJCxxyCAEu4vKH</a>
Hematoxylin and Eosin Stain Kit	VectorLab	H-3502	<a href="https://vectorlabs.com/products/hematoxylin-and-eosin-stain-kit">https://vectorlabs.com/products/hematoxylin-and-eosin-stain-kit</a>
Calcein AM	Sigma-Aldrich	206700	<a href="https://www.sigmaaldrich.com/MO/en/product/mm/206700">https://www.sigmaaldrich.com/MO/en/product/mm/206700</a>
DAPI	Sigma-Aldrich	D9542	<a href="https://www.sigmaaldrich.com/MO/en/product/sigma/d9542">https://www.sigmaaldrich.com/MO/en/product/sigma/d9542</a>

DOI [to be added]

Seahorse XF Base Medium	Agilent	102353-100	<a href="https://www.agilent.com/cs/library/datasheets/public/XF-base-medium-data-sheet.pdf">https://www.agilent.com/cs/library/datasheets/public/XF-base-medium-data-sheet.pdf</a>
Seahorse XF Cell Mito Stress Test Kit	Agilent	103015-100	<a href="https://www.agilent.com/cs/library/usermanuals/public/XF_Cell_Mito_Stress_Test_Kit_User_Guide.pdf">https://www.agilent.com/cs/library/usermanuals/public/XF_Cell_Mito_Stress_Test_Kit_User_Guide.pdf</a>
DMEM	Thermo Fisher Scientific	11995065	<a href="https://www.thermofisher.com/order/catalog/product/11995065">https://www.thermofisher.com/order/catalog/product/11995065</a>
EDTA	Thermo Fisher Scientific	AM9260G	<a href="https://www.thermofisher.com/order/catalog/product/AM9260G?SID=srch-srp-AM9260G">https://www.thermofisher.com/order/catalog/product/AM9260G?SID=srch-srp-AM9260G</a>
Formaldehyde solution	Sigma-Aldrich	F1635	<a href="https://www.sigmaaldrich.com/MO/en/product/sigald/f1635">https://www.sigmaaldrich.com/MO/en/product/sigald/f1635</a>
Fetal bovine serum	Thermo Fisher Scientific	10270106	<a href="https://www.thermofisher.com/order/catalog/product/10270106?SID=srch-srp-10270106">https://www.thermofisher.com/order/catalog/product/10270106?SID=srch-srp-10270106</a>
Penicillin-Streptomycin	Thermo Fisher Scientific	15070063	<a href="https://www.thermofisher.com/order/catalog/product/15070063?SID=srch-srp-15070063">https://www.thermofisher.com/order/catalog/product/15070063?SID=srch-srp-15070063</a>
Rabbit IgG Isotype Control	Cell Signaling Technology	3900	<a href="https://www.cellsignal.cn/products/primary-antibodies/rabbit-dallemab-igg-xp-isotype-control/3900">https://www.cellsignal.cn/products/primary-antibodies/rabbit-dallemab-igg-xp-isotype-control/3900</a>
Mouse IgG	Abcam	Ab280974	<a href="https://www.abcam.com/en-us/products/primary-antibodies/mouse-igg1-monoclonal-r312-mouseigg1-isotype-control-ab280974">https://www.abcam.com/en-us/products/primary-antibodies/mouse-igg1-monoclonal-r312-mouseigg1-isotype-control-ab280974</a>
Nitrocellulose Membrane	BIO-RAD	1620115	<a href="https://www.bio-rad.com/en-mo/product/nitrocellulose-membrane-0-45-um?ID=9b5b2069-356c-447b-a0fd-cae196945394">https://www.bio-rad.com/en-mo/product/nitrocellulose-membrane-0-45-um?ID=9b5b2069-356c-447b-a0fd-cae196945394</a>
Western diet	Research Diets Inc.,	D12492	<a href="https://researchdiets.com/formulas/d12492">https://researchdiets.com/formulas/d12492</a>

## 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	M	16 wk	6	6	Y	Wild type+NCD
Group 2	M	16 wk	6	6	Y	Wild type+HFD
Group 3	M	16 wk	6	6	Y	Wild type+HFD+SB
Group 4	M/F	26 wk	9	9	Y	GSK3 $\beta^{fl/fl}$ ; HFD
Group 5	M/F	26 wk	9	9	Y	GSK3 $\beta^{ADKO}$ ; HFD
Group 6	M/F	26 wk	5	5	Y	GSK3 $\alpha^{fl/fl}$ ; HFD
Group 7	M/F	26 wk	5	5	Y	GSK3 $\alpha^{ADKO}$ ; HFD
Group 8	M	26 wk	5	5	Y	GSK3 $\beta^{ADKO}$ ; HFD+PT
Group 9	M	26 wk	5	5	Y	GSK3 $\beta^{ADKO}$ ; HFD+CC
Group 10	F	26 wk	6	6	Y	GSK3 $\beta^{ADKO}$ ; HFD+PT
Group 11	F	26 wk	5	5	Y	GSK3 $\beta^{ADKO}$ ; HFD+CC

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

The number of animals utilized in each experiment was determined based on the typical sample size used in the field.

**Inclusion Criteria**

All mice with correct genotype were included in the study.

**Exclusion Criteria**

No mouse was excluded.

**Randomization**

Mice were allocated to each group randomly using a random number generator.

**Blinding**

The animal experiments were conducted by researchers who were blinded to the genotype and treatment assignments. All immunostaining quantification analysis were blinded.