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Supplementary Materials for

Estrogen receptor α controls metabolism in white and brown adipocytes by regulating *Polg1* and mitochondrial remodeling

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The PDF file includes:

Other Supplementary Material for this manuscript includes the following:

(available at stm.sciencemag.org/cgi/content/full/12/555/eaax8096/DC1)

Data file S1 (Microsoft Excel format). Raw data from studies of human tissues, cells, and genetically engineered mice.
Data file S2 (Microsoft Excel format). Raw data of *ESR1*-correlated genes in subcutaneous fat from men participating in the METSIM study.
Data file S3 (Microsoft Excel format). Raw data of *ESR1*-correlated genes in subcutaneous fat from men participating in the MyoGlu study.
Data file S4 (Microsoft Excel format). Raw data of *Esr1*-correlated genes in gonadal fat from male mice of the UCLA HMDP.
Data file S5 (Microsoft Excel format). Raw data of *Esr1*-correlated genes in gonadal fat from female mice of the UCLA HMDP.
Data file S6 (Microsoft Excel format). GO of microarray data performed on gonadal fat from female FERKO and Control$^{f/f}$ mice.

Materials and methods

Immunoblot analysis

Whole quadriceps muscles from both legs were pulverized together into a powder while frozen in liquid nitrogen and a homogenous sample of pulverized muscle was used for immunoblotting. Proteins from each individual whole cell homogenate were normalized (expressed relative to the pixel densitometry) to glyceraldehyde 3-phosphate dehydrogenase (GAPDH, AM4300, Ambion). Phosphorylation-specific proteins were normalized (expressed relative to pixel densitometry) to the same unphosphorylated protein (i.e. phosphorylated Drp1 at Ser 616 was expressed relative to the pixel densitometry of Drp1 for each individual sample). Primary antibodies included: Mitochondrial Fission Protein 1 (Fis1, GTX111010, GeneTex), Mitochondrial fission factor (MFF, ab81127, Abcam), Mitofusin 1 (MFN1, 75-162, NeuroMab), Mitofusin2 (MFN2, ab56889, Abcam), Transcription factor A, Mitochondrial (TFAM, ab131607, Abcam), Dynamin-related protein 1 (Drp1, 8570, Cell Signaling), phosphorylated Drp1 Ser616 (4494, Cell Signaling), phosphorylated Drp1 Ser637 (6319, Cell Signaling), OxPhos Complex I to V (ab110413, Abcam), Optic atrophy 1 (Opa1, 612606, BD Biosciences), PTEN Induced Putative Kinase 1 (Pink1, 10006283, Cayman Chemical), Parkin (2132, Cell Signaling), phosphorylated Parkin Ser65 (ab154995, Abcam), Microtubule-associated proteins 1A/1B light chain 3B (LC3B, 2775, Cell Signaling), Sequestosome 1 (p62, 5114, Cell Signaling), Beclin-1 (3738, Cell Signaling), Autophagy Related 7 (ATG7, 8558, Cell Signaling), Protein Kinase A (PKA, 4782, Cell Signaling), Autophagy Related 10 (ATG10, PA5-20454, ThermoFisher), phospho-AMPKα Thr172 (50081, Cell Signaling), PGC1α (2178, Cell Signaling), and phospho-PKA Thr197 (5661, Cell Signaling). In some cases immunoblots were stripped and re-probed with a different antibody; thus, loading controls in specific instances were duplicated between panels.

DNA & RNA extraction, cDNA synthesis, quantitative RT-PCR, and microarrays

DNA and RNA were extracted from a portion of frozen adipose tissue homogenate (gonadal and inguinal white adipose tissue and interscapular brown adipose tissue) using DNeasy/RNeasy isolation kits (Qiagen) as described by the manufacturer. Isolated DNA and RNA were tested for concentration and purity using a NanoDrop Spectrophotometer (Thermo Scientific). Isolated RNA was converted into cDNA, checked for purity, and qPCR of the resulting cDNA was performed (*1*). All genes were normalized to the housekeeping gene Ppia or 18S. Mitochondrial DNA content was assessed as a ratio of mitochondrial DNA (mtCO2) to nuclear DNA (SDHA). See **table S5** for a list of qPCR primers. MtDNA copy number from human adipose tissue was deep sequenced and aligned reads origin from the human mitochondrial chromosome (37 genes), quantified (normalized) copy numbers and compared them between dysglycemic and normoglycemic men. We used the Rsubread package in R. Total DNA was extracted from cells using DNeasy Blood and Tissue kit (Qiagen). Expression of mtCO3 for mtDNA and 18S for nuclear DNA was assessed by real-time qPCR. The ratio of mtDNA (mtCO3) to nuDNA (18S) was used as an estimate for comparison of mtDNA content between the genotypes.

Total RNA from HMDP mouse muscle (211 females, 228 males) was hybridized to Affymetrix HT_MG-430A arrays and scanned using standard Affymetrix protocols. To reduce spurious association, RMA normalization was performed after removing all individual probes with SNPs and all probesets including 8 or more SNP-containing probes, resulting in 22,416 remaining probesets. To determine the accuracy of microarray data, qPCR was used to test the expression of a dozen genes. A correlation of r = 0.7 between qPCR and microarrays was determined. Frozen human adipose tissue biopsies were cooled in liquid nitrogen and crushed to powder by a pestle in a liquid nitrogen-cooled mortar as described by Langleite et al. (*64*). Frozen biopsies were transferred into 1 mL QIAzol Lysis Reagent (Qiagen), and homogenized using TissueRuptor (Qiagen) at full speed for 15 sec, twice. Total RNA was isolated from the homogenate using RNeasy Mini Kit (Qiagen). RNA integrity and concentration were determined using Agilent RNA 6000 Nano Chips on a Bioanalyzer 2100 (Agilent Technologies Inc). Using High-Capacity cDNA Reverse Transcription Kit (Applied Biosystems), 200 ng of total RNA was converted to cDNA for TaqMan real-time RT-PCR. The cDNA reaction mixture was diluted in water and cDNA equivalent of 25 ng RNA used for each sample. Quantitative real-time PCR was performed with reagents and instruments from Applied Biosystems in the 96 well format using a 7900HT Fast instrument and the SDS 2.3 software (Applied Biosystems). Relative target mRNA expression levels were calculated as 2−ΔCt, and normalized to beta- 2 microglobulin (B2M, Hs00984230_m1) (*63*). mRNA sequencing was performed using the Illumina HiSeq 2000 system (Illumina). cDNA sequenced read alignment was carried out using Tophat v2.0.8. Reads counted by gene feature were performed by featureCounts in Rsubread 1.14.2.

Tissue histology

White (gonadal) and brown adipose tissue (interscapular) depots from Control ERαKO models were fixed in formalin, sectioned and stained as previously described (*8*). Adipocyte nuclei and total adipocyte number and size were counted or measured using ImageJ software.

Mitochondrial isolation

Mitochondria were isolated from gastrocnemius muscle using a Dounce homogenizer and Mitochondria Isolation Kit for Tissue (Thermo Scientific) with a Percoll density method for added purification. Briefly, gastrocnemius muscles were washed in ice-cold PBS, Dounce homogenized, and centrifuged at 800g for 10 min at 4°C. The supernatant was centrifuged at 12,000g for 15 min at 4°C. The pellet was washed and purified using isolation buffer and Percoll solution. Isolated mitochondria were mixed with lysis buffer (200 uL, 12 mM sodium lauroyl sarcosine, 0.5% sodium deoxycholate, 50 mmol/L triethylammonium bicarbonate (TEAB)), then subjected to bath sonication for 10 min (Bioruptor Pico, Diagenode Inc.) and heated (95°C for 5 min).

Real-time respirometry of adipocytes

Scrambled control (Scr) and *Esr1*-KD 3T3L1 fibroblasts were seeded in 24-well Seahorse plates (Seahorse Biosciences) and differentiated to adipocytes. Mitochondrial respiration in adipocytes was measured using an XF24 Extracellular Flux Analyzer (Seahorse Biosciences). Measurements of oxygen consumption were made continuously while cells were sequentially treated with oligomycin (ATP synthase inhibitor), FCCP (an uncoupling agent), and rotenone/myxothiazol (inhibitors of complex I/III of the electron transport chain)(*28*).

Confocal microscopy

3T3-L1 cells were grown and differentiated in CELLview 4-compartment glass-bottom tissue culture dishes (Greiner Bio-One), PS, 35/10 mm. After 7 days of differentiation, 100 nM of Mtphagy Dye (Dojindo Molecular Technologies Inc.) or 1 mM of LysoTracker Green (Invitrogen) was added and cultured with preadipocytes for 30 minutes separately. Cells were imaged immediately with the alpha Plan-Apochromat 100´1.46 Oil DIC M27 objective on the Zesis LSM 880 with Airyscan. Before image analysis, raw.czi files were automatically processed into deconvoluted Airyscan images using the Zen software. Images were analyzed in Fiji (ImageJ, NIH). The areas and numbers of lysosomes and mitolysosomes were quantified. Briefly, 2-channel Airyscan images of lysosomes and mitolysosomes were subjected to a background subtraction with a rolling ball filter = 50; individual cells were cropped from larger fields, followed by thresholding, segmentation, and measurement.

ChIP

Stable ERα-expressing 3T3L1 cells (described above) were used for ChIP experiments. Cells were grown to confluence and at day 3 of differentiation were treated for 60 minutes with vehicle or 10 nM β-estradiol. Cells were harvested and ChIP analyses were performed as previously described (*8, 28)* using an antibody against ERα (ab32063, Abcam). Primers for detection of the Polg1 promoter by qPCR are listed in the **table S6**.

Transmission electron microscopy

Brown adipose tissue sections were fixed with freshly prepared pre-warmed (37°C) fixative containing 2.5% glutaraldehyde and 2% paraformaldehyde in 0.15 M cacodylate buffer. After fixation, tissues were processed for TEM analysis as described previously (*27*). Ultrathin (~60 nm) sections were viewed using a JEOL 1200EX II (JEOL) electron microscope and photographed by digital camera (Gatan). Micrographs were obtained for Control$^{f/f}$ vs. ERαKO^{BAT} brown adipose tissue samples.

FDG positron emission tomography-computed tomography imaging

PET tracers, ^{18}F-fluorodeoxyglucose (FDG) and ^{18}F-2-deoxy-2-fluoroarabinos (DFA), were synthesized as previously described. ^{18}F-FDG was obtained from the UCLA Translational Imaging Division. Mice were injected with ExiTron nano 12,000 (100μL), 3d before the PET imaging experiment. Mice were anesthetized, injected with ~2.96 MBq of ^{18}F-FDG (after overnight fast) or ^{18}F-DFA, and after 60 min imaged for 10 min on a G8 PET/CT (SOFIE Biosciences). Different groups of littermate mice were used for the room temperature vs. cold tolerance testing (4°C for 4h) studies. A blinded observer, unaware of the intervention groups, performed the PET quantification using only the CT image to examine the regions of interest. ^{18}F-DFA and ^{18}F-FDG accumulation were normalized to the respective accumulation in the brain and right forelimb triceps. Brain was selected as a reference region for the quantification of ^{18}F-DFA accumulation as specific accumulation of ^{18}F-DFA in the brain has never been observed, and the same brain region could be readily identified and quantified across individual animals. Image-derived blood ^{18}F-DFA was quantified from the left ventricle. Hepatic ^{18}F-DFA contrast, correlation, and entropy were determined using the GLCM Texture plugin in ImageJ (version 1.50i).

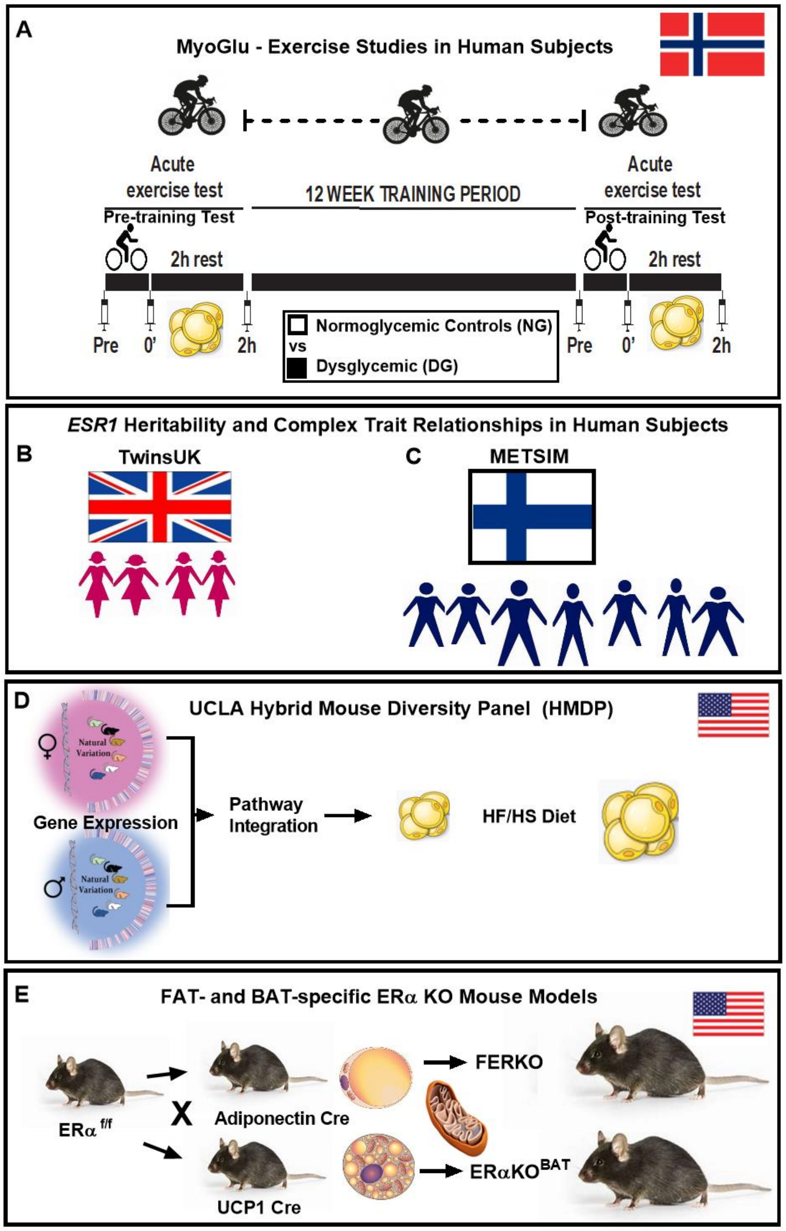

Fig. S1. Overview of the human and mouse studies included in this investigation. (A) MyoGlu exercise studies (two endurance and 2 strength training sessions, 60 min each, 4 x per week) in 13 normoglycemic (NG) and 13 dysglycemic (DG) men of age 40-65 years, with adipose tissue samples excised before and after training(*2, 14-16*). (B) TwinsUK, a study of ~766 healthy female monozygotic and dizygotic twins ages 38-85 years (median age 62, ~75% postmenopausal by FNP calculation)(*12, 13*). Adipose tissue samples were harvested and gene expression was determined by RNAseq. (C) METSIM studies in Finnish men (n=8,460) age 45-70 years included adipose tissue gene expression determined by Affymetrix microarrays and correlated with complex traits in n=770 subjects(*17-19*). (D) Studies of the UCLA Hybrid Mouse Diversity Panel (HMDP) comprised of 100 inbred and recombinant inbred male and female mice under normal chow (NC) and high fat-high sucrose (HF-HS) diet in the sedentary condition (4 mice per strain / per condition; 12 weeks of age)(*20, 21*). (E) Studies in male and female white (WAT) and brown (BAT) adipose tissue-specific ERα knockout mice, FERKO and $\text{ER}\alpha\text{KO}^{\text{BAT}}$, respectively.

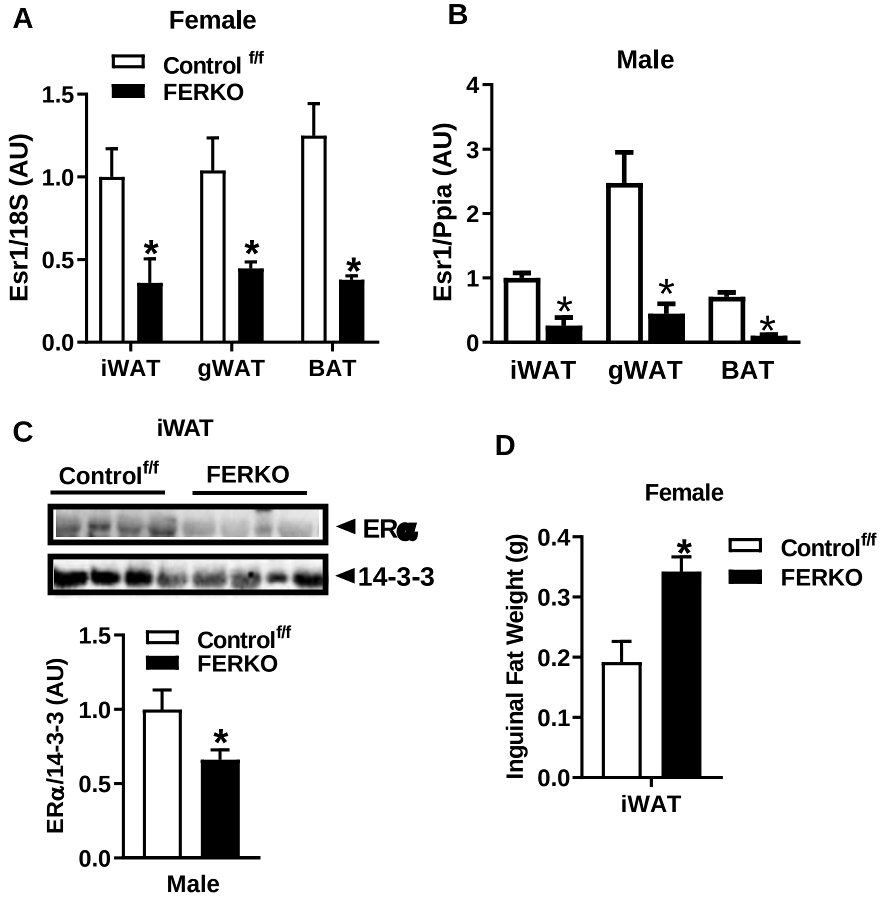

Fig. S2. Characteristics of male and female FERKO mice. (A-B) *Esr1* expression and (C) ERα protein in iWAT of female and male FERKO mice compared with Control$^{f/f}$ (n=5-9/genotype). (D) Inguinal white adipose tissue (iWAT) weight in female FERKO mice vs. Control$^{f/f}$ (n=5-7/genotype). Data are means ± SEM. Student's t-test or one-way ANOVA, *P< 0.05 between genotype difference.

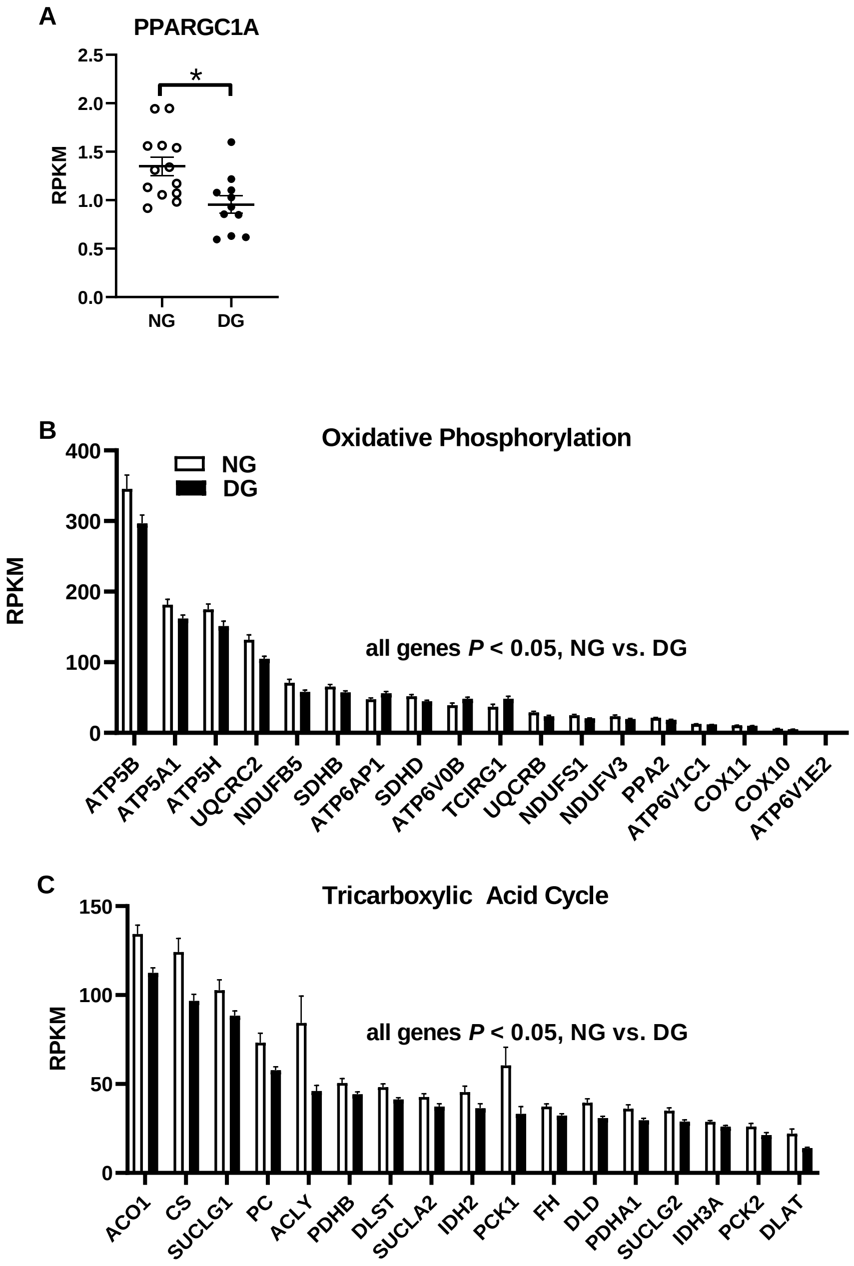

Fig. S3. Expression analyses performed on adipose tissue samples from men participating in the MyoGlu studies. Normoglycemic, NG vs. dysglycemic, DG; n=46 men aged 40-65 years. Adipose tissue expression of (A) PPARGC1A, and genes associated with (B) oxidative phosphorylation and the (C) tricarboxylic acid cycle. Values are means ± SEM. Differences detected by Student's t-test or one-way ANOVA, *$P< 0.05$ between genotype difference.

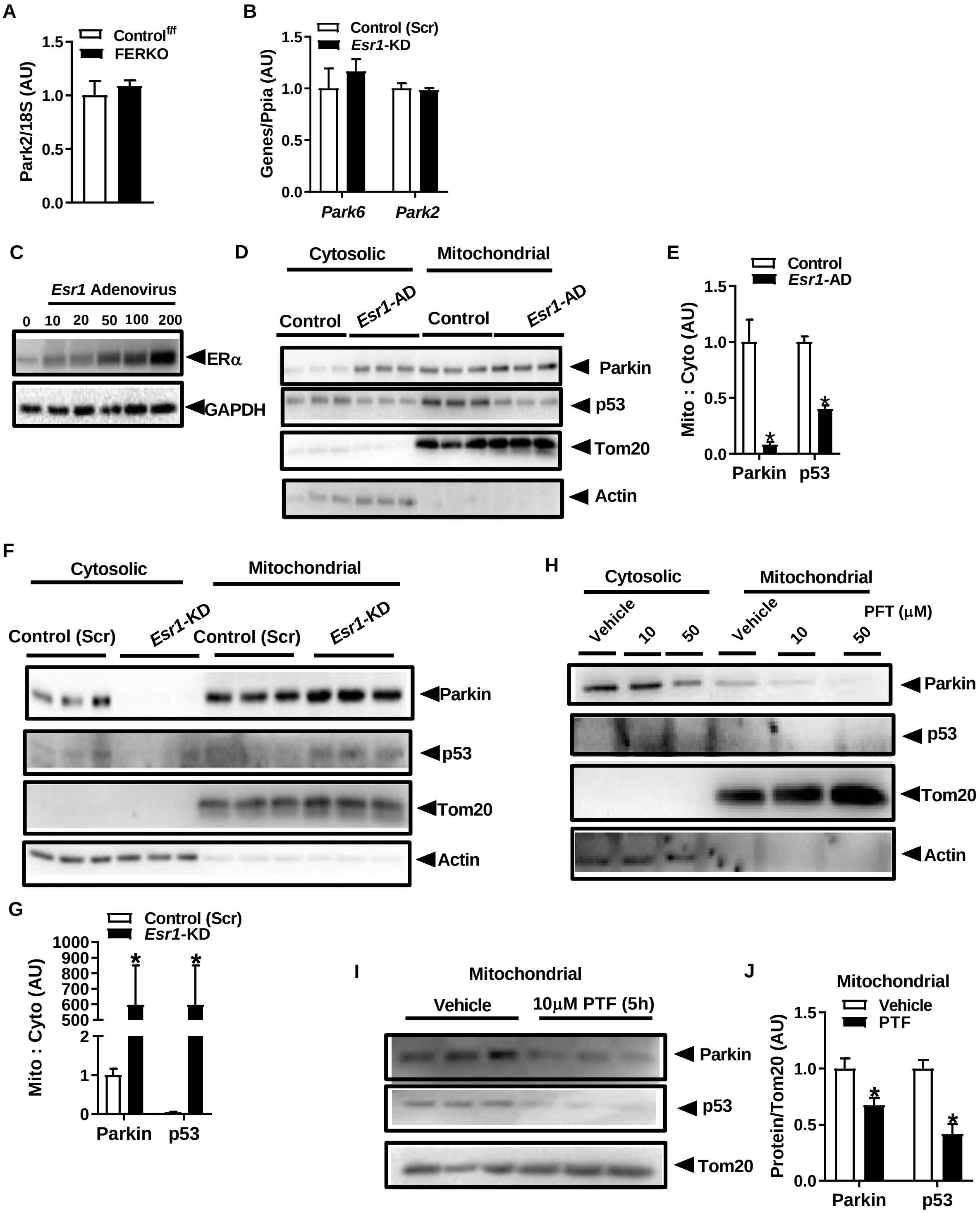

Fig. S4. The impact of *Esr1* loss and gain of expression on parkin and p53 cellular localization. (A) *Esr1* expression by increasing volumes of adenovirus in 3T3L1 adipocytes as represented by ERα immunoblotting. (B-C) *Esr1* overexpression on mitochondrial:cytosolic parkin and p53 relative to controls. (D-E) Knockdown of *Esr1* on the mitochondrial distribution of p53 and parkin compared with (Scr) controls. (F-H) The effect of p53 inhibitor Pifithrin-α (PFT 10 and 50μM, 5h) on the abundance of mitochondrial-associated p53 and parkin in control 3T3L1 adipocytes. Values are means ± SEM. Differences detected by Student's t-test or one-way ANOV, *P< 0.05 between genotype difference.

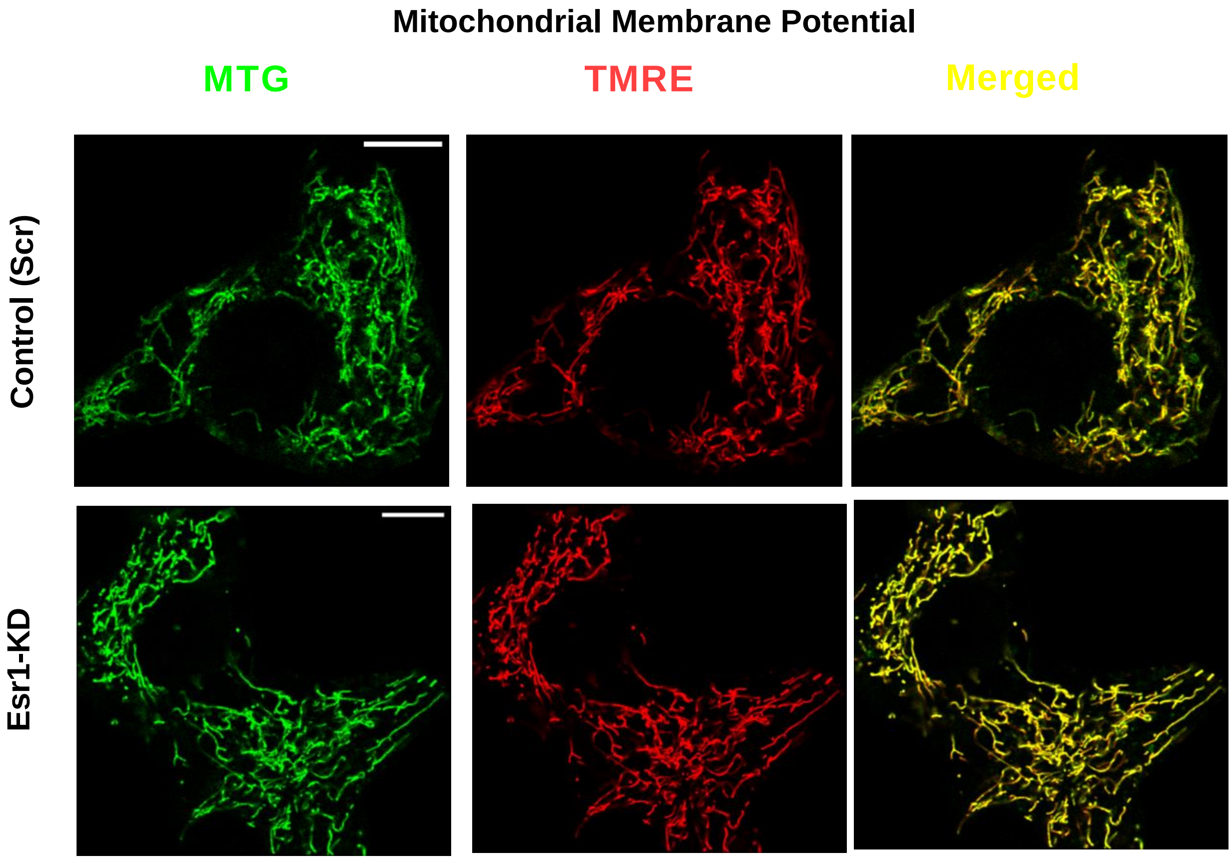

Fig. S5. Mitochondrial membrane potential in 3T3L1 adipocytes in the presence or absence of *Esr1*. Confocal microscopy analysis of mitochondrial membrane potential (ΔΨm) determined by TRME staining (middle panels) relative to MitoTracker Green (MTG; left panels) for the quantification of mitochondrial size in scrambled control (Scr) (top panels) vs. *Esr1*-KD (bottom panels) 3T3L1 adipocytes. Merged fluorescence presented in right panels.

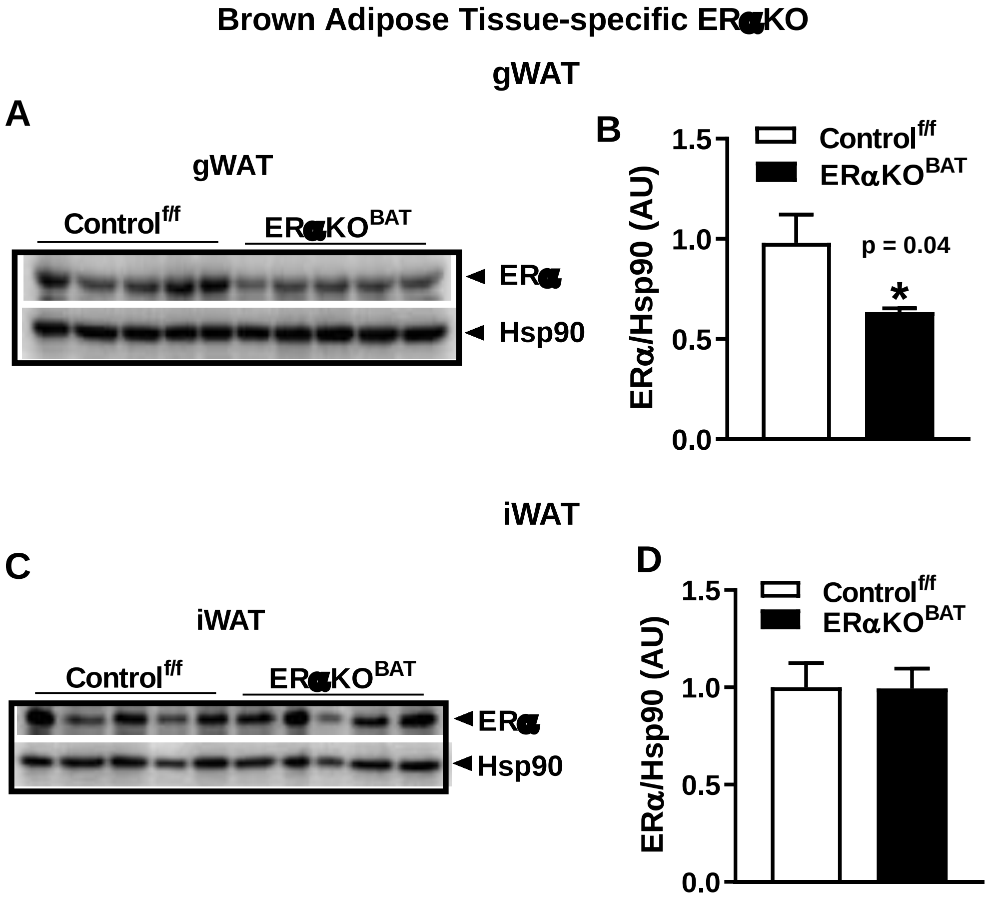

Fig. S6. ERα protein expression in gonadal and inguinal adipose tissue of BAT-specific ERα KO mice (ERαKO^{BAT}). Immunoblots and densitometry of ERα in (A-B) gonadal adipose and (C-D) inguinal fat from ERαKO^{BAT} vs. Control$^{f/f}$ (n=5/genotype). Values are means ± SEM. Differences detected by Student’s t-test, *$P < 0.05$ between genotype difference.

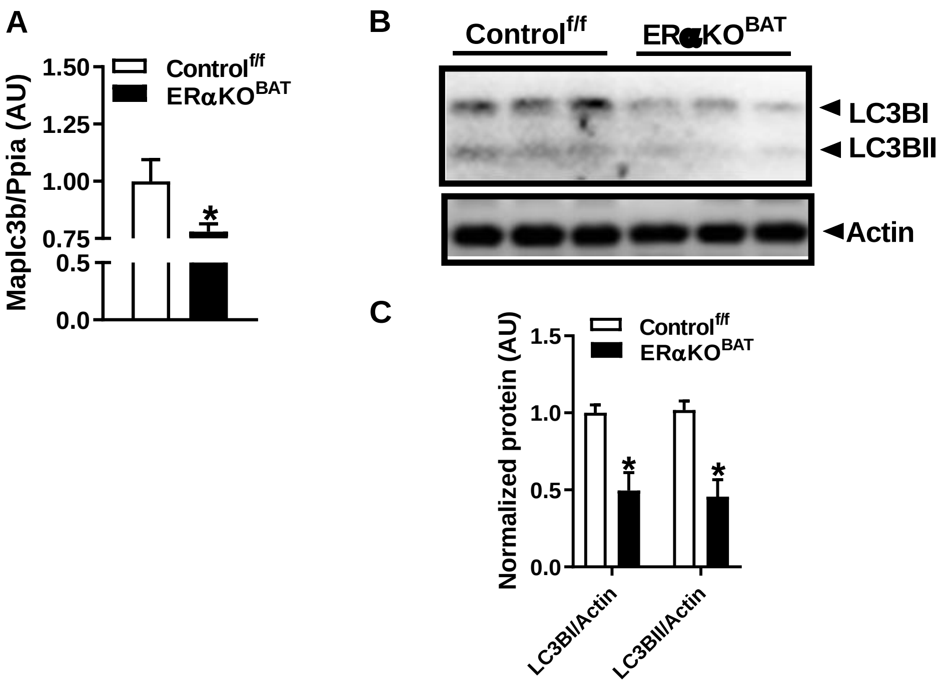

Fig. S7. LC3B expression is reduced in BAT from ERαKO^{BAT} mice. (A) Maplc3b (gene that encodes LC3B) expression in BAT from female ERαKO^{BAT} vs. Control f/f mice. (B-C) LC3BI/II protein levels in BAT of ERαKO^{BAT} vs. Control$^{f/f}$ mice. Values are means ± SEM. Differences detected by Student's t-test, *$P < 0.05$ between genotype difference.

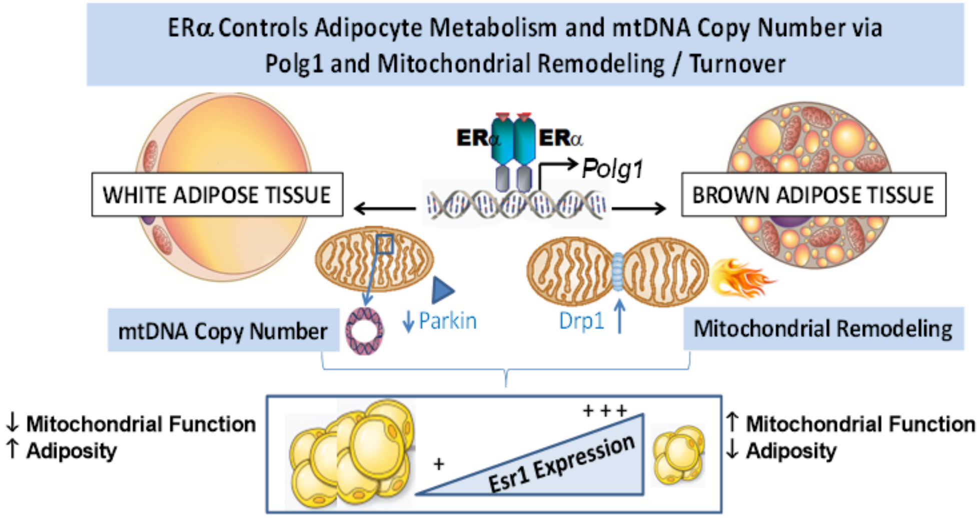

Fig. S8. Schematic overview of the mechanisms by which ERα controls adipocyte metabolism and adiposity. Collectively our findings show that the ERα target gene *Polg1* is reduced in expression in both white and brown adipocytes in the context of *Esr1* deletion. *Polg1,* via its role in the control of mtDNA replication, is intimately associated with fission-fusion-mitophagy dynamics. However the precise feedback from *Polg1* to the signaling nodes controlling mitochondrial remodeling and turnover appears to be adipocyte-specific. In white adipose tissue *Esr1* deletion reduced mtDNA copy number by heightened parkin-mediated mitophagic flux. In brown adipose tissue, *Esr1* deletion impaired mitochondrial fission via reduced Drp1 signaling. Impaired Drp1 signaling prevented fatty acid utilization and *Ucp1* induction during cold exposure. The alteration in mitochondrial fission signaling disrupted thermogenesis and glucose homeostasis. A loss of ERα from white or brown adipose tissue increased lipid deposition and adiposity. Our findings indicate that ERα combats obesity by controlling mitochondrial content and function in white and brown adipocytes.

Table S1. Genes significantly correlated with *ESR1/Esr1* and overlapping between the METSIM, MyoGlu, and HMDP studies. (Gene overlap reflected in Fig. 1K).

ACADSB
ACTN1
ANAPC5
AP3M1
API5
ARPC2
BAG3
BAG4
CAPN7
CDT1
CHPF2
COL5A2
DNAJA2
DPM1
ECHDC2
GNA12
GNAI1
GPR137B
LTBP2
NEK6
NLN
OSBPL1A
PCGF6
PCK1
PHF3
PLA2G15
RAB31
RAD17
RBM18
SCN1A
SENP2
SLC25A4
SLC31A2
SLC39A1
TERF2IP
TMSB10
VAMP2
VAMP3
VMA21
YKT6

Table S2. Genes associated with *Esr1* in gWAT from male and female C57BL6/J mice. (Overlap represented in Fig. 2A).

Gene Symbol	Female Bicor	Female P-Value	Male Bicor	Male P-Value
Syne1	0.46	1.18E-12	0.27	4.84E-05
Syne1	0.46	1.18E-12	0.27	4.84E-05
Mrps2	0.46	1.41E-12	0.15	2.57E-02
Grb10	0.45	3.96E-12	0.34	1.36E-07
Pdpk1	0.45	4.55E-12	0.31	1.23E-06
Sfswap	0.45	5.97E-12	0.32	5.85E-07
Tmem158	-0.44	3.28E-11	-0.21	1.28E-03
Ikbkb	0.43	4.55E-11	0.25	1.68E-04
Bnip2	-0.43	5.08E-11	-0.05	4.16E-01
Ermp1	-0.43	5.90E-11	0.01	8.90E-01
Lrr1	-0.43	7.45E-11	0.06	3.95E-01
Capn7	-0.43	7.81E-11	-0.11	9.11E-02
Akap8l	0.43	9.34E-11	0.22	7.46E-04
Il18rap	-0.43	9.37E-11	-0.31	2.35E-06
Luzp1	-0.43	1.03E-10	0.30	4.43E-06
Bag4	0.42	1.68E-10	0.35	4.66E-08
Clcc1	0.42	1.71E-10	0.23	3.53E-04
Gigyf1	0.42	2.11E-10	0.29	6.55E-06
Afp	-0.42	2.17E-10	-0.20	1.96E-03
Eral1	0.42	2.20E-10	0.27	3.43E-05
Mgme1	0.42	2.26E-10	0.17	8.11E-03
Car15	0.42	2.39E-10	0.28	1.74E-05
Myl12a	-0.42	2.76E-10	-0.08	2.54E-01
Ccdc47	0.42	2.89E-10	0.26	9.08E-05
Ppp6r2	0.42	3.14E-10	0.34	1.47E-07
Hoxa9	0.41	3.87E-10	0.21	1.66E-03
Zfp689	0.41	4.10E-10	0.29	6.27E-06
Slc9a8	0.41	4.67E-10	0.24	3.07E-04
Naa15	-0.41	4.72E-10	0.00	9.96E-01
Tcn2	0.41	4.88E-10	0.08	2.58E-01
Pacsin3	0.41	5.02E-10	0.33	3.51E-07
Psmf1	0.41	5.04E-10	0.34	1.40E-07
Naip5	-0.41	5.11E-10	-0.45	9.33E-13
Crebzf	0.41	5.69E-10	0.12	6.30E-02
Ppm1a	0.41	5.89E-10	0.25	1.39E-04
Foxm1	-0.41	6.22E-10	-0.06	3.53E-01
Med12	0.41	6.56E-10	0.21	1.11E-03
Runx2	-0.41	6.89E-10	0.22	9.91E-04
Tex16	0.41	7.62E-10	0.27	3.25E-05
4922502D21Rik	-0.41	8.13E-10	-0.18	5.32E-03
Foxm1	-0.41	8.35E-10	-0.41	1.84E-10
Atp1a2	0.41	8.87E-10	0.24	2.70E-04
Pcbd1	-0.41	9.08E-10	0.05	4.84E-01

Plagl2	0.41	9.09E-10	0.20	2.68E-03
Eef1e1	-0.40	9.88E-10	-0.35	4.19E-08
Rep15	0.40	1.01E-09	0.22	8.30E-04
Siva1	0.40	1.27E-09	0.23	4.09E-04
Chrd	0.40	1.28E-09	0.36	2.40E-08
Cdk7	-0.40	1.33E-09	-0.07	2.99E-01
Srsf9	-0.40	1.33E-09	-0.28	1.84E-05
Ptpn11	0.40	1.42E-09	0.35	3.82E-08
Mum1	0.40	1.49E-09	0.34	1.84E-07
Slc27a1	0.40	1.60E-09	0.15	2.47E-02
Nek6	-0.40	1.63E-09	-0.26	8.56E-05
Tm2d3	0.40	1.63E-09	0.25	1.52E-04
Txndc12	0.40	1.97E-09	0.06	3.75E-01
Atp5g3	0.40	2.31E-09	0.36	2.49E-08
Pdcd1	0.40	2.37E-09	0.25	1.79E-04
Syne2	0.40	2.39E-09	0.37	6.67E-09
Mrpl24	0.40	2.42E-09	0.23	5.02E-04
Polr2e	0.40	2.45E-09	0.02	7.45E-01
Retn	0.40	2.58E-09	0.23	5.19E-04
Fam3c	-0.40	2.62E-09	-0.08	2.15E-01
D10Wsu102e	-0.40	2.62E-09	-0.36	1.52E-08
Rnf6	-0.40	2.64E-09	0.09	1.84E-01
Ampd2	-0.40	2.67E-09	-0.01	8.49E-01
Eral1	0.40	2.67E-09	0.21	1.47E-03
Apbb3	0.39	2.74E-09	0.36	1.84E-08
Stat2	0.39	2.83E-09	0.24	2.49E-04
Eps15l1	0.39	2.87E-09	0.20	1.98E-03
Cpsf1	0.39	3.20E-09	0.16	1.65E-02
Tmem186	0.39	3.33E-09	0.28	1.67E-05
Dapk1	0.39	3.34E-09	0.14	3.05E-02
Tardbp	0.39	3.41E-09	0.31	1.89E-06
Ddrgk1	0.39	3.76E-09	0.27	4.55E-05
Skil	-0.39	3.80E-09	-0.10	1.20E-01
Rbbp8	-0.39	3.90E-09	0.01	8.52E-01
Car5b	0.39	3.92E-09	0.28	1.65E-05
Fbxw5	0.39	4.15E-09	0.17	1.15E-02
Akirin2	-0.39	4.19E-09	-0.31	1.95E-06
Bcr	0.39	4.25E-09	0.31	1.83E-06
Clk4	0.39	4.39E-09	0.21	1.56E-03
E130309D02Rik	-0.39	4.43E-09	-0.21	1.83E-03
Bad	-0.39	4.51E-09	-0.09	1.75E-01
Clpp	0.39	4.81E-09	0.29	8.98E-06
Pvrl3	-0.39	4.84E-09	-0.09	1.79E-01
Ccnh	-0.39	4.90E-09	-0.04	5.21E-01
Aplp2	0.39	4.93E-09	0.32	1.13E-06
Sh3kbp1	-0.39	4.95E-09	0.13	4.82E-02

Zbtb12	0.39	5.09E-09	0.29	1.18E-05
Ptpn21	0.39	5.37E-09	0.38	3.08E-09
Bsnd	0.39	5.43E-09	0.26	9.68E-05
Pcbp3	-0.39	5.52E-09	-0.11	1.03E-01
Gp1ba	0.39	5.58E-09	0.27	4.41E-05
Mettl7a1	0.39	5.62E-09	0.33	3.16E-07
Iqgap1	-0.39	5.64E-09	0.04	5.23E-01
Dnmt1	-0.39	5.88E-09	-0.15	2.05E-02
Zfp369	0.39	6.06E-09	0.33	2.22E-07
Vasn	-0.39	6.15E-09	0.10	1.44E-01
Gna15	-0.39	6.25E-09	-0.21	1.41E-03
Kifc2	0.39	6.26E-09	0.12	6.35E-02
Ganc	0.39	6.32E-09	0.29	1.10E-05
Dnah11	-0.39	6.36E-09	0.01	9.00E-01
Brd8	0.39	6.60E-09	0.25	1.02E-04
Mfn1	0.39	6.60E-09	0.30	5.19E-06
Eml5	0.39	6.80E-09	0.34	1.05E-07
Aldh2	0.39	6.88E-09	0.31	1.74E-06
Cuedc2	-0.39	6.93E-09	-0.02	7.47E-01
Fxyd1	0.39	6.96E-09	0.25	1.59E-04
Tab2	-0.39	6.96E-09	-0.15	2.09E-02
Cops4	0.39	7.11E-09	0.28	1.49E-05
Strn3	-0.39	7.28E-09	-0.08	2.57E-01
Mpst	0.39	7.30E-09	0.28	1.46E-05
Zfp503	0.38	7.61E-09	0.31	2.38E-06
Kpna4	-0.38	7.74E-09	0.07	3.14E-01
Il12b	-0.38	7.88E-09	-0.07	3.09E-01
Umod	-0.38	8.13E-09	-0.12	8.24E-02
Tmem2	-0.38	8.18E-09	-0.07	3.03E-01
Lamb3	-0.38	8.30E-09	-0.16	1.50E-02
Slain2	-0.38	8.39E-09	0.03	6.21E-01
Apeh	0.38	8.43E-09	0.16	1.38E-02
Cyhr1	0.38	8.44E-09	0.26	6.43E-05
Bre	0.38	8.54E-09	0.21	1.24E-03
Golga4	0.38	8.69E-09	0.23	4.07E-04
Stx17	0.38	9.12E-09	0.29	7.56E-06
Hes3	0.38	9.38E-09	0.23	5.50E-04
Phf13	0.38	9.52E-09	0.25	1.13E-04
Tfpt	0.38	9.72E-09	0.27	3.33E-05
Gmfb	-0.38	1.03E-08	0.06	3.79E-01
Acot12	0.38	1.04E-08	0.18	6.86E-03
1810055G02Rik	-0.38	1.05E-08	-0.29	9.99E-06
Fbxo45	0.38	1.07E-08	0.21	1.74E-03
Rfc5	-0.38	1.08E-08	-0.34	2.17E-07
Ptms	0.38	1.08E-08	0.35	4.47E-08
Nupl1	-0.38	1.09E-08	-0.17	9.04E-03

Tcf25	0.38	1.10E-08	0.20	2.29E-03
Atp5g1	0.38	1.15E-08	0.17	8.27E-03
Bsn	0.38	1.17E-08	0.19	3.85E-03
Wnt3a	0.38	1.24E-08	0.28	1.27E-05
Pvt1	0.38	1.27E-08	0.03	7.06E-01
Osbpl1a	0.38	1.28E-08	0.32	9.94E-07
Pcmtd1	0.38	1.31E-08	0.24	2.42E-04
Ros1	0.38	1.34E-08	0.27	5.05E-05
Olfr1509	0.38	1.41E-08	0.28	1.55E-05
Acadsb	0.38	1.44E-08	0.25	9.94E-05
Adamts5	-0.38	1.47E-08	0.11	1.10E-01
Rock1	-0.38	1.48E-08	0.21	1.45E-03
Hnrnpdl	0.38	1.54E-08	0.13	4.79E-02
Zfp518b	-0.38	1.55E-08	0.09	1.59E-01
Cntrob	0.38	1.57E-08	0.20	2.42E-03
Ltbp2	-0.38	1.70E-08	-0.35	5.82E-08
Tiam1	-0.38	1.76E-08	0.07	2.67E-01
Ppp2r5c	-0.38	1.77E-08	0.14	3.56E-02
Adcy6	0.38	1.81E-08	0.29	9.33E-06
Taf13	-0.37	1.93E-08	-0.28	1.87E-05
Lamb1	0.37	1.97E-08	0.21	1.65E-03
Gpr137b	-0.37	1.97E-08	-0.34	1.18E-07
Wdr4	0.37	2.02E-08	0.08	2.40E-01
Zbtb18	-0.37	2.03E-08	-0.18	6.46E-03
Huwe1	0.37	2.07E-08	0.19	4.64E-03
Anapc5	0.37	2.09E-08	0.28	1.29E-05
Prpf4b	0.37	2.14E-08	0.27	2.56E-05
Wdr12	-0.37	2.15E-08	-0.07	2.89E-01
2610524H06Rik	-0.37	2.19E-08	-0.20	2.41E-03
Rps6kb2	0.37	2.26E-08	0.19	4.03E-03
Gdf3	-0.37	2.33E-08	-0.23	5.40E-04
Pdgfra	0.37	2.33E-08	0.07	3.22E-01
Rac3	-0.37	2.36E-08	-0.11	8.37E-02
Fgf13	-0.37	2.38E-08	-0.21	1.55E-03
Rarg	0.37	2.42E-08	0.21	1.38E-03
Sbno1	0.37	2.58E-08	0.11	9.30E-02
Clint1	-0.37	2.59E-08	-0.29	6.55E-06
Crem	-0.37	2.60E-08	-0.06	3.83E-01
Rhbdd1	-0.37	2.65E-08	-0.33	5.07E-07
Clock	-0.37	2.72E-08	-0.13	4.65E-02
Vamp2	0.37	2.80E-08	0.29	9.01E-06
Morf4l2	-0.37	2.81E-08	-0.12	6.78E-02
Ddx54	-0.37	2.84E-08	-0.29	1.07E-05
Synj2bp	-0.37	2.88E-08	0.08	2.30E-01
Gna12	-0.37	2.92E-08	-0.37	5.68E-09
Skp2	-0.37	2.92E-08	-0.04	5.08E-01

Btbd1	-0.37	3.03E-08	-0.01	8.34E-01
Ctnnb1	-0.37	3.06E-08	0.06	3.89E-01
Myef2	-0.37	3.10E-08	-0.21	1.42E-03
Slc39a13	-0.37	3.15E-08	-0.20	2.07E-03
Dlx1	0.37	3.19E-08	0.14	3.94E-02
Oas1b	0.37	3.23E-08	0.23	3.75E-04
Arpc4	-0.37	3.26E-08	-0.24	2.35E-04
Csnk2b	0.37	3.26E-08	0.12	7.47E-02
Sparc	-0.37	3.27E-08	-0.11	9.46E-02
Lrrfip1	-0.37	3.30E-08	0.11	8.67E-02
Zfp354c	0.37	3.42E-08	0.29	1.07E-05
Usp21	0.37	3.55E-08	0.14	3.73E-02
Tbcel	-0.37	3.60E-08	0.11	1.08E-01
Gnai2	-0.37	3.68E-08	-0.18	7.05E-03
Safb	0.37	3.72E-08	0.22	6.67E-04
Tmem147	0.37	3.80E-08	0.13	4.66E-02
Fam193b	0.37	3.85E-08	0.23	3.81E-04
Rab10	-0.37	3.89E-08	0.01	8.68E-01
Terf2ip	0.37	3.93E-08	0.33	3.86E-07
Tomm7	0.37	4.04E-08	0.31	2.20E-06
Psmd11	0.37	4.23E-08	0.04	5.62E-01
Sh3gl2	0.37	4.33E-08	0.36	2.34E-08
Scarb1	0.37	4.35E-08	0.07	3.07E-01
Ndufs7	0.37	4.41E-08	0.24	2.59E-04
Wasl	-0.37	4.49E-08	0.37	1.31E-08
Cog4	0.37	4.54E-08	0.20	2.66E-03
Il31ra	0.37	4.56E-08	0.23	3.74E-04
Eral1	0.37	4.59E-08	0.15	2.36E-02
Fuca2	-0.37	4.76E-08	0.14	3.49E-02
Ngf	0.37	4.76E-08	0.33	3.65E-07
Mapk1	-0.36	4.80E-08	0.03	6.17E-01
Serf1	-0.36	4.83E-08	0.00	9.64E-01
Pmm1	0.36	4.84E-08	0.17	1.02E-02
Fcgrt	0.36	4.85E-08	0.15	1.93E-02
Cdipt	-0.36	4.91E-08	-0.16	1.32E-02
Vma21	-0.36	4.97E-08	-0.01	8.95E-01
Cadm1	-0.36	5.20E-08	-0.16	1.76E-02
Slc30a1	-0.36	5.35E-08	-0.31	1.37E-06
Nras	-0.36	5.45E-08	-0.21	1.52E-03
Nfatc2ip	-0.36	5.70E-08	0.16	1.71E-02
Cyp21a1	0.36	5.74E-08	0.22	7.82E-04
Nr2c2ap	-0.36	5.80E-08	-0.27	4.79E-05
Pmm1	0.36	5.83E-08	0.14	3.73E-02
Mettl7a2	0.36	5.88E-08	0.30	3.08E-06
Snap47	-0.36	5.89E-08	0.00	9.47E-01
S100b	-0.36	6.09E-08	0.17	8.70E-03

Rnf146	0.36	6.20E-08	0.31	1.40E-06
Eif2ak2	0.36	6.25E-08	0.30	3.41E-06
Cd70	0.36	6.33E-08	0.25	1.47E-04
Rusc1	0.36	6.34E-08	0.08	2.56E-01
Dguok	0.36	6.44E-08	0.24	2.19E-04
Ywhaz	-0.36	6.48E-08	-0.19	3.73E-03
Sf3b4	-0.36	6.49E-08	-0.34	1.67E-07
Lgals12	0.36	6.69E-08	0.28	1.24E-05
Zfp768	0.36	6.84E-08	0.31	1.58E-06
Igf2os	0.36	6.84E-08	0.31	2.68E-06
Hif1a	-0.36	6.86E-08	0.16	1.40E-02
Agpat3	0.36	6.95E-08	0.22	6.34E-04
Kpna3	-0.36	7.19E-08	-0.24	1.87E-04
Polr2l	0.36	7.26E-08	0.22	7.40E-04
Cp	0.36	7.39E-08	0.34	1.47E-07
Cnot4	-0.36	7.41E-08	0.32	7.34E-07
Denr	-0.36	7.56E-08	-0.03	6.11E-01
Sart3	0.36	7.66E-08	0.26	6.45E-05
Hells	-0.36	7.75E-08	-0.38	2.91E-09
Cdo1	0.36	7.78E-08	0.22	8.83E-04
Gpx3	0.36	7.91E-08	0.19	3.94E-03
Clk4	0.36	8.04E-08	0.21	1.71E-03
Dtnbp1	0.36	8.20E-08	0.05	4.73E-01
Hhatl	0.36	8.21E-08	0.32	1.00E-06
Rorc	0.36	8.26E-08	0.23	6.03E-04
Slc5a9	0.36	8.45E-08	0.44	4.10E-12
Galnt3	-0.36	8.48E-08	0.12	7.31E-02
Ssr1	-0.36	8.61E-08	-0.04	5.05E-01
Spag7	0.36	8.62E-08	0.26	6.64E-05
Mut	0.36	8.69E-08	0.25	1.01E-04
Pa2g4	0.36	8.70E-08	0.24	2.33E-04
Mettl7a1	0.36	8.76E-08	0.33	4.21E-07
Clec4d	-0.36	8.79E-08	-0.27	3.27E-05
Ufm1	-0.36	8.79E-08	-0.09	1.85E-01
Prl8a9	0.36	9.01E-08	0.19	4.48E-03
Klhdc3	-0.36	9.07E-08	0.04	5.55E-01
Zdhhc2	-0.36	9.10E-08	-0.02	7.70E-01
Odf2	0.36	9.26E-08	0.30	4.36E-06
Rnmt	-0.36	9.40E-08	-0.35	4.56E-08
Nek6	-0.36	9.42E-08	-0.32	9.24E-07
Trf	0.36	9.54E-08	0.20	2.46E-03
Nbr1	0.36	9.86E-08	0.21	1.35E-03
Rab6a	-0.36	1.01E-07	-0.26	5.18E-05
Nacc2	-0.36	1.04E-07	0.17	1.17E-02
Elmod3	0.36	1.05E-07	0.22	9.49E-04
Commd9	-0.36	1.06E-07	-0.10	1.45E-01

Stat5b	0.36	1.06E-07	-0.01	8.26E-01
Rbfox2	0.36	1.08E-07	0.23	5.75E-04
Ralgps2	-0.36	1.12E-07	0.27	4.13E-05
Rcl1	0.36	1.13E-07	0.16	1.58E-02
Pbld1	0.36	1.15E-07	0.17	1.05E-02
Slc25a44	0.35	1.18E-07	0.25	1.86E-04
Slc1a3	0.35	1.19E-07	0.25	1.43E-04
Neat1	0.35	1.20E-07	0.19	4.93E-03
Gusb	-0.35	1.21E-07	-0.27	4.78E-05
Kif17	0.35	1.23E-07	0.30	4.37E-06
Sema4f	0.35	1.24E-07	0.23	5.81E-04
Ppp1r18	-0.35	1.30E-07	-0.30	4.01E-06
Lama4	0.35	1.32E-07	0.33	2.29E-07
Alkbh4	0.35	1.33E-07	0.18	6.53E-03
Gid4	0.35	1.39E-07	0.18	7.51E-03
Tnfrsf21	-0.35	1.40E-07	-0.19	3.17E-03
Olfr49	0.35	1.40E-07	0.27	3.51E-05
Actn1	-0.35	1.40E-07	-0.19	4.06E-03
Rbm18	-0.35	1.41E-07	-0.21	1.27E-03
0610012G03Rik	0.35	1.42E-07	0.09	1.78E-01
Luc7l	0.35	1.42E-07	0.31	1.76E-06
Set	-0.35	1.43E-07	-0.27	3.41E-05
Atf6	-0.35	1.43E-07	-0.32	9.35E-07
Tfpi2	-0.35	1.43E-07	-0.19	4.11E-03
Hp1bp3	0.35	1.44E-07	0.23	5.38E-04
1700123O20Rik	-0.35	1.50E-07	-0.25	1.12E-04
Cadm1	-0.35	1.51E-07	-0.19	4.97E-03
Urm1	-0.35	1.51E-07	-0.15	2.01E-02
Svs5	0.35	1.55E-07	0.22	1.04E-03
Ddr1	-0.35	1.56E-07	0.10	1.53E-01
Hibch	0.35	1.57E-07	0.25	1.28E-04
Kpna1	-0.35	1.58E-07	-0.12	7.25E-02
Tspan6	-0.35	1.59E-07	0.01	8.68E-01
Gtf2a1l	0.35	1.62E-07	0.28	1.36E-05
Grb14	-0.35	1.63E-07	-0.14	3.79E-02
Vps72	0.35	1.63E-07	0.19	3.30E-03
Sema3a	0.35	1.64E-07	0.33	2.25E-07
Pcx	0.35	1.65E-07	0.11	9.62E-02
Scaf4	0.35	1.66E-07	0.33	4.99E-07
Rcbtb1	0.35	1.67E-07	0.25	1.24E-04
Mapre2	-0.35	1.68E-07	-0.09	1.62E-01
Kpna1	-0.35	1.68E-07	-0.15	2.15E-02
Cabp2	0.35	1.69E-07	0.30	4.72E-06
Trove2	0.35	1.70E-07	0.16	1.77E-02
Cnbd2	0.35	1.72E-07	0.33	4.36E-07
Derl1	0.35	1.75E-07	0.21	1.21E-03

Chek1	-0.35	1.75E-07	-0.01	9.23E-01
Rtn4r	0.35	1.79E-07	0.22	7.55E-04
Ubp1	0.35	1.79E-07	0.06	4.04E-01
Timm50	0.35	1.82E-07	0.24	2.18E-04
Fbxo42	-0.35	1.85E-07	-0.34	1.70E-07
0610010K14Rik	0.35	1.90E-07	0.13	5.28E-02
Mrpl9	0.35	1.94E-07	0.21	1.18E-03
Pdcd10	-0.35	1.94E-07	-0.08	2.34E-01
Abcc5	0.35	1.96E-07	0.10	1.34E-01
Polrmt	0.35	1.99E-07	0.15	1.93E-02
Sp1	0.35	2.04E-07	0.18	7.10E-03
Nkx1-2	0.35	2.05E-07	0.30	3.09E-06
Bptf	0.35	2.08E-07	0.33	3.43E-07
Rps6kc1	-0.35	2.14E-07	-0.31	1.73E-06
Gpr3	-0.35	2.16E-07	-0.26	9.62E-05
Ociad1	0.35	2.16E-07	0.18	6.55E-03
Arf6	-0.35	2.18E-07	-0.26	6.46E-05
Ctnnal1	-0.35	2.18E-07	0.02	7.97E-01
Add3	0.35	2.19E-07	0.24	3.43E-04
Bub1	-0.35	2.20E-07	-0.01	8.80E-01
Twf2	-0.35	2.20E-07	-0.28	1.54E-05
Rhbdd2	0.35	2.26E-07	0.41	1.78E-10
Lrrc16a	-0.35	2.26E-07	-0.02	7.73E-01
4930549C01Rik	0.35	2.30E-07	0.31	1.49E-06
Prdm1	-0.35	2.37E-07	-0.35	5.02E-08
Ankib1	-0.35	2.39E-07	-0.13	4.83E-02
Pam	-0.35	2.42E-07	-0.20	3.08E-03
Xbp1	0.35	2.44E-07	0.16	1.31E-02
Mrps26	0.35	2.46E-07	0.15	2.05E-02
Il21r	0.35	2.48E-07	0.28	2.11E-05
Scarb1	0.35	2.50E-07	0.05	4.83E-01
Ndst3	0.35	2.51E-07	0.15	2.08E-02
Gdap1	0.35	2.54E-07	0.25	1.27E-04
Tecr	0.35	2.55E-07	0.20	2.09E-03
Rhoc	-0.35	2.58E-07	-0.18	5.35E-03
Slc25a39	0.35	2.61E-07	0.12	6.82E-02
Car6	-0.35	2.62E-07	-0.20	1.91E-03
Fgf13	-0.35	2.65E-07	-0.22	7.06E-04
Safb	0.35	2.68E-07	0.21	1.52E-03
Zcchc14	0.35	2.72E-07	0.41	1.08E-10
Slc39a1	-0.34	2.75E-07	-0.29	9.54E-06
Ptms	0.34	2.77E-07	0.32	9.72E-07
Mlf2	0.34	2.77E-07	0.19	4.93E-03
Asb6	-0.34	2.81E-07	-0.41	8.55E-11
Ccdc96	0.34	2.88E-07	0.38	3.34E-09
Oma1	0.34	2.89E-07	0.11	9.63E-02

Ptpn12	-0.34	2.89E-07	-0.27	2.55E-05
E4f1	0.34	2.90E-07	0.23	5.25E-04
Clec3b	0.34	2.90E-07	0.18	6.08E-03
Pbx3	-0.34	2.95E-07	-0.25	1.24E-04
Gins1	-0.34	2.98E-07	-0.32	5.46E-07
Ripk1	-0.34	3.01E-07	-0.08	2.23E-01
Zfp52	-0.34	3.08E-07	-0.22	1.01E-03
Birc6	-0.34	3.08E-07	0.21	1.28E-03
Tmem134	0.34	3.09E-07	0.20	2.41E-03
Bmpr1a	-0.34	3.09E-07	0.04	5.43E-01
Ankef1	0.34	3.10E-07	0.36	3.10E-08
Nfe2l2	-0.34	3.10E-07	-0.30	4.10E-06
Nudcd2	-0.34	3.10E-07	-0.17	8.59E-03
Topors	0.34	3.11E-07	0.21	1.42E-03
Zfyve21	0.34	3.11E-07	0.28	1.59E-05
Ddx39b	0.34	3.14E-07	0.22	1.06E-03
Wrnip1	0.34	3.14E-07	0.30	4.71E-06
Klhl42	-0.34	3.18E-07	-0.11	9.02E-02
Tpst1	0.34	3.19E-07	0.17	1.11E-02
Tyr	0.34	3.21E-07	0.28	2.09E-05
BC024139	0.34	3.22E-07	0.15	2.07E-02
Mark1	-0.34	3.33E-07	0.02	7.47E-01
Orc3	0.34	3.38E-07	0.24	2.65E-04
Hsd17b1	0.34	3.38E-07	0.29	6.60E-06
Trpt1	0.34	3.38E-07	0.20	2.94E-03
Lrp1b	0.34	3.41E-07	0.18	6.08E-03
Mif	0.34	3.43E-07	0.11	8.64E-02
Hibch	0.34	3.43E-07	0.23	3.47E-04
Olah	-0.34	3.46E-07	0.16	1.70E-02
Cfd	0.34	3.47E-07	0.26	5.29E-05
Gdap1	-0.34	3.49E-07	-0.13	4.41E-02
Hoxd4	0.34	3.50E-07	0.26	9.01E-05
Tubb3	-0.34	3.55E-07	-0.18	5.75E-03
Ptprs	-0.34	3.57E-07	-0.13	5.18E-02
Srek1	0.34	3.60E-07	0.27	2.84E-05
Brox	0.34	3.62E-07	0.14	3.34E-02
Hnrnph3	0.34	3.63E-07	0.30	3.53E-06
Zswim1	-0.34	3.66E-07	-0.24	2.25E-04
Smim11	0.34	3.67E-07	0.26	5.37E-05
Amn	-0.34	3.71E-07	-0.19	4.92E-03
Orc4	-0.34	3.79E-07	0.22	6.94E-04
AI462493	0.34	3.81E-07	0.26	5.66E-05
Fam129b	-0.34	3.84E-07	-0.24	3.44E-04
Pter	-0.34	3.84E-07	0.03	6.75E-01
Cd247	0.34	3.88E-07	0.19	4.33E-03
Psmd4	0.34	3.91E-07	0.19	3.93E-03

Agl	0.34	3.94E-07	0.00	9.91E-01
Cnot8	0.34	3.97E-07	0.16	1.27E-02
Sparc	-0.34	3.97E-07	-0.18	7.34E-03
Frat1	0.34	3.98E-07	0.15	2.15E-02
Ccnl2	0.34	3.98E-07	0.27	3.12E-05
Rabgef1	-0.34	4.01E-07	0.04	5.11E-01
Mtmr10	-0.34	4.04E-07	-0.28	1.46E-05
Cnot3	0.34	4.06E-07	0.14	3.54E-02
Dpp3	-0.34	4.07E-07	-0.30	5.23E-06
Mbd6	0.34	4.07E-07	0.16	1.41E-02
Farp2	0.34	4.09E-07	0.11	9.20E-02
Alpk2	-0.34	4.09E-07	-0.16	1.63E-02
Ighmbp2	0.34	4.10E-07	0.25	1.25E-04
Dock8	-0.34	4.22E-07	0.07	3.23E-01
Bre	0.34	4.28E-07	0.17	1.02E-02
Pcdhb8	0.34	4.29E-07	0.35	8.82E-08
Amfr	0.34	4.33E-07	0.20	2.83E-03
Dopey2	-0.34	4.33E-07	0.18	6.21E-03
Mlxipl	0.34	4.39E-07	0.22	6.99E-04
Bub3	-0.34	4.45E-07	-0.12	6.10E-02
Dgkg	0.34	4.46E-07	0.35	4.83E-08
Sqrdl	0.34	4.55E-07	0.26	7.60E-05
Slc35f6	-0.34	4.59E-07	-0.32	9.89E-07
Hsd17b10	0.34	4.69E-07	0.29	7.90E-06
Ccnl2	0.34	4.69E-07	0.25	1.08E-04
Nsfl1c	0.34	4.74E-07	0.22	7.76E-04
Pi15	0.34	4.75E-07	0.20	2.11E-03
Trp53inp2	-0.34	4.75E-07	-0.17	8.84E-03
Uba7	0.34	4.76E-07	0.18	6.21E-03
Taf4a	0.34	4.77E-07	0.12	7.52E-02
Fam83g	0.34	4.84E-07	0.17	9.12E-03
Ppil2	0.34	4.85E-07	0.10	1.26E-01
Ankrd24	0.34	4.89E-07	0.22	1.03E-03
Il2	0.34	4.99E-07	0.16	1.85E-02
Ndufa6	0.34	5.02E-07	0.28	1.87E-05
Npr3	-0.34	5.03E-07	0.25	1.08E-04
Txn2	0.34	5.09E-07	0.26	7.84E-05
Cebpa	0.34	5.11E-07	0.25	1.81E-04
Hils1	0.34	5.13E-07	0.15	2.65E-02
Hsd17b10	0.34	5.14E-07	0.26	6.69E-05
Plekhh1	0.34	5.20E-07	0.33	2.97E-07
Phf2	0.34	5.25E-07	0.29	1.20E-05
Terf2	0.34	5.26E-07	0.31	2.20E-06
Rrp9	-0.34	5.26E-07	-0.40	5.16E-10
Znrf1	0.34	5.27E-07	0.20	2.44E-03
Cdon	0.34	5.28E-07	0.28	1.75E-05

Mos	0.34	5.28E-07	0.31	1.24E-06
Rell1	-0.34	5.29E-07	-0.25	1.57E-04
Ppp1r1a	0.34	5.30E-07	0.17	1.15E-02
Ttc28	-0.34	5.32E-07	0.02	7.19E-01
Morc1	-0.34	5.33E-07	-0.13	4.46E-02
Insig2	0.34	5.37E-07	0.24	2.03E-04
Vti1b	0.34	5.41E-07	0.23	3.68E-04
Prkar2a	-0.34	5.41E-07	-0.22	7.16E-04
Rtkn2	0.34	5.44E-07	0.24	3.27E-04
Pex5	0.34	5.44E-07	0.16	1.78E-02
Prkcg	0.34	5.47E-07	0.26	5.79E-05
Prps2	-0.34	5.52E-07	-0.06	3.94E-01
Ankrd6	0.34	5.57E-07	0.29	1.00E-05
Olr1	-0.34	5.59E-07	-0.28	1.94E-05
Kcnn4	-0.34	5.60E-07	-0.26	8.08E-05
Msantd4	-0.34	5.61E-07	-0.31	1.73E-06
Ginm1	0.34	5.64E-07	0.28	2.46E-05
Srp14	-0.34	5.65E-07	-0.19	4.23E-03
Xdh	0.34	5.74E-07	0.25	1.75E-04
Ykt6	-0.34	5.77E-07	0.02	7.11E-01
Lsm10	0.34	5.83E-07	0.15	2.63E-02
Rbms2	0.34	5.84E-07	0.20	1.87E-03
Prss39	0.34	5.85E-07	0.30	4.09E-06
Fam102a	-0.34	5.91E-07	0.05	4.97E-01
Kctd5	-0.34	6.04E-07	-0.22	8.35E-04
Cenpq	-0.34	6.05E-07	-0.35	5.73E-08
Ercc6l	-0.34	6.12E-07	-0.31	1.84E-06
Tcerg1	-0.34	6.20E-07	0.13	4.77E-02
St6galnac5	0.34	6.27E-07	0.27	2.85E-05
Uqcr10	0.34	6.28E-07	0.31	1.26E-06
Snrpe	-0.33	6.34E-07	-0.30	2.74E-06
Lbh	-0.33	6.35E-07	0.11	9.53E-02
Uba5	-0.33	6.35E-07	-0.07	3.19E-01
Mfap1a	0.33	6.40E-07	0.21	1.16E-03
Pex5	0.33	6.48E-07	0.13	4.69E-02
Tpd52	-0.33	6.49E-07	-0.22	1.06E-03
Dlgap5	-0.33	6.52E-07	-0.35	7.33E-08
Mib2	0.33	6.60E-07	0.25	1.25E-04
Pde3a	0.33	6.79E-07	0.22	9.80E-04
Leng8	0.33	6.85E-07	0.12	6.67E-02
Dck	-0.33	6.85E-07	0.03	6.12E-01
Mphosph8	-0.33	7.01E-07	-0.08	2.19E-01
Kmt2e	0.33	7.02E-07	0.27	2.74E-05
Tmod3	-0.33	7.13E-07	0.14	3.02E-02
Scarb1	0.33	7.14E-07	0.03	6.82E-01
Tank	-0.33	7.16E-07	-0.29	9.64E-06

Asprv1	0.33	7.20E-07	0.34	2.01E-07
Iqsec1	-0.33	7.26E-07	0.10	1.24E-01
Adra2c	0.33	7.38E-07	0.26	5.73E-05
Bmpr1a	-0.33	7.38E-07	-0.04	5.67E-01
Spta1	-0.33	7.43E-07	-0.04	5.62E-01
Pnpla2	0.33	7.48E-07	0.20	1.88E-03
Nr1h4	0.33	7.50E-07	0.18	7.39E-03
Map1lc3b	0.33	7.51E-07	0.18	7.77E-03
Ddx42	0.33	7.63E-07	0.21	1.61E-03
Ccne2	-0.33	7.70E-07	-0.32	7.22E-07
Zdhhc14	-0.33	7.70E-07	-0.27	2.68E-05
Junb	-0.33	7.76E-07	-0.23	3.71E-04
Id1	0.33	7.78E-07	0.33	3.19E-07
Itpk1	-0.33	7.82E-07	-0.17	9.15E-03
Apba3	0.33	7.90E-07	0.11	8.95E-02
Opn3	0.33	7.90E-07	0.20	2.85E-03
Creb3	-0.33	7.96E-07	-0.22	7.99E-04
Lmf1	0.33	8.00E-07	0.19	4.36E-03
Tpx2	-0.33	8.13E-07	-0.07	2.62E-01
Birc3	-0.33	8.22E-07	-0.26	6.04E-05
Casr	0.33	8.28E-07	0.19	5.05E-03
Gabarapl1	0.33	8.33E-07	0.14	3.76E-02
Srrm1	0.33	8.36E-07	0.38	2.10E-09
Ceacam12	0.33	8.36E-07	0.19	3.78E-03
Mbd2	0.33	8.37E-07	0.23	3.60E-04
Kcna1	0.33	8.39E-07	0.26	8.84E-05
Acin1	0.33	8.44E-07	0.32	1.15E-06
Poldip3	-0.33	8.47E-07	-0.17	8.14E-03
Stoml2	0.33	8.47E-07	0.27	2.69E-05
Smdt1	0.33	8.49E-07	0.04	5.97E-01
Trip12	-0.33	8.52E-07	0.17	9.51E-03
Col18a1	-0.33	8.52E-07	0.08	2.24E-01
Hrh1	0.33	8.56E-07	0.09	1.73E-01
Capza1	-0.33	8.61E-07	-0.30	3.45E-06
Mtpn	-0.33	8.64E-07	0.04	5.62E-01
Pxk	0.33	8.67E-07	0.10	1.35E-01
Nlk	-0.33	8.67E-07	-0.08	2.53E-01
Sra1	0.33	8.80E-07	0.24	2.20E-04
Sema4a	0.33	8.91E-07	0.25	1.26E-04
Cog1	0.33	8.99E-07	0.05	4.51E-01
Eri3	0.33	9.02E-07	0.15	2.21E-02
Nras	-0.33	9.17E-07	-0.32	1.02E-06
Six4	0.33	9.17E-07	0.20	2.48E-03
Aip	0.33	9.33E-07	0.08	2.12E-01
Spon1	0.33	9.36E-07	0.21	1.59E-03
Nudt6	0.33	9.48E-07	0.17	1.13E-02

Cdkn1c	0.33	9.61E-07	0.24	3.17E-04
Bsg	0.33	9.62E-07	0.31	1.63E-06
Wnt7b	-0.33	9.64E-07	-0.09	1.62E-01
Ndufs3	0.33	9.78E-07	0.31	2.14E-06
Fam210b	0.33	9.88E-07	0.34	1.04E-07
Rock1	-0.33	1.00E-06	0.04	5.51E-01
Tmem185b	-0.33	1.01E-06	-0.33	3.45E-07
Pcdh10	0.33	1.01E-06	0.16	1.79E-02
Eftud2	-0.33	1.01E-06	-0.05	4.73E-01
Mlst8	-0.33	1.02E-06	-0.03	6.40E-01
Sp4	0.33	1.03E-06	0.25	1.36E-04
Hmces	0.33	1.05E-06	0.30	4.10E-06
Fscn1	-0.33	1.06E-06	0.22	8.83E-04
Strn3	-0.33	1.06E-06	-0.12	7.43E-02
Prmt6	-0.33	1.07E-06	-0.34	1.08E-07
Poldip3	-0.33	1.07E-06	-0.29	1.05E-05
Trpm7	0.33	1.08E-06	0.20	2.87E-03
Six4	0.33	1.08E-06	0.13	4.20E-02
Uggt2	0.33	1.09E-06	0.17	1.19E-02
Rasa3	0.33	1.09E-06	0.10	1.27E-01
Crebzf	0.33	1.09E-06	0.08	2.34E-01
Unc119b	0.33	1.10E-06	0.25	1.65E-04
Syne1	0.33	1.12E-06	0.24	2.98E-04
Syne1	0.33	1.12E-06	0.24	2.98E-04
Taldo1	0.33	1.12E-06	0.16	1.85E-02
Evi5	0.33	1.13E-06	0.28	2.11E-05
Fabp4	0.33	1.13E-06	0.16	1.37E-02
Yipf5	-0.33	1.13E-06	-0.27	2.67E-05
Lrrc18	0.33	1.15E-06	0.30	4.76E-06
Ncor1	0.33	1.16E-06	0.23	3.75E-04
Nono	-0.33	1.16E-06	-0.21	1.15E-03
Glrb	-0.33	1.17E-06	-0.16	1.76E-02
Thap7	-0.33	1.18E-06	-0.11	1.07E-01
Prkag2	0.33	1.19E-06	0.19	3.50E-03
Api5	-0.33	1.20E-06	-0.11	1.07E-01
Ell	0.33	1.20E-06	-0.05	4.10E-01
Dusp9	-0.33	1.21E-06	-0.19	3.70E-03
Cox8a	0.33	1.23E-06	0.25	1.07E-04
Mapk14	0.33	1.24E-06	-0.07	2.74E-01
Slc25a4	0.33	1.25E-06	0.36	2.89E-08
Por	0.33	1.25E-06	0.20	1.88E-03
Ccdc101	0.33	1.25E-06	0.23	4.18E-04
Stam2	-0.33	1.27E-06	-0.03	6.88E-01
Rab18	0.33	1.28E-06	0.20	2.08E-03
Abhd5	0.33	1.28E-06	0.10	1.15E-01
Calm1	-0.33	1.29E-06	-0.15	2.82E-02

Mtch2	0.33	1.30E-06	0.24	2.39E-04
Rae1	0.33	1.31E-06	0.18	5.14E-03
Ache	0.33	1.32E-06	0.21	1.36E-03
Spata6	-0.33	1.32E-06	0.04	5.52E-01
Fignl1	-0.33	1.34E-06	-0.30	4.97E-06
Vmn1r58	0.33	1.35E-06	0.28	1.95E-05
Rad50	-0.33	1.35E-06	-0.04	5.67E-01
Parp2	0.33	1.35E-06	-0.04	5.23E-01
Tsku	-0.33	1.35E-06	-0.38	2.99E-09
Skil	-0.33	1.37E-06	-0.24	2.50E-04
Canx	-0.33	1.38E-06	-0.20	2.14E-03
Isl1	0.33	1.39E-06	0.15	2.12E-02
Apc	-0.33	1.39E-06	0.26	6.74E-05
Tle4	-0.32	1.41E-06	-0.22	9.16E-04
Slc2a3	0.32	1.41E-06	0.19	3.76E-03
S100a3	-0.32	1.41E-06	-0.21	1.46E-03
Dsc2	-0.32	1.41E-06	0.01	8.65E-01
Polr3g	-0.32	1.41E-06	-0.27	3.09E-05
Pkhd1	-0.32	1.42E-06	-0.05	4.54E-01
Polr1c	0.32	1.42E-06	0.11	8.64E-02
Ube4b	0.32	1.42E-06	0.13	4.77E-02
Ces4a	0.32	1.43E-06	0.21	1.46E-03
Vav3	-0.32	1.44E-06	-0.22	9.38E-04
Rbbp6	0.32	1.44E-06	0.29	9.83E-06
Srgap1	0.32	1.45E-06	0.23	3.91E-04
Fut4	0.32	1.46E-06	0.30	5.52E-06
Cggbp1	-0.32	1.47E-06	-0.18	6.63E-03
Zfp574	0.32	1.48E-06	0.26	7.37E-05
S100a8	-0.32	1.48E-06	-0.22	7.12E-04
Grhpr	0.32	1.49E-06	0.29	1.10E-05
Lifr	-0.32	1.49E-06	0.12	7.90E-02
Iqgap1	-0.32	1.51E-06	-0.18	5.12E-03
Uck2	0.32	1.51E-06	0.22	6.23E-04
Uck2	0.32	1.51E-06	0.22	6.23E-04
Minpp1	-0.32	1.52E-06	-0.27	4.27E-05
D4Wsu53e	0.32	1.52E-06	0.13	5.00E-02
Endou	-0.32	1.52E-06	0.07	3.23E-01
Sp5	0.32	1.52E-06	0.28	1.61E-05
Zadh2	0.32	1.52E-06	0.23	5.19E-04
Palld	-0.32	1.53E-06	-0.21	1.51E-03
Zfp418	-0.32	1.53E-06	-0.19	4.78E-03
Hspa2	-0.32	1.53E-06	0.21	1.15E-03
Rad51b	0.32	1.54E-06	0.16	1.30E-02
Zfp92	0.32	1.54E-06	0.33	2.72E-07
4921530L21Rik	-0.32	1.58E-06	-0.19	4.18E-03
Cadm1	-0.32	1.58E-06	-0.19	4.58E-03

Brat1	0.32	1.59E-06	0.32	7.78E-07
Pex6	0.32	1.63E-06	0.16	1.31E-02
Pfdn5	0.32	1.63E-06	0.24	2.38E-04
Etv1	-0.32	1.64E-06	-0.11	8.49E-02
Prkg2	0.32	1.64E-06	0.36	1.66E-08
Cav1	-0.32	1.64E-06	0.02	7.61E-01
Dgat1	0.32	1.69E-06	0.08	2.05E-01
Fbxl15	-0.32	1.70E-06	-0.12	6.00E-02
Il1rapl2	-0.32	1.70E-06	0.10	1.21E-01
Zfp148	-0.32	1.70E-06	0.25	1.55E-04
Ccr7	-0.32	1.71E-06	-0.22	7.49E-04
Bace1	-0.32	1.71E-06	-0.09	1.99E-01
Sec63	-0.32	1.72E-06	0.18	5.47E-03
Dnajc12	-0.32	1.72E-06	-0.23	5.39E-04
Aktip	-0.32	1.73E-06	0.18	5.54E-03
Atg12	-0.32	1.74E-06	0.08	2.03E-01
Cyb5r4	-0.32	1.74E-06	-0.38	4.68E-09
Wif1	-0.32	1.74E-06	-0.10	1.45E-01
Nr3c1	0.32	1.76E-06	0.12	7.81E-02
Nme3	0.32	1.77E-06	0.31	2.55E-06
Brk1	-0.32	1.80E-06	-0.29	7.10E-06
Rab34	0.32	1.81E-06	0.17	9.84E-03
Sytl1	0.32	1.82E-06	0.20	2.16E-03
Chuk	0.32	1.82E-06	0.22	9.02E-04
Igf1r	0.32	1.83E-06	0.31	1.29E-06
Mterfd2	0.32	1.83E-06	0.26	5.13E-05
Rab38	-0.32	1.86E-06	-0.24	3.37E-04
Kcnab2	-0.32	1.87E-06	-0.17	8.51E-03
Bbs2	0.32	1.87E-06	0.30	3.02E-06
Spp1	-0.32	1.88E-06	-0.25	1.50E-04
Cebpg	0.32	1.88E-06	0.24	2.85E-04
Srek1	0.32	1.89E-06	0.22	6.25E-04
Actn1	-0.32	1.89E-06	-0.29	7.12E-06
Kras	-0.32	1.90E-06	-0.14	3.00E-02
Sel1l	-0.32	1.91E-06	0.09	1.63E-01
Ppp3ca	-0.32	1.92E-06	-0.29	1.05E-05
Rqcd1	-0.32	1.93E-06	-0.31	1.38E-06
Rab27b	-0.32	1.96E-06	0.06	3.60E-01
Uhrf1	-0.32	1.97E-06	-0.25	1.33E-04
Lingo1	0.32	1.99E-06	0.24	2.23E-04
Cept1	0.32	2.00E-06	0.07	3.12E-01
Atg3	0.32	2.01E-06	0.18	5.81E-03
Gla	-0.32	2.01E-06	-0.22	6.52E-04

Table S3. Mitochondrial-associated genes differentially expressed in gWAT from female FERKO versus Control$^{f/f}$ mice. (Functional annotation in Fig. 2D).

Gene Name	**Transcription Factor**
1700123O20Rik	*FOXN4*
Abce1	*ZF5*
Acadsb	*BEN*
Acp6	*ELK-1*
Aldh2	*TEL1*
Atp5c1	*GABPa*
Atp5g3	*E2F-3*
Car5b	*PEA3*
Clpp	*GABP*
Cox8a	*E2F-4*
Dguok	*SP100*
Eci2	*E2F*
Fen1	
Gstp1	
Hibch	
Hsd17b10	
Iars2	
Mfn1	
Mpst	
Mrpl24	
Mrpl42	
Mrpl9	
Mrps21	
Mrps34	
Mrps35	
Mrps5	
Ndufa6	
Ndufb9	
Ndufs3	
Ndufs6	
Ndufs7	
Ndufv3	
Rhbdd1	
Sh3bp5	
Slc25a24	
Sqrdl	
Stk11	
Stoml2	
Syne2	
Txn2	
Uqcr11	
Uqcrh	
Wwox	

Table S4. Mouse strains studied from the UCLA HMDP. (n=4 mice/strain).

A/J
AKR/J
AXB12/PgnJ
AXB15/PgnJ
AXB19/PgnJ
AXB19a/PgnJ
AXB19b/PgnJ
BALB/cJ
BUB/BnJ
BXA11/PgnJ
BXA14/PgnJ
BXA16/PgnJ
BXA2/PgnJ
BXA24/PgnJ
BXA4/PgnJ
BXA7/PgnJ
BXA8/PgnJ
BXD12/TyJ
BXD14/TyJ
BXD15/TyJ
BXD19/TyJ
BXD20/TyJ
BXD21/TyJ
BXD31/TyJ
BXD34/TyJ
BXD38/TyJ
BXD40/TyJ
BXD43/RwwJ
BXD44/RwwJ
BXD45/RwwJ
BXD48/RwwJ
BXD49/RwwJ
BXD5/TyJ
BXD50/RwwJ
BXD51/RwwJ
BXD55/RwwJ
BXD56/RwwJ
BXD6/TyJ
BXD60/RwwJ
BXD61/RwwJ
BXD62/RwwJ
BXD64/RwwJ
BXD66/RwwJ
BXD68/RwwJ
BXD70/RwwJ
BXD71/RwwJ
BXD73/RwwJ
BXD74/RwwJ
BXD75/RwwJ
BXD79/RwwJ
BXD84/RwwJ
BXD85/RwwJ
BXD86/RwwJ
BXD87/RwwJ
BXD9/TyJ
BXH19/TyJ
BXH20/KccJ
BXH22/KccJ
BXH8/TyJ
BXH9/TyJ
C3H/HeJ
C57BL/6J
C57BLKS/J
C58/J
CBA/J
CE/J
CXB11/HiAJ
CXB12/HiAJ
CXB13/HiAJ
CXB4/ByJ
CXB6/ByJ
CXB7/ByJ
DBA/2J
FVB/NJ
KK/HlJ
MA/MyJ
NOD/ShiLtJ
NZW/LacJ
PL/J
RIIIS/J
SEA/GnJ
SJL/J
SM/J
SWR/J

Table S5. qPCR primers used to assess gene expression in adipose tissue from WT C57BL/6J, *Esr1* Control$^{f/f}$, FERKO, and ERαKO^{BAT} mice.

Gene Symbol	Forward (5' -> 3')	Reverse (5' -> 3')
18S	CGCCGCTAGAGGTGAAATTCT	CGAACCTCCGACTTTCGTTCT
Acta1	CCAGCCTTCCTTTATCGGTATG	CGGTCAGCGATACCAGGG
Atg12	CCACAGCCCATTTCTTTGTT	GAAACAGCCACCCCAGAG
Atg3	ATTCTTCCCCTGTAGCCCAT	GAAGTGGCCGAGTACCTGAC
Atg5	ACAGCTTCTGGATGAAAGGC	TGGGACTGCAGAATGACAGA
Atg7	GCCAGGTACTCCTGAGCTGT	ACTTGACCGGTCTTACCCTG
Beclin-1	CCCCGATCAGAGTGAAGCTA	AGGAGAGACCCAGGAGGAAG
Ctnnb1	CAGCTTGAGTAGCCATTGTCC	GAGCCGTCAGTGCAGGAG
Cav1	ATGTCTGGGGGCAAATACGTG	CGCGTCATACACTTGCTTCT
Col6A1	TCGGTCACCACGATCAAGTA	CAAGTACTTCGGGAAAGGCA
Dnm1l	CGTGGACTAGCTGCAGAATG	TGCCTCAGATCGTCGTAGTG
Esr1	GCCAGAATGGCCGAGAGAG	CCCCATAATGGTAGCCAGAGG
Gfm2	ACCGTCCAACACCCTCAAG	AAGAACGAGAAAGGGGCATT
Itgam	CCCCAATTACGTAGCGAATG	TGCTGCGAAGATCCTAGTTG
Maplc3b	AATCACTGGGATCTTGGTGG	AGTCAGATCGTCTGGCTCG
mtCO2	CTACAAGACGCCACAT	GAGAGGGGAGAGCAAT
Fis1	AGGAGCTGGAACGCCTGATTGATA	AGGATTTGGACTTGGAGACAGCCA
MFF	GCAGTTGGCAGGCTAAAAAG	TCAGGTAGCATATGGGGAGG
Mgme1	TGTTAGGTTCTCCTGGGGTG	TTTGGAGAGGTGGAAAGAGC
Mrpl9	GCAACCACCACACCAAGATT	GATCCAGACAAAGGCAGGAG
Mrps2	CGGTGAAGTTCAAAGCCAGT	CCGAGTACACCTGGGACATAA
Mrps24	GGAAAGGTGCCCATCATAAA	ACTACATCGCACACCGAAAG
MFN2	ATTGATCACGGTGCTCTTCC	GTCCTGGACGTCAAAGGGTA
MFN1	GCTTCCGACGGACTTACAAC	TGAATAACCGTTGGGATGCT
Myod1	AGGCCGTGGCAGCGA	GCTGTAATCCATCATGCCATCA
Myog	CAACCAGGAGGAGCGCGATCTCCG	AGGCGCTGTGGGAGTTGCATTCACT
Myh4	AGCTCGTGCTGGATCTTACG	GCAGGACTTGGTGGACAAAC
Myh6	CTTCATCCATGGCCAATTCT	GCGCATTGAGTTCAAGAAGA
Myh7	CTCAACTGGGAAGAGCATCCA	CCTCCAGCAAACTCTGGAGGC
Nrf1	GAACTGCCAACCACAGTCAC	CGTCTGGATGGTCATTTCAC
Opa1	TCCTGGTGAAGAGCTTCAATG	TTTGCAGAAGACGGTGAGAA
Park2	ATCGACCTCCACTGGGAAG	GCGTAGGTCCTTCTCGACC
Park7	AACACACCCACTGGCTAAGG	GTGCCTCCACAATGGCTAGT
Ppia	AGCCAAATCCTTTCTCTCCAG	CACCGTGTTCTTCGACATCA
PGC1α	TGAGGACCGCTAGCAAGTTT	TGAAGTGGTGTAGCGACCAA
Polg1	TAGCTGGCTGGTCCAAGAGT	CGACGTGGAGGTCTGCTT
Polg2	CCGTTTTCCAGCGTAGTCTC	TTCTGTGTGGCCTGGCTATT

Polrmt	CTCATCTCAGGTGTGCCCTC	TCTGCAGCTCAAGAAGGAGC
Peo1	GCCCAGTCACCAGTTTCCTA	ACTCTGGTCATTCACCCTCG
Ppp3cc	GCGATTGATCCCAAGTTGTC	TGCCCTCCTTCATGAGATGT
Pink1	GGATGTCGTCCTGAAGGGAG	GCTTCGCTGGAGGAACCTG
Rcan	TGTGGCAAACGATGATGTCT	GCAGATAAGGGGTTGCTGAA
Sqstm1	TTTCTGGGGTAGTGGGTGTC	CTGAAGAATGTGGGGGAGAG
S1pr3	TCTTAGCTGAGACACGGCAG	TCAGGGAACAATTGGGAGAG
Sdha	TACTACAGCCCCAAGTCT	TGGACCCATCTTCTATGC
Tfam	AGCTTGTAAATGAGGCTTGGA	AGATGTCTCCGGATCGTTTC
Tnni1	CCCTACTGGGCTCTAAGCACA	GCCTCCACATTCTTCCTCCA
Tnni2	CTGTCAGAACACTGCCCGC	GCTCCTTGCTGCTCTTCTGC
Ulk1	TAGTCAGCCAGGTCTCCACC	CTGCTGGGAAAGGAAATCAA
Vegfa	AATGCTTTCTCCGCTCTGAA	CTCACCAAAGCCAGCACATA

Table S6. qPCR primers used for ChIP studies to assess the binding of ERα to the Polg1 proximal promoter in 3T3L1 adipocytes.

Set 1: F: 5’-GGATAAGGCGTCTGACTTCG-3’; R: 5’-CCCTGACAGTTGTTTGCTCA-3’

Set 2: F: 5’-CTATGGACCGCAAAGGCTAA-3’; R: 5’-GAGCTGGGAGCAGAAACAAC-3’

Set 6: F: 5’-CCCACTGATACCAACCAAGC-3’; R: 5’-GAGGGTCAGAGCAGCTTCAT-3’

Set 7: F: 5’-TGGACCACTACCTGAGTGACC-3’; R: 5’-CTCTTATGAGCCACCCTTGC-3’

Positive control (Pgr):

F: 5’-CCAACATACTTCATGCTGCAC-3’; R: 5’-TTCAGCAAGGCAAGAAACAA-3’

Data file S1. Raw data from studies of human tissues, cells, and genetically engineered mice. (Excel)

Data file S2. Raw data of *ESR1*-correlated genes in subcutaneous fat from men participating in the METSIM study. (Excel)

Data file S3. Raw data of *ESR1*-correlated genes in subcutaneous fat from men participating in the MyoGlu study. (Excel)

Data file S4. Raw data of *Esr1*-correlated genes in gonadal fat from male mice of the UCLA HMDP. (Excel)

Data file S5. Raw data of *Esr1*-correlated genes in gonadal fat from female mice of the UCLA HMDP. (Excel)

Data file S6. GO of microarray data performed on gonadal fat from female FERKO and Control$^{f/f}$ mice. (Excel)