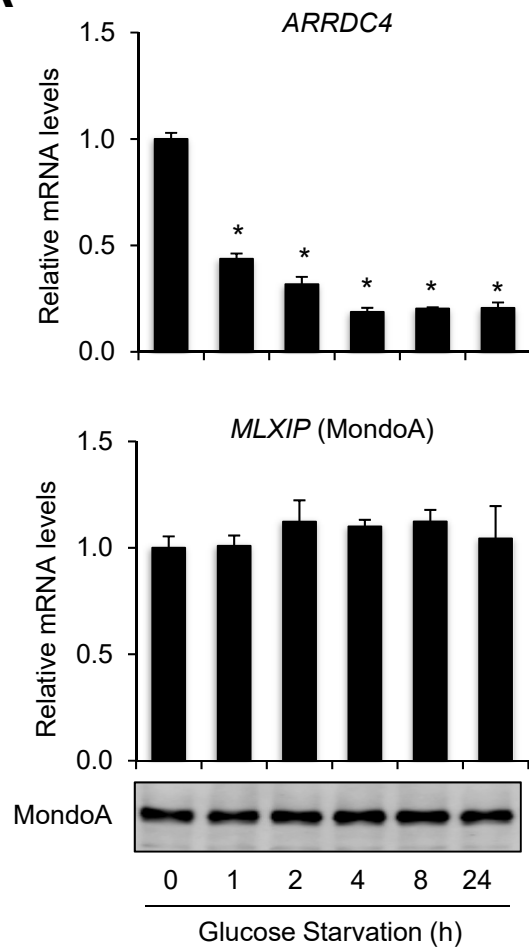
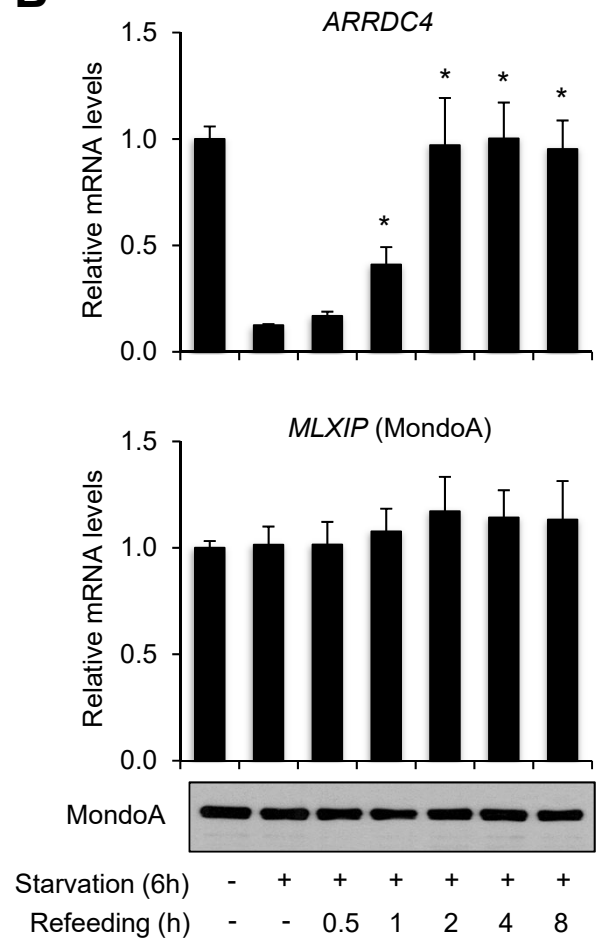
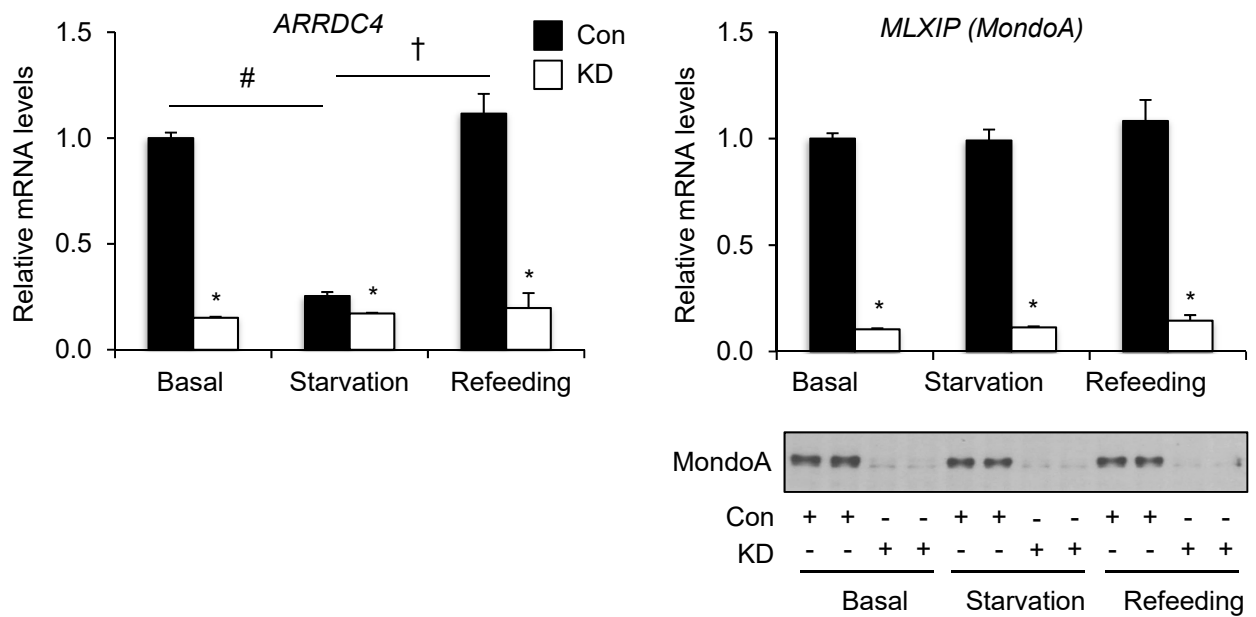
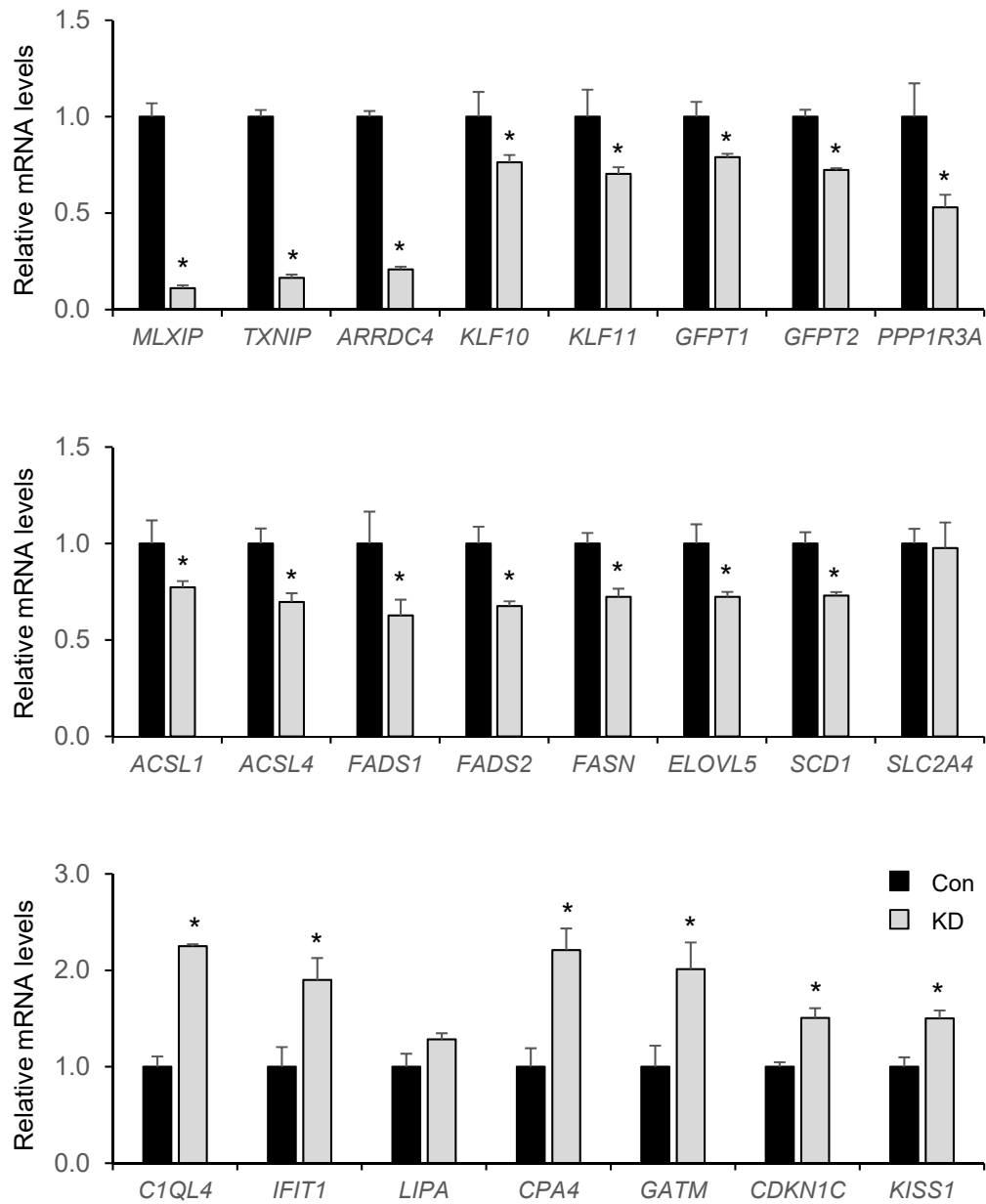
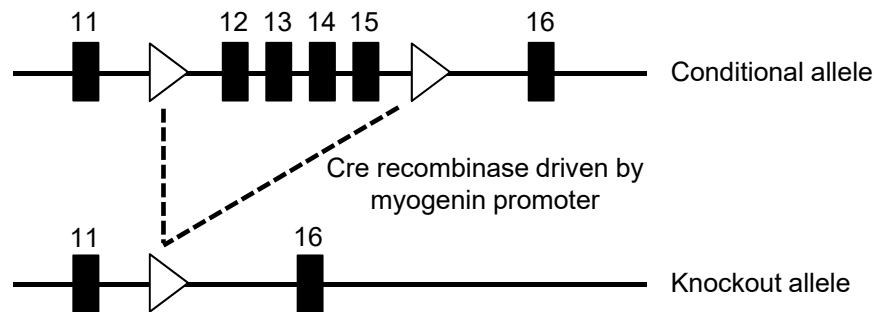
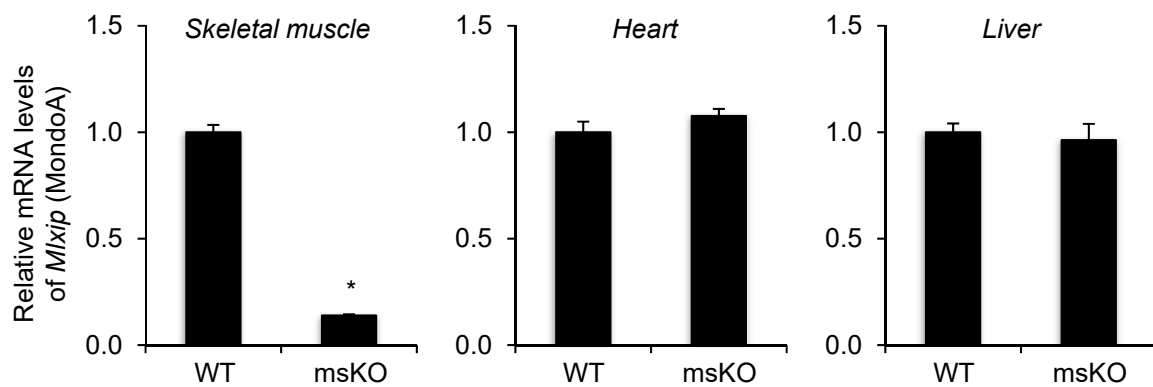
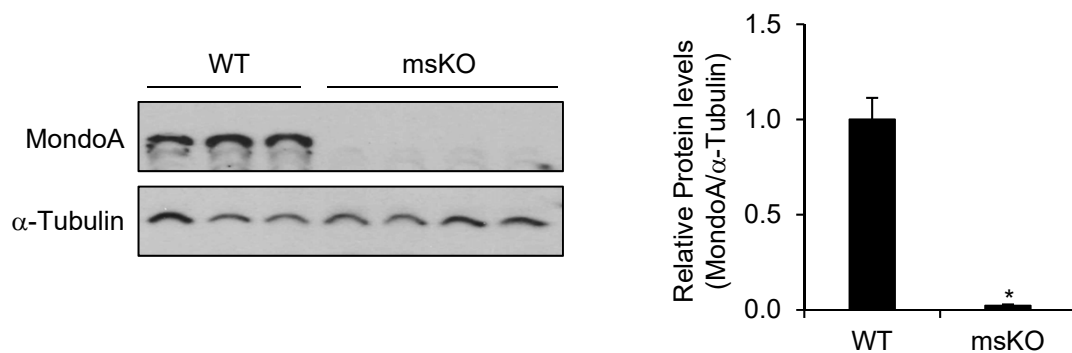


A**B****C**

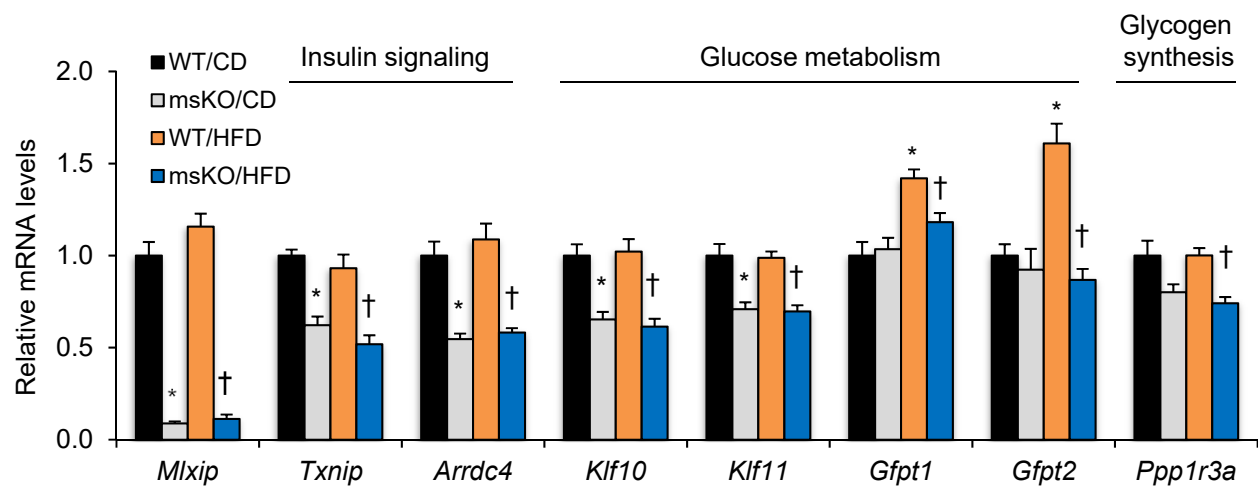
Supplemental Figure 1. Glucose-mediated regulation of *ARRDC4* is dependent on *MondoA* in human skeletal myotubes. **(A)** (top) *ARRDC4* and *MLXIP* (*MondoA*) mRNA levels were determined by qRT-PCR in human skeletal myotubes following deprivation of glucose at the indicated time (n=4). (bottom) Representative Western blot analysis of *MondoA* demonstrating the effect of glucose deprivation. *p<0.05 vs. 0h. **(B)** (top) *ARRDC4* and *MLXIP* (*MondoA*) expression in human myotubes following a 6h glucose removal and refeeding at the times indicated (n=4). (bottom) Corresponding Western blot analysis. *p<0.05 vs Starvation 6h. **(C)** (top) Expression of *ARRDC4* and *MLXIP* in human myotubes following deprivation and refeeding of glucose in the absence or presence of siRNA-mediated *MondoA* KD (n=4). (bottom) Corresponding Western blot analysis. *p<0.05 vs siControl. # p<0.05. § p<0.05. The data represents mean $\pm$ SD. All statistical significance determined by one-way ANOVA with Tukey multiple comparison post-hoc test.



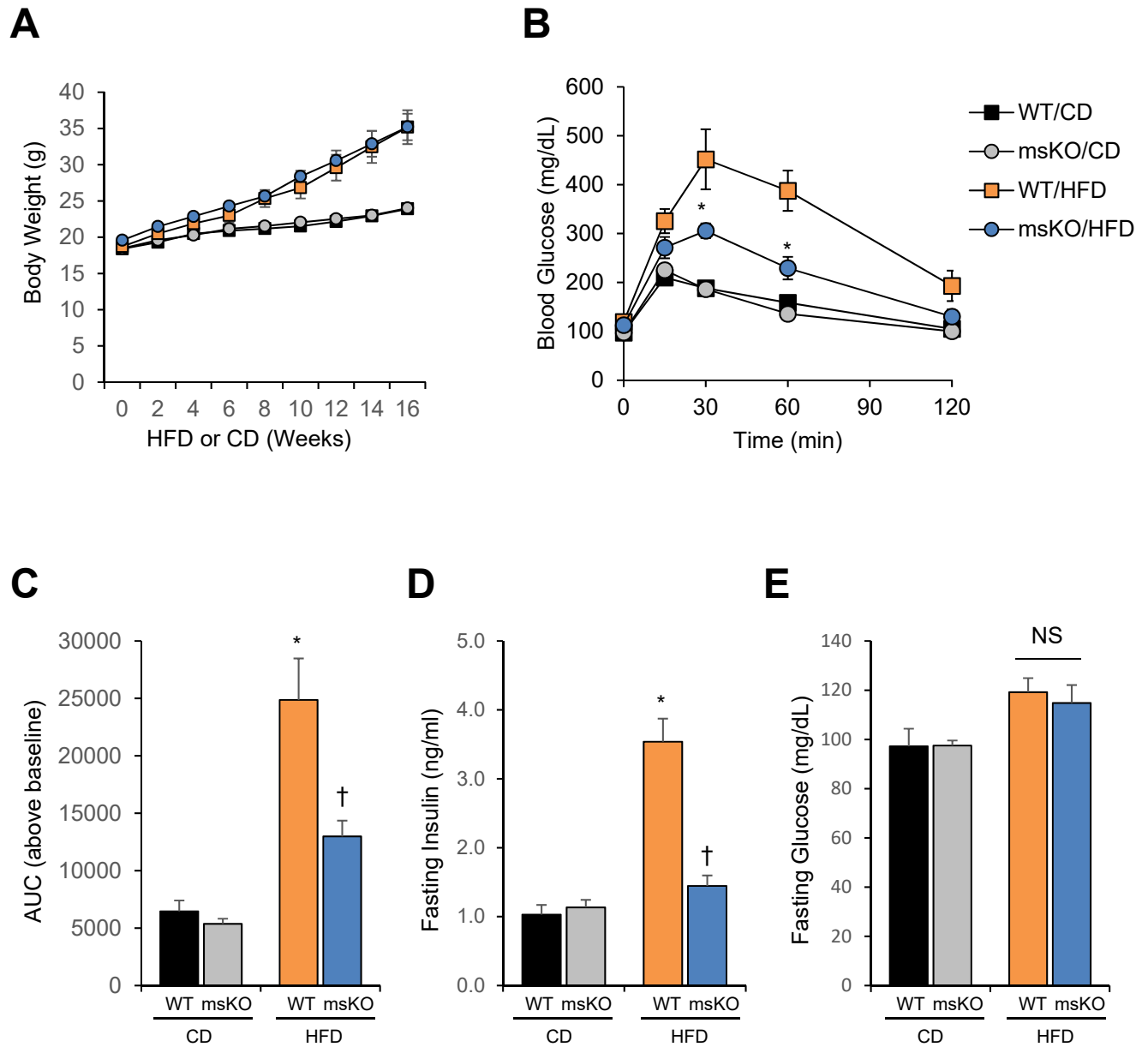
Supplemental Figure 2. Validation of RNA-seq results by qRT-PCR in human myotubes. Expression of a subset of downregulated and upregulated genes was assessed in human myotubes following the absence or presence of siRNA-mediated MondoA KD (n=3). The data represents mean $\pm$ SD. * $p < 0.05$ vs Control (Con) by Mann-Whitney test.

A**B****C**

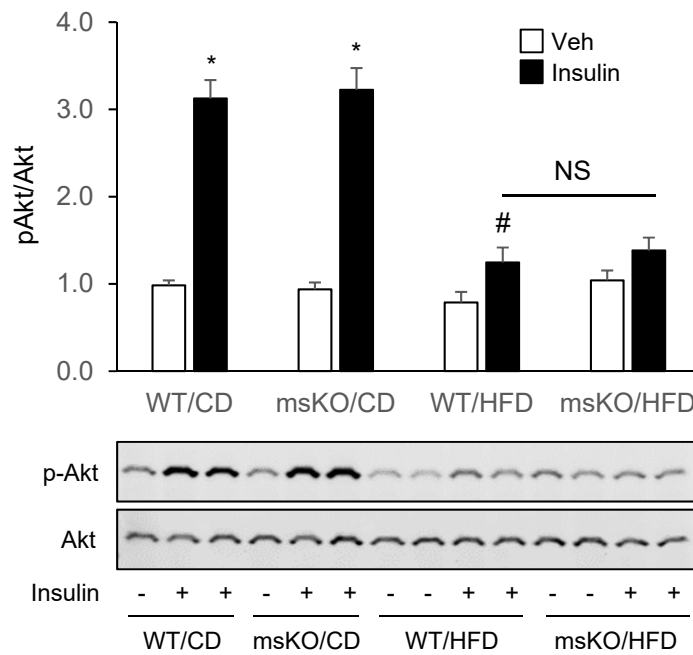
Supplemental Figure 3. Generation of skeletal muscle-specific MondoA deficient mice (msMondoA^{-/-}). (A) Schematic diagram of conditional and knockout allele of *Mlxip* (MondoA). Black boxes depict exons. White triangles depict LoxP. (B) qRT-PCR analysis of *Mlxip* (MondoA) expression in gastrocnemius muscle, heart and liver (n= 6-7 per group). (C) Western blot analysis of MondoA protein levels in gastrocnemius muscle lysates. * p<0.05 vs WT by Mann-Whitney test. The data represents mean $\pm$ SEM.



Supplemental Figure 4. Loss of MondoA reduces target gene expression in skeletal muscle. Target gene expression was measured by quantitative RT-PCR in gastrocnemius muscle in mice maintained on a control diet (CD) or HFD for 16 weeks (n = 8-10 mice per group). Data bars represent mean $\pm$ SEM. * $p < 0.05$ vs WT/CD; † $p < 0.05$ vs WT/HFD by one-way ANOVA with Tukey multiple comparison post-hoc test.

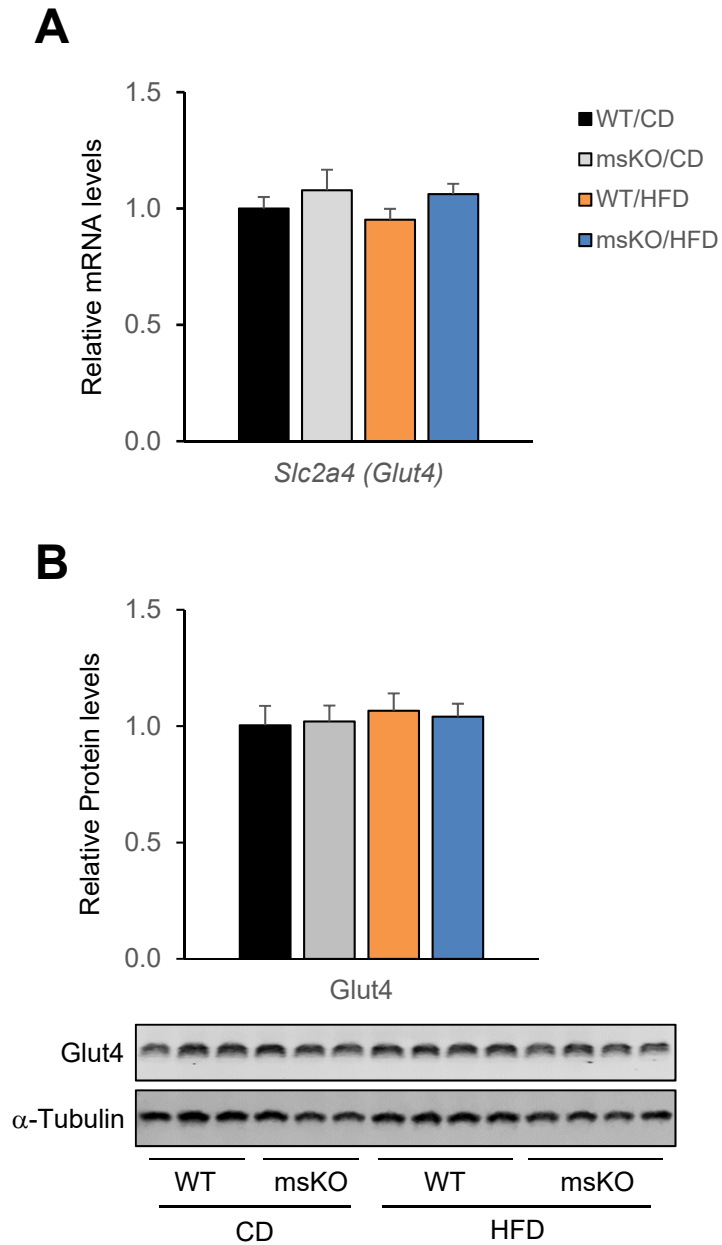


Supplemental Figure 5. Glucose tolerance is improved in female skeletal muscle-specific MondoA-deficient mice (*msMondoA*^{-/-}). (A) Body weight of wild-type (WT) and muscle-specific MondoA deficient (*msMondoA*^{-/-}; msKO) female mice fed chow diet (CD) or 60% high fat diet (HFD) for 16 weeks (n = 4-6 mice per group). (B) Glucose tolerance test (GTT) was conducted following glucose injection (1g/kg, i.p.) after a 5h fast. Data represent mean ± SEM. *p<0.05 WT/HFD vs msKO/HFD; 2-way ANOVA with Tukey multiple comparisons post-hoc test. The level of (C) Area-under-the-curve (AUC) for GTT, (D) fasting plasma insulin and (E) fasting blood glucose. The data represents mean ± SEM. *p<0.05 vs WT/CD, † p<0.05 vs WT/HFD by one-way ANOVA with Tukey multiple comparison post-hoc test.

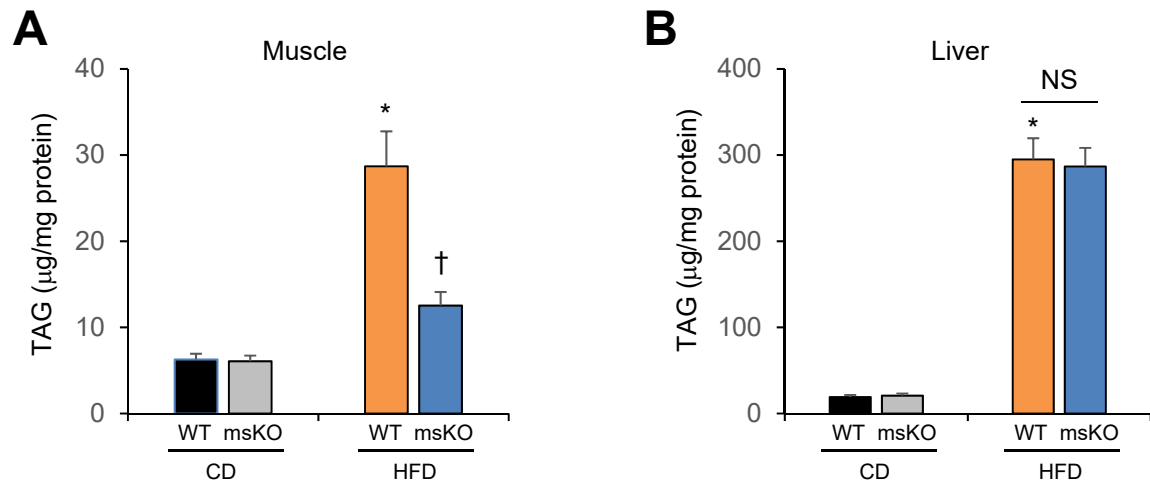


Supplemental Figure 6. Muscle-specific MondoA deficiency has no effect on insulin signaling in liver.

Western blot analysis of pAkt (S473) and total Akt in response to insulin (1.0U/kg for 10 minutes) in liver lysates (n = 4-6 mice per group). Representative Western blots are shown in the bottom panel. The data represents mean $\pm$ SEM. *p<0.05 vs WT/CD, # p<0.05 vs WT/CD with insulin by one-way ANOVA with Tukey multiple comparison post hoc test.



Supplemental Figure 7. The gene expression and protein level of Glut4 in skeletal muscle. (A) qRT-PCR analysis of *Slc2a4* (*Glut4*) expression in gastrocnemius muscle (n= 8-10 per group). (B) Western blot analysis of Glut4 protein levels in gastrocnemius muscle lysates. The data represents mean $\pm$ SEM.



Supplemental Figure 8. Loss of MondoA reduces total TAG levels in skeletal muscle.

Total triglyceride content (Biochemical assay) was measured in **(A)** gastrocnemius muscle and **(B)** liver. Data bars represent mean $\pm$ SEM. * $p<0.05$ vs WT/CD; † $p<0.05$ vs WT/HFD by one-way ANOVA with Tukey multiple comparison post-hoc test

Supplemental Table 1. Top 50 up- and downregulated genes from RNA-seq analysis of human skeletal myotubes (Control vs MondoA KD).

A. Down-regulated genes		
GENE ID	Name	Fold Change
ARRDC4	Arrestin domain containing 4	-4.187
RPTN	Repetin	-3.842
TXNIP	Thioredoxin interacting protein	-3.812
PUDPP2	Pseudouridine 5'-phosphatase pseudogene 2	-3.486
MLXIP	MLX interacting protein	-1.957
MYBPC1	Myosin binding protein C, slow type	-1.804
OLFML2A	Olfactomedin like 2A	-1.790
PRDX3	Peroxiredoxin 3	-1.778
AC117505.1	AC117505.1	-1.772
NR2F6	Nuclear receptor subfamily 2 group F member 6	-1.742
MAP1LC3B2	Microtubule associated protein 1 light chain 3 beta 2	-1.738
AC090181.1	AC090181.1	-1.705
TMEM64	Transmembrane protein 64	-1.681
TOMM5	Translocase of outer mitochondrial membrane 5	-1.659
FERMT2	Fermitin family member 2	-1.645
MAP1LC3B	Microtubule associated protein 1 light chain 3 beta	-1.638
MYH2	Myosin heavy chain 2	-1.614
AC125618.1	AC125618.1	-1.590
CDC42SE2	CDC42 small effector 2	-1.589
TPM3	Tropomyosin 3	-1.573
ACAA2	Acetyl-CoA acyltransferase 2	-1.568
IER3IP1	Immediate early response 3 interacting protein 1	-1.551
SPT2D1	SPT2 chromatin protein domain containing 1	-1.533
KLHL7	Kelch like family member 7	-1.533
MAP3K7CL	MAP3K7 C-terminal like	-1.528
AC243960.2	AC243960.2	-1.506
SLC2A5	Solute carrier family 2 member 5	-1.499
PFKM	Phosphofructokinase, muscle	-1.499
SDC4	Syndecan 4	-1.488
GNPTAB	N-acetylglucosamine-1-phosphate transferase alpha and beta subunits	-1.488
MLLT11	Myeloid/lymphoid or mixed-lineage leukemia; translocated to, 11	-1.487
AC010149.1	AC010149.1	-1.487
ASB14	Ankyrin repeat and SOCS box containing 14	-1.482
ERLEC1	Endoplasmic reticulum lectin 1	-1.449
MYL2	Myosin light chain 2	-1.442
UBN1	Ubinuclein 1	-1.433
SLC40A1	Solute carrier family 40 member 1	-1.428
PCYOX1	Prenylcysteine oxidase 1	-1.427
USP12	Ubiquitin specific peptidase 12	-1.425
POLR2M	RNA polymerase II subunit M	-1.424
FADS2	Fatty acid desaturase 2	-1.423

RWDD4	RWD domain containing 4	-1.421
FADS1	Fatty acid desaturase 1	-1.412
CUL4A	Cullin 4A	-1.403
SMG5	SMG5, nonsense mediated mRNA decay factor	-1.398
TMEM167A	Transmembrane protein 167A	-1.388
CBX3	Chromobox 3	-1.384
NXPE3	Neurexophilin and PC-esterase domain family member 3	-1.380
XPOT	Exportin for tRNA	-1.379
SCARB2	Scavenger receptor class B member 2	-1.344

B. Up-regulated genes

GENE ID	Gene Name	Fold Change
C1QL4	Complement C1q like 4	2.292
MIR3687-1	MicroRNA 3687-1	2.272
LINC01934	Long Intergenic Non-Protein Coding RNA 1934	2.130
CPA4	Carboxypeptidase A4	2.071
IFIT1	Interferon induced protein with tetratricopeptide repeats 1	1.898
FNDC1	Fibronectin type III domain containing 1	1.862
IFI6	Interferon alpha inducible protein 6	1.811
BBOX1	Gamma-butyrobetaine hydroxylase 1	1.770
IFIT2	Interferon induced protein with tetratricopeptide repeats 2	1.755
FBXL22	F-box and leucine rich repeat protein 22	1.754
PGA4	Pepsinogen 4, group I (pepsinogen A)	1.724
PGA3	Pepsinogen 3, group I (pepsinogen A)	1.718
AP003037.1	AP003037.1	1.704
PGA5	Pepsinogen 5, group I (pepsinogen A)	1.700
LINC02262	Long Intergenic Non-Protein Coding RNA 2262	1.698
BBOX1-AS1	BBOX1 Antisense RNA 1	1.675
RGS4	Regulator of G-protein signaling 4	1.639
PAMR1	Peptidase domain containing associated with muscle regeneration 1	1.620
UNQ6494	UNQ6494	1.608
PACSIN1	Protein kinase C and casein kinase substrate in neurons 1	1.580
GATM	Glycine amidinotransferase	1.553
GALNT10	Polypeptide N-acetylgalactosaminyltransferase 10	1.543
CDKN1C	Cyclin dependent kinase inhibitor 1C	1.540
KRT86	Keratin 86	1.528
XRCC4	X-ray repair cross complementing 4	1.509
SAP30L-AS1	SAP30L Antisense RNA 1	1.508
AP002026.1	AP002026.1	1.502
PSKH1	Protein serine kinase H1	1.492
KISS1	KiSS-1 metastasis-suppressor	1.488
PCED1B	PC-esterase domain-containing protein 1B	1.482
FOLR1	Folate receptor 1	1.454
AP000812.1	AP000812.1	1.447
PKP1	Plakophilin 1	1.446
DDX60	DExD/H-box helicase 60	1.428

ARNT2	Aryl hydrocarbon receptor nuclear translocator 2	1.407
STK39	Serine/threonine kinase 39	1.388
LIPA	Lipase A, lysosomal acid type	1.387
AL049569.1	AL049569.1	1.369
LRP4	LDL receptor related protein 4	1.369
AC145207.2	AC145207.2	1.368
ATP13A2	ATPase 13A2	1.366
FILIP1L	Filamin A interacting protein 1 like	1.366
KIFC3	Kinesin family member C3	1.345
SIRPA	Signal regulatory protein alpha	1.343
ADAM19	ADAM metalloproteinase domain 19	1.342
ARHGDIA	Rho GDP dissociation inhibitor alpha	1.327
ITGA4	Integrin subunit alpha 4	1.327
ABLIM1	Actin binding LIM protein 1	1.324
TRAM2	Translocation associated membrane protein 2	1.315
DDX60L	DEAD-box helicase 60-like	1.313

Supplemental Table 2. KEGG pathway results from up- and downregulated genes.**A. Pathways of downregulated genes****a. Insulin resistance**

GENE ID	Gene Name	Fold Change	p-value
MLXIP	MLX interacting protein	-1.983	8.6E-74
MLX	MLX, MAX dimerization protein	-1.146	1.5E-05
PPARGC1A	PPARG coactivator 1 alpha	-1.500	1.1E-12
GFPT1	glutamine--fructose-6-phosphate transaminase 1	-1.213	8.3E-12
GFPT2	glutamine-fructose-6-phosphate transaminase 2	-1.138	3.7E-05
IL6	interleukin 6	-1.235	3.2E-04
MTOR	mechanistic target of rapamycin	-1.151	2.2E-06
MAPK9	mitogen-activated protein kinase 9	-1.201	9.2E-08
PPARA	peroxisome proliferator activated receptor alpha	-1.144	1.7E-05
PIK3R2	phosphoinositide-3-kinase regulatory subunit 2	-1.240	1.2E-06
PYGM	phosphorylase, glycogen, muscle	-1.172	4.5E-04
PRKAA1	protein kinase AMP-activated catalytic subunit alpha 1	-1.121	2.6E-05
PRKAA2	protein kinase AMP-activated catalytic subunit alpha 2	-1.172	3.2E-07
PRKCQ	protein kinase C theta	-1.387	5.8E-07
PPP1R3A	protein phosphatase 1 regulatory subunit 3A	-1.255	1.7E-05
PTPN11	protein tyrosine phosphatase, non-receptor type 11	-1.120	6.0E-05
RPS6KB1	ribosomal protein S6 kinase B1	-1.106	5.4E-04
SLC2A4	solute carrier family 2 member 4	-1.844	6.5E-06
SREBF1	sterol regulatory element binding transcription factor 1	-1.138	1.1E-04
TRIB3	tribbles pseudokinase 3	-1.154	4.7E-04

b. Fatty acid metabolism

GENE ID	Gene Name	Fold Change	p-value
ELOVL5	ELOVL fatty acid elongase 5	-1.263	8.93E-18
ACAA2	acetyl-CoA acyltransferase 2	-1.589	3.74E-66
ACADM	acyl-CoA dehydrogenase, C-4 to C-12 straight chain	-1.184	1.43E-09
ACOX3	acyl-CoA oxidase 3, pristanoyl	-1.141	8.25E-05
ACSBG1	acyl-CoA synthetase bubblegum family member 1	-1.146	4.90E-05
ACSL1	acyl-CoA synthetase long-chain family member 1	-1.282	7.39E-18
ACSL3	acyl-CoA synthetase long-chain family member 3	-1.132	9.68E-06
ACSL4	acyl-CoA synthetase long-chain family member 4	-1.303	3.48E-21
FADS1	fatty acid desaturase 1	-1.431	1.44E-34
FADS2	fatty acid desaturase 2	-1.441	7.52E-36
SCD5	stearoyl-CoA desaturase 5	-1.255	3.05E-11
SCD	stearoyl-CoA desaturase	-1.414	5.80E-27

c. Adipocytokine signaling pathway

GENE ID	Gene Name	Fold Change	p-value
PPARGC1A	PPARG coactivator 1 alpha	-1.255	1.7E-05
ACSBG1	acyl-CoA synthetase bubblegum family member 1	-1.146	4.9E-05
ACSL1	acyl-CoA synthetase long-chain family member 1	-1.282	7.4E-18
ACSL3	acyl-CoA synthetase long-chain family member 3	-1.132	9.7E-06

ACSL4	acyl-CoA synthetase long-chain family member 4	-1.303	3.5E-21
CHUK	conserved helix-loop-helix ubiquitous kinase	-1.120	2.7E-04
LEPR	leptin receptor	-1.109	2.3E-04
MTOR	mechanistic target of rapamycin	-1.151	2.2E-06
MAPK9	mitogen-activated protein kinase 9	-1.201	9.2E-08
PPARA	peroxisome proliferator activated receptor alpha	-1.144	1.7E-05
PRKAA1	protein kinase AMP-activated catalytic subunit alpha 1	-1.121	2.6E-05
PRKAA2	protein kinase AMP-activated catalytic subunit alpha 2	-1.172	3.2E-07
PRKCQ	protein kinase C theta	-1.387	5.8E-07
PTPN11	protein tyrosine phosphatase, non-receptor type 11	-1.120	6.0E-05
SLC2A4	solute carrier family 2 member 4	-1.844	6.5E-06

B. Pathways of upregulated genes

a. Focal adhesion

GENE ID	Gene Name	Fold Change	p-value
BRAF	B-Raf proto-oncogene, serine/threonine kinase	1.153	5.2E-04
JUN	Jun proto-oncogene, AP-1 transcription factor subunit	1.202	3.4E-08
ACTN4	actinin alpha 4	1.196	7.5E-11
BIRC3	baculoviral IAP repeat containing 3	1.335	3.6E-06
COL1A1	collagen type I alpha 1 chain	1.403	5.9E-11
COL4A1	collagen type IV alpha 1 chain	1.164	3.6E-07
COL4A2	collagen type IV alpha 2 chain	1.205	2.0E-11
COL11A2	collagen type XI alpha 2 chain	1.542	4.0E-05
CCND1	cyclin D1	1.126	5.7E-05
EGFR	epidermal growth factor receptor	1.268	3.8E-07
FLNA	filamin A	1.231	2.6E-14
FLNB	filamin B	1.274	1.1E-17
FLNC	filamin C	1.116	6.2E-05
IGF1R	insulin like growth factor 1 receptor	1.325	6.5E-08
ITGA4	integrin subunit alpha 4	1.309	1.1E-19
MYLK	myosin light chain kinase	1.184	4.9E-10
PAK3	p21 (RAC1) activated kinase 3	1.413	1.9E-04
PXN	paxillin	1.133	4.4E-05
PGF	placental growth factor	1.116	4.7E-04
PDGFC	platelet derived growth factor C	1.221	8.5E-09
PRKCA	protein kinase C alpha	1.169	4.8E-05
PTK2	protein tyrosine kinase 2	1.111	4.7E-04
TLN1	talin 1	1.162	1.2E-07
TNC	tenascin C	1.139	1.7E-05
THBS1	thrombospondin 1	1.131	1.4E-06
VEGFC	vascular endothelial growth factor C	1.469	3.0E-17
VASP	vasodilator-stimulated phosphoprotein	1.188	1.9E-07

b. Rap1 signaling pathway

GENE ID	Gene Name	Fold Change	p-value
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BRAF	B-Raf proto-oncogene, serine/threonine kinase	1.153	5.2E-04
RAPGEF5	Rap guanine nucleotide exchange factor 5	1.392	4.1E-08
CALM2	calmodulin 2	1.155	9.7E-08
EFNA5	ephrin A5	1.261	1.6E-06
EGFR	epidermal growth factor receptor	1.268	3.8E-07
FGF1	fibroblast growth factor 1	1.261	4.1E-09
FGF13	fibroblast growth factor 13	1.356	1.7E-14
FGF2	fibroblast growth factor 2	1.119	5.1E-04
FGF5	fibroblast growth factor 5	1.384	3.2E-05
ID1	inhibitor of DNA binding 1, HLH protein	1.145	8.3E-05
IGF1R	insulin like growth factor 1 receptor	1.325	6.5E-08
MAGI1	membrane associated guanylate kinase, WW and PDZ domain containing 1	1.188	4.1E-04
MAGI2	membrane associated guanylate kinase, WW and PDZ domain containing 2	1.205	4.7E-04
NGFR	nerve growth factor receptor	1.199	6.6E-08
NGF	nerve growth factor	1.571	2.6E-06
PLCB4	phospholipase C beta 4	1.257	1.4E-06
PGF	placental growth factor	1.116	4.7E-04
PDGFC	platelet derived growth factor C	1.221	8.5E-09
PRKCA	protein kinase C alpha	1.169	4.8E-05
PRKD1	protein kinase D1	1.221	2.1E-05
SIPA1L1	signal induced proliferation associated 1 like 1	1.182	6.4E-06
TLN1	talin 1	1.162	1.2E-07
THBS1	thrombospondin 1	1.131	1.4E-06
VEGFC	vascular endothelial growth factor C	1.469	3.0E-17
VASP	vasodilator-stimulated phosphoprotein	1.188	1.9E-07

Supplementary Table 3. Lipidomic DAG and TAG species profile from WT to msMondoA^{-/-} skeletal muscle on Chow (CD) or High Fat Diet (HFD).

Lipid (nmol/mg protein)	MASS	WT/CD	msKO/CD	WT/HFD	msKO/HFD
Diacylglycerol (DAG)					
C28:0	598.50	0.03±0.00	0.03±0.00	0.03±0.00	0.03±0.00
C30:1	624.52	0.00±0.00	0.00±0.00	0.00±0.00	0.00±0.00
C32:2	650.54	0.02±0.00	0.02±0.00	0.03±0.00	0.02±0.00
C32:1	652.55	0.06±0.00	0.07±0.01	0.08±0.01	0.07±0.00
C32:0	654.57	0.17±0.01	0.17±0.01	0.16±0.01	0.16±0.01
C34:3	676.55	0.03±0.00	0.03±0.00	0.05±0.01	0.04±0.01
C34:2	678.57	1.75±0.03	1.73±0.06	2.04±0.05*	1.81±0.07†
C34:1	680.58	0.19±0.01	0.19±0.01	0.36±0.05*	0.25±0.03†
C34:0	682.60	0.07±0.01	0.07±0.01	0.07±0.01	0.07±0.00
C36:4	702.57	0.06±0.00	0.06±0.00	0.11±0.01	0.09±0.01
C36:3	704.58	0.09±0.01	0.09±0.01	0.33±0.04*	0.24±0.03†
C36:2	706.60	0.07±0.01	0.08±0.01	0.35±0.06*	0.16±0.04†
C36:1	708.61	0.03±0.01	0.04±0.01	0.05±0.01	0.03±0.00
C36:0	710.63	0.05±0.01	0.06±0.03	0.03±0.00	0.03±0.00
C38:6	726.57	0.21±0.02	0.13±0.01	0.06±0.00*	0.05±0.00
C38:5	728.58	0.04±0.00	0.03±0.00	0.04±0.00	0.03±0.00
C38:4	730.60	0.07±0.01	0.06±0.01	0.11±0.01	0.09±0.01
C38:3	732.61	0.03±0.00	0.03±0.00	0.03±0.00	0.03±0.00
C38:2	734.63	0.01±0.00	0.01±0.01	0.01±0.00	0.01±0.00
C38:1	736.65	0.03±0.01	0.02±0.01	0.01±0.00	0.01±0.00
C40:8	750.57	0.06±0.00	0.05±0.00	0.02±0.00	0.02±0.00
C40:7	752.58	0.12±0.01	0.10±0.01	0.08±0.01	0.07±0.01
C40:6	754.60	0.12±0.01	0.08±0.01	0.05±0.00	0.03±0.00
C40:5	756.61	0.01±0.00	0.01±0.00	0.01±0.00	0.01±0.00
Sum		3.34±0.08	3.16±0.18	4.10±0.14*	3.34±0.16†
Triacylglycerol (TAG)					
C44:2	753.66	0.19±0.01	0.16±0.02	0.19±0.03	0.25±0.06
C44:1	755.67	0.19±0.02	0.16±0.03	0.22±0.04	0.29±0.06
C44:0/C45:7	757.69	0.14±0.02	0.12±0.02	0.21±0.05	0.27±0.06
C46:3	779.67	0.14±0.01	0.12±0.02	0.16±0.03	0.20±0.04
C46:2	781.69	0.25±0.04	0.20±0.02	0.30±0.07	0.33±0.07
C46:1/C47:8	783.71	0.34±0.05	0.25±0.02	0.37±0.04	0.36±0.05
C46:0/C47:7	785.72	0.25±0.03	0.20±0.02	0.32±0.04	0.35±0.04
C47:2/C48:9	795.71	0.13±0.04	0.08±0.01	0.14±0.03	0.19±0.04
C47:1/C48:8	797.72	0.19±0.05	0.13±0.01	0.19±0.04	0.24±0.05
C47:0/C48:7	799.74	0.31±0.05	0.22±0.02	0.41±0.10	0.57±0.14
C48:4	805.69	0.12±0.01	0.10±0.01	0.17±0.03	0.18±0.03
C48:3	807.71	0.45±0.07	0.45±0.07	0.76±0.15	0.73±0.14
C48:2/C49:9	809.72	0.95±0.09	0.93±0.15	1.71±0.08*	1.23±0.09†
C48:1/C49:8	811.74	1.34±0.08	1.05±0.13	2.08±0.08*	1.53±0.11†
C48:0/C49:7	813.75	0.47±0.04	0.36±0.05	0.92±0.05*	0.73±0.05

C49:6	815.67	0.10±0.02	0.07±0.01	0.22±0.07	0.38±0.12
C49:3/C50:10	821.72	0.16±0.04	0.13±0.02	0.30±0.09	0.47±0.12
C49:2/C50:9	823.74	0.24±0.05	0.20±0.02	0.28±0.04	0.29±0.04
C49:1/C50:8	825.75	0.43±0.07	0.36±0.04	0.56±0.05	0.51±0.07
C49:0/C50:7	827.67	0.21±0.03	0.18±0.03	0.28±0.03	0.26±0.03
C50:6	829.69	0.14±0.01	0.12±0.01	0.18±0.02	0.31±0.11
C50:5	831.71	0.16±0.02	0.16±0.01	0.29±0.04	0.34±0.06
C50:4	833.72	0.50±0.06	0.63±0.10	1.23±0.05	0.93±0.06
C50:3/C51:10	835.74	1.79±0.18	2.08±0.32	5.70±0.24*	3.93±0.34†
C50:2/C51:9	837.75	2.86±0.35	2.71±0.35	12.00±0.53*	8.93±0.46†
C50:1/C51:8	839.77	1.39±0.10	1.23±0.13	7.84±0.49*	5.61±0.40†
C50:0/C51:7	841.78	0.20±0.02	0.16±0.01	0.54±0.05	0.53±0.07
C51:6	843.71	0.06±0.01	0.05±0.01	0.12±0.03	0.18±0.04
C51:5	845.72	0.08±0.01	0.07±0.01	0.14±0.03	0.22±0.04
C51:4/C52:11	847.74	0.12±0.02	0.11±0.02	0.27±0.07	0.40±0.10
C51:2/C52:9	851.77	0.56±0.06	0.62±0.08	1.51±0.07*	1.08±0.06†
C51:1/C52:8	853.69	0.42±0.04	0.42±0.05	1.27±0.07*	0.93±0.04†
C51:0/C52:7	855.71	0.24±0.02	0.23±0.03	0.83±0.05*	0.69±0.05
C52:6	857.72	0.17±0.01	0.19±0.01	0.40±0.03	0.46±0.13
C52:5	859.74	0.54±0.07	0.73±0.09	2.12±0.11*	1.60±0.14†
C52:4/C53:11	861.75	1.76±0.26	2.35±0.32	10.37±0.66*	7.16±0.73†
C52:3/C53:10	863.77	2.88±0.38	3.50±0.45	25.84±1.80*	17.38±1.68†
C52:2/C53:9	865.78	1.82±0.19	1.97±0.21	22.87±1.69*	15.53±1.29†
C52:1/C53:8	867.80	0.32±0.03	0.27±0.02	2.64±0.19	2.02±0.12
C52:0/C53:7	869.81	0.15±0.02	0.12±0.01	0.25±0.04	0.31±0.04
C53:6	871.74	0.07±0.01	0.06±0.00	0.12±0.03	0.31±0.13
C53:5/C54:12	873.75	0.09±0.01	0.08±0.00	0.17±0.02	0.25±0.05
C53:4/C54:11	875.77	0.30±0.07	0.35±0.07	0.99±0.18*	0.97±0.16
C53:3/C54:10	877.78	0.61±0.06	0.77±0.08	2.66±0.16*	1.93±0.12†
C53:2/C54:9	879.71	0.49±0.05	0.57±0.06	3.05±0.22*	2.00±0.14†
C53:1/C54:8	881.72	0.33±0.03	0.35±0.03	2.37±0.14*	1.64±0.07
C53:0/C54:7	883.74	0.21±0.01	0.24±0.02	0.62±0.03*	0.54±0.05
C54:6	885.75	0.47±0.04	0.60±0.05	2.04±0.11*	1.60±0.15
C54:5/C55:12	887.77	0.95±0.15	1.25±0.15	7.44±0.57*	5.09±0.52†
C54:4/C55:11	889.78	1.51±0.26	1.92±0.24	17.89±1.46*	11.84±1.19†
C54:3/C55:10	891.80	1.21±0.18	1.35±0.16	18.24±1.44*	11.83±1.07†
C54:2/C55:9	893.81	0.31±0.03	0.33±0.03	4.04±0.36*	2.76±0.21
C54:1/C55:8	895.83	0.11±0.00	0.10±0.01	0.46±0.04	0.47±0.08
C54:0/C55:7	897.85	0.19±0.03	0.18±0.03	0.24±0.04	0.40±0.10
C55:6	899.77	0.08±0.01	0.07±0.00	0.12±0.01	0.94±0.70
C55:5/C56:12	901.78	0.16±0.01	0.18±0.01	0.40±0.03	0.56±0.21
C55:4/C56:11	903.80	0.30±0.03	0.38±0.03	1.54±0.12*	1.10±0.08†
C55:3/C56:10	905.72	0.28±0.03	0.34±0.03	2.16±0.17*	1.41±0.09†
C55:2/C56:9	907.74	0.23±0.02	0.26±0.02	1.93±0.13*	1.27±0.07†
C55:1/C56:8	909.75	0.20±0.01	0.24±0.02	0.67±0.03	0.55±0.06
C55:0/C56:7	911.77	0.22±0.01	0.25±0.02	0.83±0.04*	0.62±0.04†
C56:6	913.78	0.15±0.01	0.16±0.01	1.00±0.05*	0.76±0.05†

C56:5/C57:12	915.80	0.12±0.01	0.12±0.01	0.87±0.05*	0.70±0.04†
C56:4/C57:11	917.81	0.13±0.01	0.14±0.01	0.75±0.05*	0.58±0.05†
C56:3/C57:10	919.83	0.14±0.01	0.14±0.01	0.62±0.04*	0.52±0.05
C56:2/C57:9	921.85	0.11±0.02	0.09±0.00	0.31±0.02	0.94±0.56
C56:1/C57:8	923.86	0.27±0.02	0.25±0.03	0.28±0.04	0.84±0.51
C57:4/C58:11	931.74	0.05±0.00	0.05±0.00	0.10±0.01	0.13±0.03
C57:3/C58:10	933.75	0.06±0.00	0.07±0.00	0.12±0.01	0.12±0.02
C57:2/C58:9	935.77	0.11±0.01	0.11±0.01	0.20±0.01	0.26±0.07
C57:1/C58:8	937.78	0.13±0.01	0.13±0.01	0.29±0.02*	0.30±0.07
C57:0/C58:7/C59:14	939.80	0.13±0.02	0.11±0.01	0.27±0.02	0.32±0.08
C58:6/C59:13	941.81	0.06±0.01	0.05±0.01	0.15±0.01	0.23±0.07
C58:4/C59:11	945.85	0.05±0.00	0.05±0.00	0.18±0.01	0.19±0.05
C58:3/C59:10	947.86	0.11±0.00	0.08±0.00	0.21±0.01	0.24±0.05
C58:2/C59:9	949.88	0.04±0.00	0.03±0.00	0.06±0.01	0.60±0.45
C58:1/C59:8/C60:15	951.89	0.14±0.01	0.12±0.01	0.10±0.02	0.54±0.39
C59:4/C60:11	959.77	0.04±0.00	0.04±0.00	0.07±0.01	0.18±0.11
C59:3/C60:10	961.78	0.03±0.00	0.03±0.00	0.08±0.01	0.15±0.07
C60:6/C61:13	969.85	0.04±0.00	0.04±0.00	0.11±0.01	0.21±0.09
C60:5/C61:12	971.86	0.14±0.02	0.17±0.03	0.24±0.02	0.24±0.04
C60:4/C61:11	973.88	0.04±0.00	0.04±0.00	0.14±0.01	0.27±0.15
Sum		33.16±2.29	35.06±3.32	180.32±9.42*	134.27±7.96†

TAG Fatty acyl chain content	MASS				
14:0	228.00	4.22±0.49	3.80±0.35	9.50±0.72*	9.24±0.80
16:0	256.00	20.44±1.60	20.80±2.54	111.32±7.35*	96.77±16.79
16:1	254.00	14.22±1.60	15.66±2.04	41.94±1.49*	30.49±2.01†
18:0	284.00	4.15±0.25	3.92±0.20	25.73±1.52*	21.50±1.36†
18:1	282.00	23.51±2.80	27.06±3.18	216.46±14.84*	143.58±12.47†
18:2	280.00	12.66±1.45	15.66±1.79	79.42±5.70*	55.67±4.86†
18:3	278.00	3.49±0.19	3.28±0.19	10.54±0.48*	11.79±1.63
20:0	312.00	2.42±0.20	2.27±0.18	5.30±0.73*	6.77±1.15
20:1	310.00	2.69±0.18	2.54±0.20	6.22±0.60*	6.65±0.73
20:3	306.00	1.78±0.18	1.63±0.17	4.21±0.51*	4.96±0.69
20:4	304.00	2.64±0.28	2.50±0.20	10.46±0.52*	8.47±0.58†
20:5	302.00	4.54±1.12	4.43±0.71	9.59±2.23*	10.18±1.62
22:0	340.00	2.61±0.06	2.28±0.15	5.54±0.56*	5.68±0.69
22:1	338.00	2.72±0.44	2.87±0.53	5.07±1.24*	6.19±1.09
22:2	336.00	1.49±0.15	1.22±0.10	2.80±0.48*	4.75±1.26
22:3	334.00	2.07±0.10	1.83±0.13	3.12±0.43*	6.77±2.96
22:6	328.00	2.54±0.13	2.30±0.10	4.05±0.54*	5.50±1.02
Sum		108.18±7.16	114.06±9.07	551.28±26.47*	434.96±26.79†

Data represents mean ± SEM. * p<0.05 vs. WT/CD, † p<0.05 vs. WT/HFD

Supplementary Table 4. Primer sequences for qRT-PCR and ChIP-qPCR.**A. qRT-PCR**

Human Gene	Forward (5' to 3')	Reverse (5' to 3')
<i>ARRDC4</i>	TCCCACCTGTTACTCCATCC	CACTAATGGCAGTTCGAGCA
<i>MLXIP</i> (MondoA)	GCTCACCAAGCTCTTCGAGT	GCCGGATCTTGTCTCTCCAC
<i>TXNIP</i>	AGTTTCCTGCATGTTTCATTCT	CCACAATTCGGGAACATGTATT
<i>ACSL1</i>	GGCTCAGCACTGATCCAGAA	GAACGATCACCATCGAATAAGCA
<i>ACSL4</i>	GCCGAATGGATGATTGCAGC	GCCTCAGATTTCATTTAGCCCA
<i>FADS1</i>	GTGGCTAGTGATCGACCGTA	GGCCCTTGTTGATGTGGAAG
<i>FADS2</i>	CTGGAATTCGTGGGCAAGTTC	GTTTCATGTCCTCAGCCGTCTT
<i>FASN</i>	GATGCCTCCTTCTTCGGAGT	CCTCGGAGTGAATCTGGGTT
<i>ELOVL5</i>	GTGCACATTCCCTCTTGTTG	ATGGACCCATTCTGGTGGTC
<i>SCD1</i>	CTTCTCTCACGTGGGTTGGC	CATCAGCAAGCCAGGTTTGTAG
<i>SLC2A4</i> (GLUT4)	TATCATCTCTCAGTGGCTTGGA	CCAAGGATGAGCATTTCATAGG
<i>KLF10</i>	ATCTGAAGGCCACACGAG	GCCTGTGTCTGGACAGTTCAT
<i>KLF11</i>	ATGTCACCACCACTGTGCAT	GATGGCTCCACGAGATCAGG
<i>GFPT1</i>	GCCAGAGTCTGTCTGAACA	AATCAAACGCCGGCATCTCT
<i>GFPT2</i>	GCAAGAGATCATCCGTGGCT	CCATCACCAGCAGCGATCT
<i>PPP1R3A</i>	GGACAAGGAAGATTTGGAAGCC	TCCTTTCATCTCTGGAAGCAGT
<i>C1QL4</i>	CAGGCGTCTACTTCTTCGCT	TGCTGGCGTAGTCGTAGTTC
<i>CDKN1C</i>	TGAGCCAATTTAGAGCCCAA	GTTGCTGCTACATGAACGGT
<i>CPA4</i>	TGCAACACAATGAAGGGCAAG	CGGCAATGTTGTCCATCTCG
<i>GATM</i>	AGAGGCCAGGAACATTCCG	GCACCCATCCTGTCAAGGTT
<i>IFIT1</i>	GAGGAGCCTGGCTAAGCAAA	GCTCCAGACTATCCTTGACCTG
<i>KISS1</i>	CCACCCTCTGGACATTCAC	GCTGCCAAGAAACCAGTGAG
<i>LIPA</i>	TTCCTCATGGGAGGAAGAAC	CTGCTGTTGGCAAGGTTTGT
<i>RPLP0</i> (36B4)	TCTACAACCCTGAAGTGCTTGAT	GATAGAATGGGGTACTGATGCAA

Mouse Gene	Forward (5' to 3')	Reverse (5' to 3')
<i>Acsl3</i>	CAGTGCAGGCTCTAGGAGTG	GGAATTCCTGTGGACCCACTT
<i>Acsl4</i>	TTGGCTCATGTGCTGGAAC	ACAATCACCCTTGCTTCCCTT
<i>Arrdc4</i>	CAGCCTCCTCAGAAGTGGAAT	TCAGACGGAAGCTGAAAGCG

<i>Dgat1</i>	GTGCACAAGTGGTGCATCAG	CAGTGGGATCTGAGCCATCA
<i>Dgat2</i>	GCATTTGACTGGAACACGCC	CTGGTGGTCAGCAGGTTGTG
<i>Elovl5</i>	AGATCACCGTGCTCCATGTC	ATGAAGCTGTTGAGTGTCGC
<i>Elovl6</i>	CGTAGCGACTCCGAAGATCA	AGCGTACAGCGCAGAAAACA
<i>Fasdl</i>	GGAAC TTCCTTGGTGCCCTT	GTCGAGGTGCCAAAGACTGA
<i>Fasn</i>	CCAAGCAGGCACACACAATG	GTTTCGTCCTCGGAGTGAGG
<i>Gfpt1</i>	TCTGATGCAAGTGCCGTGAT	GATGGTCTCCTGCAGTTCGT
<i>Gfpt2</i>	CTGAGCGTGATTCCACTCCA	CAGGTGACGACAGTCTTGTGA
<i>Klf10</i>	ACCATGCTCAACTTCGGCG	AGTCACTCTGCTCAGCTTTGT
<i>Klf11</i>	CAGCTGCACCTGATCTACCA	GGCAGTGACCATGCATCCTT
<i>Mxip</i> (MondoA)	TGCTACCTGCCACAGGAGTC	GACTCAAACAGTGGCTTGATGA
<i>Ppp1r3a</i>	GACGAACACAATGGAAAGGAGC	AGCTTGCTTCTTCTCTGACCC
<i>Scd1</i>	CCAAGCTGGAGTACGTCTGG	CAGAGCGCTGGTCATGTAGT
<i>Txnip</i>	GTCTCAGCAGTGCAAACAGACTT	GCTCGAAGCCGAACTTGTACTC
<i>Rplp0</i> (36B4)	TGGAAGTCCAACTACTTCCTCAA	ATCTGCTGCATCTGCTTGGAG

B. ChIP-qPCR

Human promoter	Forward (5' to 3')	Reverse (5' to 3')
<i>TXNIP ChoRE</i>	CCGGGCAGCCAATGGGAG	GCAGGAGGCGGAAACGTCTC
<i>ARRDC4 ChoRE</i>	CGGAGATAACCCTGTTCCGC	CAGGCCGTTTACTGGCTGA