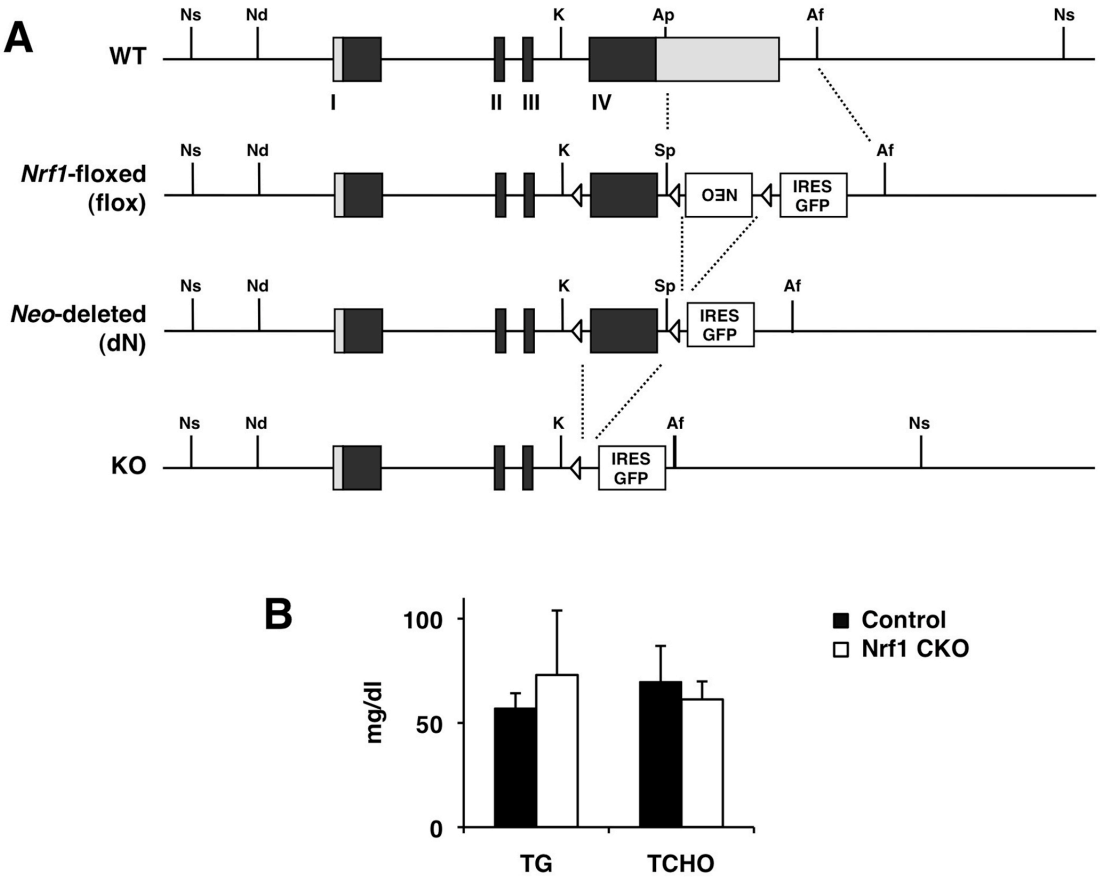

FIG. S1. Generation of *Nrf1* CKO mice using the *Neo*-deleted (dN) allele. (A) The structure of the *Nrf1* wild-type (WT), *Nrf1*-floxed (Ohtsuji et al., 2008), dN, and *Nrf1*-deleted (KO) alleles is shown. *Neo* gene was removed from *Nrf1*-floxed allele to generate dN allele by mating with *Ayu1-Cre* mice that express ubiquitous Cre recombinase. (B) Serum triglyceride (TG) and serum total cholesterol (TCHO) in the control and *Nrf1* CKO mice. The data represent the mean ± SD (n = 3-4)

Table S1. Oligonucleotides used for qRT-PCR, ChIP-qPCR and EMSA.

Name	Sequence
Primers used for qRT-PCR	
Acox1 forward	5'-GCCCAACTGTGACTTCCATC-3'
Acox1 reverse	5'-CCAGGACTATCGCATGATTG-3'
Ahcy forward	5'-GAGAACGCGGTGGAGAAAG-3'
Ahcy reverse	5'-CGCCCATTCTTTAGCCAGTA-3'
Akr1d1 forward	5'-AGGCCATCAGAGAAAAGATAGC-3'
Akr1d1 reverse	5'-CATTGATGGGACATGCTCTG-3'
Fads1 forward	5'-AACATGCACCCCCTCTTCTT-3'
Fads1 reverse	5'-TGGTTGTATGGCATGTGCTT-3'
Gnmt forward	5'-GCTGGACGTAGCCTGTGG-3'
Gnmt reverse	5'-CACGCTCATCACGCTGAA-3'
Hadh forward	5'-TGAAGCTGAAGAACGAGCTG-3'
Hadh reverse	5'-TTGCTGGCAAAGATGGTGT-3'
Hmgcs2 forward	5'-TTTTCATTCCGAGTGTCCAA-3'
Hmgcs2 reverse	5'-CACACTAGACACCAGTTTCTCCA-3'
Hprt forward	5'-CTGGTGAAAAGGACCTCTCG-3'
Hprt probe	5'-FAM-ATCCAACAAAGTCTGGCCTGTATCCAAC-TAMRA-3'
Hprt reverse	5'-TGAAGTACTCATTATAGTCAAGGG-3'
Lipin1 forward	5'-TCCCAGTTCGGACAGAGAAT-3'
Lipin1 probe	5'-FAM-TCCCCCAGCCCCAGCAG-TAMRA-3'
Lipin1 reverse	5'-GGAGTCCTCTGGCAATCTACC-3'
Mat1a forward	5'-TCTGAGGCGCTCTGGTGT-3'
Mat1a reverse	5'-CCTGCATGTACTGAACTGTTACCT-3'
Nnmt forward	5'-TGTGATCTTGAAGGCAACAGA-3'
Nnmt reverse	5'-CTTGATTGCACGCCTCAAC-3'
Nrf1 forward	5'-ACAGCAGTGGCAAGATCTCA-3'
Nrf1 probe	5'-FAM-TGGAAATGCAGGCTATGGAAGTAAATACAT-TAMRA-3'
Nrf1 reverse	5'-GCAAGGCTGTAGTTGGTGCT-3'
Nrf2 forward	5'-CAAGACTTGGGCCACTTAAAAGAC-3'
Nrf2 probe	5'-FAM-AGGCGGCTCAGCACCTTGTATCTTG-TAMRA-3'
Nrf2 reverse	5'-AGTAAGGCTTTCCATCCTCATCAC-3'
PGC-1α forward	5'-ACCGCAGTCGCAACATGCTCA-3'
PGC-1α reverse	5'-GGAACCCTTGGGGTCATTTGGTG-3'
PGC-1β forward	5'-GACGTGGACGAGCTTTCACT-3'
PGC-1β probe	5'-FAM-TACAGAAGCTCCTCCTGGCCACAT-TAMRA-3'
PGC-1β reverse	5'-GAGCGTCAGAGCTTGCTGTT-3'
PPARα forward	5'-GCTCCGAGGGCTCTGTCATC-3'
PPARα probe	5'-FAM-ACACCCTCTCTCCAGCTTCC-TAMRA-3'
PPARα reverse	5'-GGGCAGCTGACTGAGGAAGG-3'
PPARγ forward	5'-CATGCTTGTGAAGGATGCAAG-3'
PPARγ reverse	5'-TTCTGAAACCGACAGTACTGACAT-3'
SREBP1 forward	5'-GATGTGCGAACTGGACACAG-3'
SREBP1 reverse	5'-CATAGGGGGCGTCAAACAG-3'
Primers used for ChIP-qPCR	
Lipin1 intron forward	5'-CAGAGGCACACTTGCTGAGT-3'
Lipin1 intron reverse	5'-GTTAGCTCCATCTGTGTGGAATTA-3'
Lipin1 promoter forward	5'-GCCCTAGGCAGTGTTTTGTC-3'
Table S1 (continued)	

Lipin1 promoter reverse	5’-CCTCAGTTCTCTGGCTGAGTC-3’
Nqo1 promoter forward	5’-GCACGAATTCATTTCACACGAGG-3’
Nqo1 promoter probe	5’-FAM-AACGGATGGGCTCAAATTTTGC-TAMRA-3’
Nqo1 promoter reverse	5’-GGAAGTCACCTTTGCACGCTAG-3’
PGC-1β intron forward	5’-TAGATGCTTCTGGGCCTAGC-3’
PGC-1β intron reverse	5’-CACAGACTGAGTGGGTGTAT-3’
PPARα 3’ UTR forward	5’-ATCCTGGTGAGGGTTGAGC-3’
PPARα 3’ UTR reverse	5’-AAGCACTGAGGACTGGCTGT-3’
PPARα promoter forward	5’-CCCACTTGGAGACTCATCATGGGGT-3’
PPARα promoter reverse	5’-AGGAAGGGATGCGTTTGCTCTGA-3’
Txs intron3 forward	5’-GCAATAGGACTATCATGCGC-3’
Txs intron3 reverse	5’-ATGACAGGTCCAAACGAGAG-3’
Txs intron3 probe	5’-FAM-GAAGATGCCTTCAAAGGACAAGTACCC-TAMRA-3’
Oligonucleotides used for EMSA	
Lipin1 intron ARE WT forward	5’-CGCGGAGGCACACTTGCTGAGTCAGCACCCCGGGAGT-3’
Lipin1 intron ARE WT reverse	5’-CTAGACTCCCGGGGTGCTGACTCAGCAAGTGTGCCTC-3’
Lipin1 intron ARE Mut forward	5’-CGCGGAGGCACACTTTCTGAGTCAGAACCCCGGGAGT-3’
Lipin1 intron ARE Mut reverse	5’-CTAGACTCCCGGGGTTCTGACTCAGAAAGTGTGCCTC-3’
Lipin1 promoter ARE WT forward	5’-CGCGTGCCGCTGAGCTGTGACTCAGCCAGAGAACTGA-3’
Lipin1 promoter ARE WT reverse	5’-CTAGTCAGTTCTCTGGCTGAGTCACAGCTCAGCGGCA-3’
Lipin1 promoter ARE Mut forward	5’-CGCGTGCCGCTGAGCTGTGACTCAGACAGAGAACTGA-3’
Lipin1 promoter ARE Mut reverse	5’-CTAGTCAGTTCTCTGTCTGAGTCACAGCTCAGCGGCA-3’
Nqo1 promoter ARE WT forward	5’-CGCGTCTAGAGTCACAGTGAGTCGGCAAAATTTGAGC-3’
Nqo1 promoter ARE WT reverse	5’-CTAGGCTCAAATTTTGCCGACTCACTGTGACTCTAGA-3’
Nqo1 promoter ARE Mut forward	5’-CGCGTCTAGAGTCACAGTGAGTCGACAAAATTTGAGC-3’
Nqo1 promoter ARE Mut reverse	5’-CTAGGCTCAAATTTTGTCGACTCACTGTGACTCTAGA-3’
PGC-1β intron ARE WT forward	5’-CGCGGAGGGGAACATGCTGACTCAGCAGCTCCGAATA-3’
PGC-1β intron ARE WT reverse	5’-CTAGTATTCGGAGCTGCTGAGTCAGCATGTTCCCCTC-3’
PGC-1β intron ARE Mut forward	5’-CGCGGAGGGGAACATTCTGACTCAGAAGCTCCGAATA-3’
PGC-1β intron ARE Mut reverse	5’-CTAGTATTCGGAGCTTCTGAGTCAGAATGTTCCCCTC-3’

Table S2. The pathway analysis in *Nrf1* CKO mice.

Enriched events in downregulated genes in *Nrf1* CKO mice	
p-value	**Name of Event / List of Genes**
1.52E-18	**Metabolism of amino acids and derivatives**
	SLC38A4, SLC25A2, PSMD7, UROC1, ACADSB, PSMB1, MCCC2, GLS2, PAOX, PSMD4, HIBADH, IVD, TAT, PSMA6, GAMT, BBOX1, DLST, SLC3A1, SLC16A10, GPT2, HAAO, GCDH, BCKDHB, SLC38A3, FAH, PSMC2, PAH, SLC38A2, AFMID, PSMC6, GPT, AADAT, AGMAT, ALDH7A1, PSMA5, PSMC3, ASL, PSMC1, OTC, PSMD9, PSMB7, SHMT1, AGXT, PSMA7, AASS, SLC6A6, PSMD2, SLC6A12, PSMD3, PSMD12, ALDH6A1, HPD, OAZ1, SLC7A2, FTCD, ASS, HIBCH, QDPR, ARG1, TDO2, PSMB4
1.50E-07	**Respiratory electron transport, ATP synthesis by chemiosmotic coupling, and heat production by uncoupling proteins. (Oxidative phosphorylation)**
	NDUFV2, ATP5I, UQCR, SDHB, NDUFS7, ATP5C1, NDUFA5, UQCRH, NDUFB8, SDHA, NDUFA11, ATP5H, NDUFA1, NDUFB9, NDUFB5, NDUFA10, NDUFS8, NDUFA2, NDUFB7, NDUFA6, ATP5A1, NDUFA9, ATP5G1, ATP5J, ATP5E, NDUFB10
2.57E-06	**Metabolism of lipids and lipoproteins ***
	CYP17A1, SRD5A1, AGT, TM7SF2, PPM1L, STARD5, PEX11A, RXRA, MUT, ELOVL2, CPT1A, APOC3, SLC27A2, DGAT1, LIPE, GPAM, STAR, PRKAG2, DECR1, EBP, DGAT2, PRKAA2, ACSL1, ABCG8, SLC10A1, CYP39A1, MGLL, NCOR1, AKR1D1, ACOX1, DCI, CYP7B1, PRKACB, LCAT, LPIN1, APOA2, HADHSC, HSD3B2, PPARBP, PCCB, HMGCS2, FADS1, IDH1, SLC27A5, ABCC3, ACLY, ACAA1, SLC10A2, HSD11B1
2.69E-06	**Proteasome cleavage of substrate (Proteasome subunit genes)**
	PSMD7, PSMA5, PSMC3, PSMB1, PSMC1, PSMD9, PSMB7, PSMD4, PSMA7, PSMA6, PSMD2, PSMD3, PSMD12, PSMC2, PSMC6, PSMB4
2.61E-0.2	**Pyruvate metabolism and Citric Acid (TCA) cycle**
	DLST, PDHB, SDHB, IDH1, SDHA, PDK1, PDK2, IDH3B
Enriched events in upregulated genes in *Nrf1* CKO mice	
p-value	**Name of Event / List of Genes**
2.41E-20	**Cell Cycle, Mitotic**
	RFC3, TUBA1, BUB1, AURKB, CDH1, CDC25B, RPA2, CKS1B, MCM3, MCM5, CDC6, ANAPC1, MCM6, LIG1, DNCLC1, XPO1, POLA2, SKP2, MCM2, CDC45L, PRKAR2B, PKMYT1, MCM4, CENPJ, CDK6, KIF18A, CDC20, CENPH, NEK2, NUP43, SEC13L1, KIF2C, BIRC5, KIF20A, RRM2, TUBB4, MLF1IP, PLK1, CCNB1, SGOL1, CDC7, AURKA, TSGA14, ANAPC4, CENPF, SGOL2, FEN1, INCENP, UBE2C, CDCA1, CENPE, KNTC1, TUBGCP2, BUB1B, NUP107, CDKN1A, MAD2L1, CCND1, E2F1, PLK4, ORC1L, RFC4, TUBA3, CCNA2, POLD1, FSHPRH1, CCNB2, CCNE2, CDC25C, POLE2, KNTC2, MCM7, E2F2, POLE, CDCA8, PRIM1
3.34E-13	**DNA replication**
	RFC3, KIF20A, MLF1IP, BUB1, PLK1, SGOL1, CDC7, AURKB, CDH1, CENPF, RPA2, MCM3, SGOL2, INCENP, FEN1, MCM5, CDC6, CDCA1, MCM6, LIG1, XPO1, CENPE, KNTC1, BUB1B, POLA2, NUP107, CDKN1A, MAD2L1, CDC45L, MCM2, ORC1L, RFC4, POLD1, FSHPRH1, MCM4, KIF18A, CDC20, POLE2, CENPH, KNTC2, MCM7, POLE, NUP43, CDCA8, SEC13L1, KIF2C, PRIM1, BIRC5

***** PPARα target genes are underlined.

Table S3. Metabolome analysis of *Nrf1* CKO mouse liver.

Pathway / Metabolites	Concentration (nmol/g of wet liver tissue)					
	Control [1]			*Nrf1* CKO [2]		
	1	2	3	1	2	3
Amino acid						
Ala	2,678	2,375	2,454	2,766	2,336	2,487
Arg	8.3	5.9	9.1	28	18	19
Asn	101	100	103	158	127	126
Asp	534	1,627	1,070	531	563	1,247
Cys	1.4	N.D.[3]	0.8	2.2	N.D.	0.9
Gln	3,575	5,213	4,734	4,826	4,327	3,369
Glu	1,063	1,922	1,425	2,148	2,676	2,757
Gly	2,701	2,252	2,371	2,859	2,254	3,242
His	685	671	599	651	440	799
Ile	120	114	148	195	163	188
Leu	297	183	222	414	250	374
Lys	1,133	635	866	1,175	519	1,272
Met	29	22	21	24	19	25
Phe	85	67	86	150	103	111
Pro	210	151	162	259	203	263
Ser	356	340	364	445	276	680
Thr	281	215	260	410	283	413
Trp	32	27	30	41	35	46
Tyr	77	80	91	156	119	165
Val	335	202	274	399	285	388
Amino acid metabolism / Amino acid derivative						
S-Adenosylmethionine	81	78	93	112	106	85
Anthranilic acid	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
Betaine	668	896	698	967	512	937
Betaine aldehyde +H2O	22	26	26	17	12	38
Carnosine	1.1	1.1	2	1.7	1.3	0.6
Choline	187	174	208	237	281	445
Citrulline	58	42	52	56	45	93
Creatine	276	161	188	280	154	266
Creatinine	4.2	4.3	5.2	4.5	4	5.9
N,N-Dimethylglycine	31	37	35	65	44	38
GABA	18	27	22	41	31	26
Glutathione (GSH)	872	81	602	1,039	N.D.	72
Glutathione (GSSG) divalent	1,461	1,708	1,477	1,801	1,560	1,783
Glycerol 3-phosphate	10,103	4,286	6,438	6,435	6,185	5,993
Glycolic acid	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
Glyoxylic acid	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
Homoserine	3.9	4.4	5	5.9	5.1	5.7
2-Hydroxybutyric acid	108	60	83	125	99	138
3-Hydroxybutyric acid	764	1,257	1,343	793	1,494	1,141
Hydroxyproline	20	28	35	33	24	27
Ornithine	389	270	288	388	311	561
2-Oxoisovaleric acid	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
Putrescine	6.1	5.8	6.7	17	12	13
Sarcosine	27	53	34	73	28	67
Spermidine	114	111	99	125	86	118
Spermine	18	23	17	14	12	18
Tyramine	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.

Table S3 (continued 1)

Glycolysis / Gluconeogenesis / Pentose phosphate pathway /TCA cycle						
Acetyl CoA divalent	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
cis-Aconitic acid	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
Citric acid	118	181	148	93	111	107
Dihydroxyacetone phosphate	135	119	125	127	95	88
Erythrose 4-phosphate	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
Fructose 1,6-diphosphate	103	165	129	144	78	68
Fructose 6-phosphate	102	193	89	178	114	33
Fumaric acid	401	648	424	151	139	293
Glucose 1-phosphate	113	158	96	164	93	31
Glucose 6-phosphate	295	655	316	683	407	113
Glyceraldehyde 3-phosphate	19	16	19	16	16	8.3
Isocitric acid	9	10	9.1	6.2	6.9	5.1
Lactic acid	35,846	13,736	19,255	26,387	22,028	13,047
Malic acid	2,457	4,633	2,873	1,087	950	2,161
Malonyl CoA (divalent)	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
2-Oxoglutaric acid	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
2-Phosphoglyceric acid	6.8	6.6	5	11	4.6	6.5
3-Phosphoglyceric acid	91	80	65	157	42	76
6-Phosphogluconic acid	32	37	31	29	29	12
Phosphoenolpyruvic acid	6.8	4	3.6	14	4.4	5
5-phosphoribosyl-α-1-pyrophosphate	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
Pyruvic acid	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
Ribose 5-phosphate	28	24	22	33	20	25
Ribulose 5-phosphate	755	575	494	670	472	435
Sedoheptulose 7-phosphate	204	430	193	249	253	90
Succinic acid	2,019	1,442	1,465	1,632	2,497	1,442
Purine / Pyrimidine metabolism						
Adenine	6.8	7.3	7.9	9	9.1	7.7
Adenosine	26	31	26	26	23	20
ADP	658	806	779	376	602	619
AMP	5,621	3,212	3,367	3,455	2,001	3,330
ATP	35	97	88	32	113	70
cAMP	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
CDP	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
cGMP	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
CMP	135	91	110	74	76	82
CTP	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
Cytidine	1.3	1.3	1.3	1.7	2.1	2.1
Cytosine	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
dATP	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
dCTP	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
dTDP	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
dTMP	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
dTTP	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
GDP	10	16	15	11	18	15
GMP	674	557	579	566	459	644
GTP	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
Guanine	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
Guanosine	7.6	9	7	8.4	8.1	5.7
Hypoxanthine	81	42	47	79	64	60
IMP	377	227	186	276	401	128

Table S3 (continued 2)

Inosine	152	93	85	230	144	110
Thymidine	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
Thymine	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.
UDP	7.6	12	9	6.2	18	8.3
UMP	1,459	948	1,076	951	847	1,005
Uracil	13	7.9	8.8	32	16	18
Uridine	93	65	79	269	143	122
UTP	N.D.	N.D.	N.D.	N.D.	5.3	N.D.
Others						
NAD+	1,212	1,022	906	697	883	935
NADP+	76	67	52	61	54	72
Gluconic acid	2,433	1,281	1,692	1,600	1,246	1,665
CoA (divalent)	8.3	4.6	8.7	11	6	14

[1,2] Three biological replicates (1-3) were prepared; [3] N.D., Not detected