Supplemental Table 1. Mouse real-time PCR primer sequence and shRNA sequences

Gene Names	Forward	Reverse
ACSL1	ATCTGGTGGAACGAGGCAAG	TCCTTTGGGGTTGCCTGTAG
ACSL3	TCTTGCAAACAAAGCTGAAGGA	GGTTGGAGGCTTCCCATCAA
ACSL4	CTTCCTCTTAAGGCCGGGAC	TGCCATAGCGTTTTTCTTAGATTT
ACSL5	GGCCAAACAGAATGCACAGG	GATGCAGATCTCGCCTTCGT
SREBP1C	CAAGGCCATCGACTACATCCG	CACCACTTCGGGTTTCATGC
ACC1	AGCACAGCTCCAGATTGCCA	GGAGATACCCCATACATCATAC
FASN	GTGATAGCCGGTATGTCGGG	TAGAGCCCAGCCTTCCATCT
SCD1	CTGCAGGTTGTGCTAGATGGGATGG	GCCTGGGGTCTTTGGTAAGTAGGC
DGAT1	TGGTAGTGGGCCCAAGGTAG	GAATCTTGCAGACGATGGCAC
DGAT2	GGCTACGTTGGCTGGTAACT	TCTTCAGGGTGACTGCGTTC
ELOVL3	TACTTCTTTGGCTCTCGCCC	AGCTTACCCAGTACTCCTCCA
LDLR	ACCTGCCGACCTGATGAATTC	GCAGTCATGTTCACGGTCACA
PCSK9	TTGCAGCAGCTGGGAACTT	CCGACTGTGATGACCTCTGGA
HMGCR	CTTTCAGAAACGAACTGTAGCTCAC	CTAGTGGAAGATGAATGGACATGAT
HMGCS1	TTTGATGCAGCTGTTTGAGG	CCACCTGTAGGTCTGGCATT
SREBP2	CCAAAGAAGGAGAGAGGCGG	CGCCAGACTTGTGCATCTTG
ACAT1	CAGGAAGTAAGATGCCTGGAAC	TTCACCCCCTTGGATGACATT
ACAT2	CCCGTGGTCATCGTCTCAG	GGACAGGGCACCATTGAAGG
ACLY	TGCCCCAAGATTCAGTCCCA	ACGATGGCCTTGGTATGTCG
PMVK	TCTACTGAGCGGGTCCACTT	CTCCAAGTCTGCTCTTCAGCC
SHP	CCGTGGAATGGAGTCTGG	CTTGCTGGACAGTTAGTAGTG
CYP7A1	GGGATTGCTGTGGTAGTGAGC	GGTATGGAATCAACCCGTTGTC
CYP8B1	GATGGCACCCGGAAAGTGGA	TAGTGGTGGATCTTCTTGCC
CYP7B1	CCCTGCGTGACGAAATTGAC	AGAATAGTGCTTTCCAGGCAGA
CYP27A1	CCAGGCACAGGAGAGTACG	GGGCAAGTGCAGCACATAG
CYP46A1	CACCCTGGCAAAGTTCATGC	CAGAACCTCATCGTCCTGAGC
BAAT	GGTTGCTGTAAAACTACTGTTTTGG	TGTGCACAGGCTCATCAACA
ACOX2	TCGGCAAAAACTTCCAAATC	GGCTGTGTATCACAAACTCCTG
GAPDH	ATGGTGAAGGTCGGTGTGAA	ACTGGAACATGTAGACCATGTAGT
ACSL1 shRNA	CCGGCCGAAGATCTTGCGATAATTTCTCGAGAAATTATCGCAAGATCTTCGGTTTTTG	
Scramble shRNA	GACACGCGACTTGTACCACTTCAAGAGAGTGGTACAAGTCGCGTGTCTTTTTTACGCGT	

Supplemental Table 2. Individual BA levels of pooled serum samples of Ad-shAcsl1 and Ad-shU6-C injected mice were quantified.

	Ad-shU6-C (μM)	Ad-shAcsl1 (μM)
CDCA	31.1	n.a.
CA	39.3	50.2
DCA	59.7	61.9
LCA	41.1	38.7
TCDCA	5.9	10.9
TCA	180.8	92.7
TDCA	4.2	6.8
TLCA	5.2	6.6
Total	**367.3**	**267.8**

Supplemental Table 3. A detailed list of genes and fold changes in Reactome pathways presented in Figure 5 B, D and supplemental Figure 3 A-D.

BILE ACID METABOLISM

List of Gene	Gene Symbol	Gene Title	Fold Change	P value
1	CH25H	Cholesterol 25-hydroxylase	1.70	0.005
2	CYP7A1	Cytochrome p450 family 7 subfamily a member 1	1.30	0.160
3	ALB	Albumin	1.00	0.600
4	CYP39A1	Cytochrome p450 family 39 subfamily a member 1	1.00	0.670
5	FABP6	Fatty acid binding protein 6	-1.10	0.530
6	ABCC3	ATP binding cassette subfamily c member 3	-1.10	0.450
7	ABCB11	ATP binding cassette subfamily b member 11	-1.10	0.440
8	HSD3B7	Hydroxy-delta-5-steroid dehydrogenase, 3 beta- and steroid delta-isomerase 7	-1.10	0.400
9	SLC27A2	Solute carrier family 27 member 2	-1.10	0.099
10	SCP2	Sterol carrier protein 2	-1.20	0.026
11	SLC10A1	Solute carrier family 10 member 1	-1.30	0.099
12	CYP27A1	Cytochrome p450 family 27 subfamily a member 1	-1.30	0.046
13	SLC27A5	Solute carrier family 27 member 5	-1.30	0.042
14	CYP46A1	Cytochrome p450 family 46 subfamily a member 1	-1.30	0.014
15	HSD17B4	Hydroxysteroid 17-beta dehydrogenase 4	-1.30	0.004
16	AMACR	Alpha-methylacyl-coa racemase	-1.40	0.003
17	ACOX2	Acyl-coa oxidase 2	-1.40	0.001
18	AKR1D1	Aaldo-keto reductase family 1 member d1	-1.50	0.013
19	ACOT8	Acyl-coa thioesterase 8	-1.60	0.003
20	CYP7B1	Cytochrome p450 family 7 subfamily b member 1	-2.00	0.033
21	SLC10A2	Solute carrier family 10 member 2	-2.00	0.001
22	BAAT	Bile acid-coa:amino acid n-acyltransferase	-2.00	0.000
23	CYP8B1	Cytochrome p450 family 8 subfamily b member 1	-2.30	0.018

CHOLESTEROL METABOLISM

List of Gene	Gene Symbol	Gene Title	Fold Change	P value
1	APP	Amyloid beta precursor protein	2.20	0.000
2	CLN6	Ceroid-lipofuscinosis, neuronal 6, late infantile, variant	2.50	0.000
3	LEPR	Leptin receptor	3.20	0.000
4	CFTR	Cystic fibrosis transmembrane conductance regulator	1.60	0.000
5	CYP1B1	Cytochrome p450 family 1 subfamily b member 1	4.70	0.001
6	SOAT1	Sterol o-acyltransferase 1	2.20	0.001
7	ABCA1	ATP binding cassette subfamily a member 1	1.40	0.003
8	ABCG1	ATP binding cassette subfamily g member 1	2.00	0.004
9	CH25H	Cholesterol 25-hydroxylase	1.70	0.005
10	TRERF1	Transcriptional regulating factor 1	1.50	0.006
11	NPC1	NPC intracellular cholesterol transporter 1	1.30	0.006
12	LRP5	LDL receptor related protein 5	1.30	0.006
13	SCARB1	Scavenger receptor class b member 1	1.30	0.009
14	ERLIN1	ER lipid raft associated 1	1.40	0.015
15	STARD3	Star related lipid transfer domain containing 3	1.20	0.052
16	PRKAA1	Protein kinase amp-activated catalytic subunit alpha 1	1.20	0.060
17	NPC2	NPC intracellular cholesterol transporter 2	1.30	0.064
18	SCAP	SREBF chaperone	1.10	0.073
19	SNX17	Sorting nexin 17	1.20	0.089
20	CYB5R1	Cytochrome b5 reductase 1	1.30	0.090
21	LBR	Lamin b receptor	1.30	0.130
22	CYP7A1	Cytochrome p450 family 7 subfamily a member 1	1.30	0.160
23	SORL1	Sortilin related receptor 1	1.30	0.230
24	APOA1	Apolipoprotein a1	1.10	0.250
25	APOBR	Apolipoprotein b receptor	1.20	0.270
26	MBTPS2	Membrane bound transcription factor peptidase, site 2	1.10	0.290
27	TNFSF4	Tumor necrosis factor superfamily member 4	1.10	0.430
28	CYP11B2	Cytochrome p450 family 11 subfamily b member 2	-1.20	0.220
29	CYP39A1	Cytochrome p450 family 39 subfamily a member 1	1.00	0.670
30	CUBN	Cubilin	1.00	0.720
31	LDLRAP1	Low density lipoprotein receptor adaptor protein 1	1.00	0.750
32	OSBPL1A	Oxysterol binding protein like 1a	1.00	0.770
33	CYP11A1	Cytochrome p450 family 11 subfamily a member 1	1.00	0.930
34	SREBF2	Sterol regulatory element binding transcription factor 2	1.00	0.950
35	CEL	Carboxyl ester lipase	1.00	0.950
36	CELA3B	Chymotrypsin like elastase family member 3b	-1.00	0.980
37	CYB5R2	Cytochrome b5 reductase 2	-1.00	0.930
38	RXRA	Retinoid x receptor alpha	-1.00	0.850
39	NPC1L1	NPC1 like intracellular cholesterol transporter 1	-1.00	0.740
40	LIPC	Lipase c, hepatic type	-1.00	0.710

41	PPARD	Peroxisome proliferator activated receptor delta	-1.00	0.710
42	VLDLR	Very low-density lipoprotein receptor	-1.10	0.690
43	CLN8	Ceroid-lipofuscinosis, neuronal 8	-1.10	0.660
44	ERLIN2	ER lipid raft associated 2	-1.00	0.640
45	PRKAG2	Protein kinase amp-activated non-catalytic subunit gamma 2	-1.10	0.630
46	LCAT	Lecithin-cholesterol acyltransferase	-1.00	0.570
47	SQLE	Squalene epoxidase	-1.20	0.540
48	APOE	Apolipoprotein e	-1.00	0.520
49	HDLBP	High density lipoprotein binding protein	-1.00	0.490
50	APOB	Apolipoprotein b	-1.10	0.450
51	IL4	Interleukin 4	-1.10	0.330
52	ARV1	Arv1 homolog, fatty acid homeostasis modulator	-1.10	0.300
53	EBP	Emopamil binding protein (sterol isomerase)	-1.10	0.290
54	LEP	Leptin	-1.10	0.290
55	HMGCS2	3-hydroxy-3-methylglutaryl-coa synthase 2	-1.10	0.280
56	APOA2	Apolipoprotein a2	-1.10	0.260
57	CYP19A1	Cytochrome p450 family 19 subfamily a member 1	-1.10	0.250
58	LIPA	Lipase a, lysosomal acid type	-1.10	0.230
59	PON1	Paraoxonase 1	-1.20	0.220
60	CYP11B1	Cytochrome p450 family 11 subfamily b member 1	1.10	0.520
61	FDX1	Ferredoxin 1	-1.20	0.190
62	SOAT2	Sterol o-acyltransferase 2	-1.20	0.160
63	HMGCR	3-hydroxy-3-methylglutaryl-coa reductase	-1.20	0.110
64	CNBP	CCHC-type zinc finger nucleic acid binding protein	-1.10	0.110
65	INSIG2	Insulin induced gene 2	-1.20	0.100
66	SCARF1	Scavenger receptor class f member 1	-1.10	0.094
67	PRKAA2	Protein kinase amp-activated catalytic subunit alpha 2	-1.20	0.080
68	MVD	Mevalonate diphosphate decarboxylase	-1.30	0.078
69	NR0B2	Nuclear receptor subfamily 0 group b member 2	-1.60	0.070
70	HMGCS1	3-hydroxy-3-methylglutaryl-coa synthase 1	-1.30	0.070
71	GGPS1	Geranylgeranyl diphosphate synthase 1	-1.20	0.064
72	MBTPS1	Membrane bound transcription factor peptidase, site 1	-1.10	0.056
73	OSBPL5	Oxysterol binding protein like 5	-1.30	0.052
74	APOA4	Apolipoprotein a4	-1.20	0.047
75	CYP27A1	Cytochrome p450 family 27 subfamily a member 1	-1.30	0.046
76	ACAA2	Acetyl-coa acyltransferase 2	-1.20	0.044
77	FDXR	Ferredoxin reductase	-1.20	0.043
78	LSS	Lanosterol synthase	-1.50	0.033
79	CYP7B1	Cytochrome p450 family 7 subfamily b member 1	-2.00	0.033
80	DHCR24	24-dehydrocholesterol reductase	-1.20	0.026
81	SC5D	Sterol-c5-desaturase	-1.20	0.020
82	STAR	Steroidogenic acute regulatory protein	-1.30	0.020
83	CYP8B1	Cytochrome p450 family 8 subfamily b member 1	-2.30	0.018
84	CAT	Catalase	-1.20	0.015

85	CYP46A1	Cytochrome p450 family 46 subfamily a member 1	-1.30	0.014
86	HSD17B7	Hydroxysteroid 17-beta dehydrogenase 7	-1.40	0.014
87	AKR1D1	Aldo-keto reductase family 1 member d1	-1.50	0.013
88	IDI1	Isopentenyl-diphosphate delta isomerase 1	-1.40	0.011
89	DHCR7	7-dehydrocholesterol reductase	-1.30	0.007
90	MVK	Mevalonate kinase	-1.30	0.004
91	LIPE	Lipase e, hormone sensitive type	-1.60	0.003
92	PCSK9	Proprotein convertase subtilisin/kexin type 9	-1.70	0.003
93	FDFT1	Farnesyl-diphosphate farnesyltransferase 1	-1.40	0.003
94	ANGPTL3	Angiopoietin like 3	-1.40	0.003
95	APOA5	Apolipoprotein a5	-1.40	0.002
96	TM7SF2	Transmembrane 7 superfamily member 2	-2.30	0.001
97	APOF	Apolipoprotein f	-1.40	0.001
98	NSDHL	NAD(P) dependent steroid dehydrogenase-like	-2.10	0.001
99	LDLR	Low density lipoprotein receptor	-1.70	0.001
100	CYP17A1	Cytochrome p450 family 17 subfamily a member 1	-4.30	0.001
101	CEBPA	CCAAT/enhancer binding protein alpha	-1.40	0.001
102	FDPS	Farnesyl diphosphate synthase	-1.90	0.001
103	SREBF1	Sterol regulatory element binding transcription factor 1	-1.50	0.000
104	ACLY	ATP citrate lyase	-2.10	0.000
105	EBPL	Emopamil binding protein like	-1.60	0.000
106	INSIG1	Insulin induced gene 1	-2.30	0.000
107	PMVK	Phosphomevalonate kinase	-1.70	0.000

TCA CYCLE

List of Gene	Gene Symbol	Gene Title	Fold Change	P value
1	PCK2	Phosphoenolpyruvate carboxykinase 2, mitochondrial	2.000	0.000
2	IDH2	Isocitrate dehydrogenase (NADP (+)) 2, mitochondrial	1.100	0.450
3	SDHC	Succinate dehydrogenase complex subunit C	1.000	0.580
4	PCK1	Phosphoenolpyruvate carboxykinase 1	1.100	0.730
5	OGDH	Oxoglutarate dehydrogenase	1.000	0.760
6	CS	Citrate synthase	-1.000	0.820
7	OGDHL	Oxoglutarate dehydrogenase-like	-1.000	0.800
8	MDH2	Malate dehydrogenase 2	-1.100	0.380
9	IDH3G	Isocitrate dehydrogenase 3 (NAD (+)) gamma	-1.100	0.160
10	PDHA1	Pyruvate dehydrogenase (lipoamide) alpha 1	-1.200	0.093
11	ACO1	Aconitase 1	-1.200	0.088
12	SUCLG2	Succinate-CoA ligase GDP-forming beta subunit	-1.200	0.035
13	IDH3B	Isocitrate dehydrogenase 3 (NAD (+)) beta	-1.200	0.033
14	IDH3A	Isocitrate dehydrogenase 3 (NAD (+)) alpha	-1.200	0.026
15	IDH1	Isocitrate dehydrogenase (NADP (+)) 1, cytosolic	-1.200	0.022
16	DLD	Dihydrolipoamide dehydrogenase	-1.300	0.005
17	SUCLG1	Succinate-CoA ligase alpha subunit	-1.400	0.003
18	DLST	Dihydrolipoamide S-succinyltransferase	-1.300	0.002
19	SDHB	Succinate dehydrogenase complex iron sulfur subunit B	-1.500	0.001
20	SDHA	Succinate dehydrogenase complex flavoprotein subunit A	-1.400	0.000
21	MDH1	Malate dehydrogenase 1	-1.400	0.000
22	ACO2	Aconitase 2	-1.400	0.000
23	ACLY	ATP citrate lyase	-2.100	0.000
24	SUCLA2	Succinate-CoA ligase ADP-forming beta subunit	-1.600	0.000
25	PDHB	Pyruvate dehydrogenase (lipoamide) beta	-1.600	0.000
26	DLAT	Dihydrolipoamide S-acetyltransferase	-1.700	0.000
27	SDHD	Succinate dehydrogenase complex subunit D	-1.500	0.000

PYRUVATE METABOLISM

List of Gene	Gene Symbol	Gene Title	Fold Change	P value
1	ACSS1	Acyl-CoA synthetase short-chain family member 1	5.10	0.000
2	PCK2	Phosphoenolpyruvate carboxykinase 2, mitochondrial	2.00	0.000
3	PKM	Pyruvate kinase, muscle	1.90	0.000
4	ALDH1B1	Aldehyde dehydrogenase 1 family member B1	1.30	0.067
5	ME2	Malic enzyme 2	1.30	0.074
6	HAGHL	Hydroxyacylglutathione hydrolase-like	1.10	0.090
7	PCK1	Phosphoenolpyruvate carboxykinase 1	1.10	0.730
8	LDHB	Lactate dehydrogenase B	1.00	0.920
9	LDHA	Lactate dehydrogenase A	1.00	0.930
10	ALDH9A1	Aldehyde dehydrogenase 9 family member A1	1.00	0.950
11	LDHAL6B	Lactate dehydrogenase A like 6B	-1.10	0.450
12	ACYP2	Acylphosphatase 2	-1.10	0.380
13	MDH2	Malate dehydrogenase 2	-1.10	0.380
14	ALDH7A1	Aldehyde dehydrogenase 7 family member A1	-1.10	0.310
15	ACOT12	Acyl-CoA thioesterase 12	-1.10	0.260
16	LDHC	Lactate dehydrogenase C	-1.20	0.140
17	ME3	Malic enzyme 3	-1.20	0.110
18	PDHA1	Pyruvate dehydrogenase (lipoamide) alpha 1	-1.20	0.093
19	GRHPR	Glyoxylate and hydroxypyruvate reductase	-1.10	0.056
20	ALDH2	Aldehyde dehydrogenase 2 family (mitochondrial)	-1.20	0.048
21	ALDH3A2	Aldehyde dehydrogenase 3 family member A2	-1.20	0.039
22	ACAT1	Acetyl-CoA acetyltransferase 1	-1.20	0.033
23	ACYP1	Acylphosphatase 1	-1.30	0.012
24	LDHD	Lactate dehydrogenase D	-1.50	0.008
25	DLD	Dihydrolipoamide dehydrogenase	-1.30	0.005
26	GLO1	Glyoxalase I	-1.40	0.002
27	ACACA	Acetyl-CoA carboxylase alpha	-1.40	0.002
28	ACACB	Acetyl-CoA carboxylase beta	-1.90	0.002
29	HAGH	Hydroxyacylglutathione hydrolase	-1.50	0.001
30	MDH1	Malate dehydrogenase 1	-1.40	0.000
31	ACSS2	Acyl-CoA synthetase short-chain family member 2	-2.10	0.000
32	PKLR	Pyruvate kinase, liver and RBC	-1.50	0.000
33	PDHB	Pyruvate dehydrogenase (lipoamide) beta	-1.60	0.000
34	DLAT	Dihydrolipoamide S-acetyltransferase	-1.70	0.000
35	ME1	Malic enzyme 1	-1.90	0.000

FATTY ACID METABOLISM

List of Gene	Gene Symbol	Gene Title	Fold Change	P value
1	EHHADH	Enoyl-CoA hydratase and 3-hydroxyacyl CoA Dehydrogenase	1.60	0.000
2	ALDH1B1	Aldehyde dehydrogenase 1 family member B1	1.30	0.067
3	ACADL	Acyl-CoA dehydrogenase, long chain	1.20	0.100
4	ACOX3	Acyl-CoA oxidase 3, pristanoyl	1.00	0.690
5	ACSL3	Acyl-CoA synthetase long-chain family member 3	1.00	0.870
6	ALDH9A1	Aldehyde dehydrogenase 9 family member A1	1.00	0.950
7	HADH	Hydroxyacyl-CoA dehydrogenase	-1.00	0.880
8	ACSL4	Acyl-CoA synthetase long-chain family member 4	-1.00	0.820
9	CPT2	Carnitine palmitoyltransferase 2	-1.00	0.620
10	CPT1A	Carnitine palmitoyltransferase 1A	-1.00	0.560
11	HADHA	Hydroxyacyl-CoA dehydrogenase, alpha subunit	-1.10	0.480
12	ACSL6	Acyl-CoA synthetase long-chain family member 6	-1.10	0.410
13	ALDH7A1	Aldehyde dehydrogenase 7 family member A1	-1.10	0.310
14	CPT1C	Carnitine palmitoyltransferase 1C	-1.20	0.300
15	ACADM	Acyl-CoA dehydrogenase, C-4 to C-12 straight chain	-1.10	0.290
16	ECI2	Enoyl-CoA delta isomerase 2	-1.10	0.140
17	ACADS	Acyl-CoA dehydrogenase, C-2 to C-3 short chain	-1.20	0.051
18	ALDH2	Aldehyde dehydrogenase 2 family (mitochondrial)	-1.20	0.048
19	ACAA2	Acetyl-CoA acyltransferase 2	-1.20	0.044
20	ALDH3A2	Aldehyde dehydrogenase 3 family member A2	-1.20	0.039
21	ACOX1	Acyl-CoA oxidase 1	-1.20	0.038
22	ACADSB	Acyl-CoA dehydrogenase, short/branched chain	-1.20	0.033
23	ACAT1	Acetyl-CoA acetyltransferase 1	-1.20	0.033
24	ADH4	Alcohol dehydrogenase 4 (class II), pi polypeptide	-1.40	0.018
25	ADH5	Alcohol dehydrogenase 5 (class III), chi polypeptide	-1.30	0.014
26	ACADVL	Acyl-CoA dehydrogenase, very long chain	-1.20	0.013
27	ECHS1	Enoyl-CoA hydratase, short chain 1	-1.30	0.004
28	GCDH	Glutaryl-CoA dehydrogenase	-1.60	0.001
29	ECI1	Enoyl-CoA delta isomerase 1	-1.40	0.001
30	ACSL5	Acyl-CoA synthetase long-chain family member 5	-1.40	0.001
31	ADH7	Alcohol dehydrogenase 7	-1.80	0.000
32	ACSL1	Acyl-CoA synthetase long-chain family member 1	-2.00	0.000

TRIGLYCERIDE BIOSYNTHESIS PATHWAY

List of Gene	Gene Symbol	Gene Title	Fold Change	P value
1	LPCAT4	Lysophosphatidylcholine acyltransferase 4	1.90	0.000
2	ELOVL7	Elovl fatty acid elongase 7	2.10	0.000
3	AGPAT4	1-acylglycerol-3-phosphate o-acyltransferase 4	2.00	0.004
4	LPCAT1	Llysophosphatidylcholine acyltransferase 1	1.70	0.005
5	AGPAT1	1-acylglycerol-3-phosphate o-acyltransferase 1	1.30	0.005
6	LPIN2	Lipin 2	1.30	0.046
7	LPIN3	Lipin 3	1.20	0.110
8	GPD1L	Glycerol-3-phosphate dehydrogenase 1-like	1.10	0.170
9	AGPAT5	1-acylglycerol-3-phosphate o-acyltransferase 5	1.10	0.310
10	ELOVL2	Elovl fatty acid elongase 2	1.00	0.670
11	ACSL3	Acyl-coa synthetase long-chain family member 3	1.00	0.870
12	AGPAT3	1-acylglycerol-3-phosphate o-acyltransferase 3	-1.00	0.980
13	LCLAT1	Lysocardiolipin acyltransferase 1	-1.00	0.890
14	ACSL4	Acyl-coa synthetase long-chain family member 4	-1.00	0.820
15	ELOVL1	Elovl fatty acid elongase 1	-1.00	0.800
16	GPAT2	Glycerol-3-phosphate acyltransferase 2, mitochondrial	-1.00	0.760
17	ACSL6	Acyl-coa synthetase long-chain family member 6	-1.10	0.410
18	TECR	Trans-2,3-enoyl-coa reductase	-1.10	0.350
19	ELOVL4	Elovl fatty acid elongase 4	-1.20	0.058
20	DGAT2	Diacylglycerol o-acyltransferase 2	-1.20	0.051
21	LPIN1	Lipin 1	-1.70	0.017
22	AGPAT2	1-acylglycerol-3-phosphate o-acyltransferase 2	-1.20	0.005
23	ACACA	Acetyl-coa carboxylase alpha	-1.40	0.002
24	ACSL5	Acyl-coa synthetase long-chain family member 5	-1.40	0.001
25	ELOVL5	Elovl fatty acid elongase 5	-1.40	0.001
26	DGAT1	Diacylglycerol o-acyltransferase 1	-1.60	0.000
27	ACLY	ATP citrate lyase	-2.10	0.000
28	ELOVL3	Elovl fatty acid elongase 3	-7.90	0.000
29	HSD17B12	Hydroxysteroid 17-beta dehydrogenase 12	-1.70	0.000
30	GPAM	Glycerol-3-phosphate acyltransferase, mitochondrial	-1.70	0.000
31	GPD1	Glycerol-3-phosphate dehydrogenase 1	-1.90	0.000
32	ELOVL6	Elovl fatty acid elongase 6	-2.40	0.000
33	ACSL1	Acyl-coa synthetase long-chain family member 1	-2.00	0.000
34	FASN	Fatty acid synthase	-2.70	0.000

Supplemental Figure legends

Supplemental Figure 1. Effects of adenoviral injection on mouse body weight, food intake, liver weight, liver index and ALT levels.

Male mice fed a HFD for 8 weeks were injected with Ad-shACSL1 or Ad-shU6-C. Body weight and food intake were recorded throughout the treatment duration. After 11-days of adenoviral injection, mice were sacrificed and 4-h fasting serum and liver samples were collected. All data are mean ± SEM of 5-6 liver samples. A, Body weight measurement; B, Food intake; C, Liver weight; D, Liver index. E, ALT serum levels.

Supplemental Figure 2. Measurement of serum total bile acids in HFD-fed mice injected with AcshAcsl1 or Ad-shU6-C. Male mice fed a HFD for 8 weeks were injected with Ad-shACSL1 or Ad-shU6-C. After 11-days of adenoviral injection, mice were sacrificed and 4-h fasting serum and liver samples were collected. Serum total bile acids were measured. All data are mean ± SEM of 4-5 serum samples.

Supplemental Figure 3. Heatmap illustrations of down regulation of gene expression involved in indicated lipid metabolism pathways. Graphs show fold changes in all genes within the indicated pathway that have a p value <0.05.

Supplemental Figure 4. No effects of adenoviral injection on chow-fed mice liver phospholipids and free FA levels. Male C57BL/6J mice fed a NCD were injected with Ad-shACSL1 or Ad-shU6-C. After 11-days of adenoviral injection, mice were sacrificed for collections of fasting serum samples and liver tissues. Lipids were extracted from individual liver homogenates and PL and FFA contents were measured.

Supplementary Figure 5. Obeticholic acid (OCA) downregulated hepatic ACSL1 expression in male mice fed a high fat and high cholesterol diet. Male C57BL/6J mice were fed a HFHCD for 4 weeks and orally treated with OCA (n=4) at the daily dose of 40 mg/kg or vehicle (n=4) for 14 days. Liver tissues were collected after the treatment and analyzed for ACSL1 protein and mRNA levels.

(A) Western blot analysis of hepatic ACSL1 protein and β-actin levels. Levels of ACSL1 were normalized levels of □-actin. Significance was determined by Student's *t*-test. n = 4 mice per group. ** p<0.01.

(B) Real-time PCR was conducted to determine the relative expression levels of Acsl1 mRNAs after normalization with GAPDH mRNA levels. Significance was determined by Student's *t*-test. n = 4 mice per group. ** $p < 0.01$.