

**Supplemental Table 1. Gene Sets Altered in LIRKO livers**

RANK	NAME	FDR q-val
1	CHOLESTEROL_BIOSYNTHESIS	0.000
2	BIOSYNTHESIS_OF_STEROIDS	0.000
3	GLYCINE_SERINE_AND_THREONINE_METABOLISM	0.000
4	PROTEASOME	0.002
5	GAMMA_HEXACHLOROCYCLOHEXANE_DEGRADATION	0.007
6	AMINOACYL_TRNA_BIOSYNTHESIS	0.008
7	TRYPTOPHAN_METABOLISM	0.023
8	PORPHYRIN_AND_CHLOROPHYLL_METABOLISM	0.027
9	CIRCADIAN_EXERCISE	0.038
10	PENTOSE_PHOSPHATE_PATHWAY	0.067
11	UBIQUINONE_BIOSYNTHESIS	0.073
12	OXIDATIVE_PHOSPHORYLATION	0.069
13	PYRUVATE_METABOLISM	0.064
14	GLYCOLYSIS	0.063
15	GLUCONEOGENESIS	0.064
16	GLYCEROPHOSPHOLIPID_METABOLISM	0.064
17	NUCLEOTIDE_METABOLISM	0.082
18	UBIQUITIN_MEDIATED_PROTEOLYSIS	0.109
19	VALINE_LEUCINE_AND_ISOLEUCINE_DEGRADATION	0.111
20	GLYCOSPHINGOLIPID_METABOLISM	0.148
21	N_GLYCAN_BIOSYNTHESIS	0.170
22	BILE_ACID_BIOSYNTHESIS	0.185
23	HISTIDINE_METABOLISM	0.190
24	LYSINE_DEGRADATION	0.190
25	ATP_SYNTHESIS	0.229
26	BLOOD_CLOTTING CASCADE	0.241
27	FLAGELLAR_ASSEMBLY	0.233
28	STARCH_AND_SUCROSE_METABOLISM	0.233
29	TYPE_III_SECRETION_SYSTEM	0.235
30	TYROSINE_METABOLISM	0.232
31	GLUTATHIONE_METABOLISM	0.233
32	GLOBOSIDE_METABOLISM	0.226
33	FRUCTOSE_AND_MANNOSE_METABOLISM	0.237
34	BUTANOATE_METABOLISM	0.244
35	PROPANOATE_METABOLISM	0.247
36	CITRATE_CYCLE_TCA_CYCLE	0.241
37	ALANINE_AND ASPARTATE_METABOLISM	0.239
38	GLYCOLYSIS_AND_GLUCONEOGENESIS	0.245

39	UREA_CYCLE_AND_METABOLISM_OF_AMINO_GROUPS	0.239
40	STATIN_PATHWAY_PHARMGKB	0.373
41	PHOTOSYNTHESIS	0.410
42	METHANE_METABOLISM	0.461
43	KREBS_TCA_CYCLE	0.475
44	ARGININE_AND_PROLINE_METABOLISM	0.512
45	CARBON_FIXATION	0.543
46	RIBOSOMAL_PROTEINS	0.576
47	TRANSLATION_FACTORS	0.575
48	PROSTAGLANDIN_AND_LEUKOTRIENE_METABOLISM	0.594
49	MRNA_PROCESSING.REACTOME	0.586
50	GALACTOSE_METABOLISM	0.577
51	RNA_TRANSCRIPTION.REACTOME	0.588
52	BETA_ALANINE_METABOLISM	0.581
53	GLYCEROLIPID_METABOLISM	0.654
54	PURINE_METABOLISM	0.648
55	BIOGENIC_AMINE_SYNTHESIS	0.761
56	DNA_REPLICATION.REACTOME	0.832
57	RNA_Polymerase	0.933
58	INTEGRIN_MEDIATED_CELL_ADHESION_KEGG	0.946

**Supplemental Table 2. Primer Sequences**

Primer	Sequence
Srebp-1c-F	GGCCCGGGAAAGTCACTGT
Srebp-1c-R	GGAGCCATGGATTGCACATT
Srebp-1a-F	GGCCGAGATGTGCGAAGT
Srebp-1a-R	TTGTTGATGAGCTGGAGCATGT
Srebp2-F	GCGTTCTGGAGACCATGGA
Srebp2-R	ACAAAGTTGCTCTGAAAACAATCA
Insig1-F	TCACAGTGACTGAGCTTCAGCA
Insig1-R	TCATCTTCATCACACACCCAGGAC
Insig2a-F	CCCTCAATGAATGTACTGAAGGATT
Insig2a-R	TGTGAAGTGAAGCAGACCAATGT
Insig2b-F	CCGGGCAGAGCTCAGGAT
Insig2b-R	GAAGCAGACCAATGTTCAATGG
Hmgcr-F	CTTGTGGAATGCCTTGTGATTG
Hmgcr-R	AGCCGAAGCAGCACATGAT
Fdps-F	ATGGAGATGGCGAGTTCTTC
Fdps-R	CCGACCTTCCCCGTACA
Fdft1-F	CCAACTCAATGGGTCTGTTCC
Fdft1-R	TGGCTTAGCAAAGTCTTCCA
Cyp51-F	AGCTGTACGCAGACCTGGAT
Cyp51-R	ACGCCC GT C C T T G T A T G T A G
Ldlr-F	GAGGAGCAGCCACATGGTAT
Ldlr-R	GCTCGTCCTCTGTGGTCTTC
18S-F	GTAACCCGTTGAACCCCATT
18S-R	CCATCCAATCGGTAGTAGCG
Pcsk9-F	CCCCATGTGGAGTACATTGA
Pcsk9-R	GTGGAAGCGTGTCCCATC
Idol-F	ACCGCCCCAATACAGCTATGA
Idol-R	GTTCTCCATCGCTGACACAA
Fasn-F	GCTGCGGAAACTTCAGGAAAT
Fasn-R	AGAGACGTGTCACTCCTGGACTT
Scd1-F	CATCATTCTCATGGTCCTGCT
Scd1-R	CCCAGTCGTACACGTCATTT

## **Supplemental Information**

**Supplemental Figure S1.** *Statin/ezetimibe treatment lowers HDL and non-HDL cholesterol in LIRKO mice.* LIRKO and control mice were fed a diet with or without supplementation with statin/ezetimibe (**S/E**, 0.1% Lovastatin and 0.025% ezetimibe) for one week. Equal amounts of serum were pooled from four to six mice from each group, and subjected to FPLC fractionation. Cholesterol was measured in each fraction.

# Supplemental Figure S1

