C:\Files\WPFiles\PAPER.NEW\ACSS2 gene array paper\Supplementary Figure 1.tif

**Figure S1. (A)** The color scheme indicates the value of the differential gene expressions. **(B)** Shapes indicate the type and function of the DEG products.

C:\Files\WPFiles\PAPER.NEW\ACSS2 gene array paper\gProfiler figure.tif

**Figure S2. gProfiler analysis of organ-specific effects of Acss2 deletion.** **(A)** Upregulated DEG in liver showing enrichment of 18 biological processes (GO:BP). No transcription factor (TF) enrichment is found. **(B)** Downregulated genes in liver showing enrichment of 193 TFs. Correspondingly 38 biological processes are enriched. **(C)** Upregulated genes in brain showing enrichment of 68 TFs with 83 enriched biological processes. **(D)** Downregulated genes in brain showing enrichment of 7 biological processes but a complete lack of TF enrichment. **(E)** Upregulated genes in adipose tissue showing enrichment of 98 transcription factors and 140 biological processes. **(F)** Downregulated genes in adipose tissue showing enrichment of 235 TFs and 50 biological processes. Note Y axes are not to the same scale. GO:BP = bioprocess, GO:MF = molecular function, GO:CC = cellular components, TF = TransFac transcription factor binding motifs. Transcription factors are indicated with arrows. **gProfiler:** <https://biit.cs.ut.ee/gprofiler/page/r>.

**Table S1.** Fatty acid concentration data (μg/ml)

**Table S2**

**Table S2A - Liver.** The -log (p-value) and z-score of the top 10 statistically significant (-log (p-value) > 1.3) and differentially regulated canonical pathways in liver tissue of *Acss2*-/- compared to wild-type mice.

|  |  |  |
| --- | --- | --- |
| **Canonical Pathways** | **-log(p-value)** | **z-score** |
| eNOS Signaling | 2.91 | 0.816 |
| Aldosterone Signaling in Epithelial Cells | 2.87 | -1 |
| Ferroptosis Signaling Pathway | 2.49 | 0.707 |
| LXR/RXR Activation | 2.44 | 1.633 |
| Nitric Oxide Signaling in the Cardiovascular System | 1.82 | -0.447 |
| NER (Nucleotide Excision Repair, Enhanced Pathway) | 1.64 | -0.447 |
| Kinetochore Metaphase Signaling Pathway | 1.58 | -0.447 |
| Xenobiotic Metabolism PXR Signaling Pathway | 1.55 | 1.134 |
| Role of MAPK Signaling in Promoting the Pathogenesis of Influenza | 1.51 | -2 |
| AMPK Signaling | 1.36 | 0.447 |

**Table S2B - Brain.** The -log (p-value) and z-score of the top 10 statistically significant (-log (p-value) > 1.3) and differentially regulated canonical pathways in brain tissue of *ACSS2*-/- compared to wild-type mice.

|  |  |  |
| --- | --- | --- |
| **Canonical Pathways** | **-log(p-value)** | **z-score** |
| Sirtuin Signaling Pathway | 4.95 | 1.414 |
| Oxidative Phosphorylation | 4.33 | -2.828 |
| 3-phosphoinositide Biosynthesis | 2.62 | 2.646 |
| PI3K/AKT Signaling | 2.2 | -2.646 |
| Superpathway of Inositol Phosphate Compounds | 2.18 | 2.646 |
| BEX2 Signaling Pathway | 1.93 | -2 |
| Cyclins and Cell Cycle Regulation | 1.91 | -2 |
| Fcγ Receptor-mediated Phagocytosis in Macrophages and Monocytes | 1.66 | 2 |
| Neuropathic Pain Signaling In Dorsal Horn Neurons | 1.59 | 2 |
| D-myo-inositol (1,4,5,6)-Tetrakisphosphate Biosynthesis | 1.31 | 2 |

**Table S2C - Adipose.** The -log (p-value) and z-score of the top 10 statistically significant (-log (p-value) > 1.3) and differentially regulated canonical pathways in adipose tissue of *Acss2*-/- compared to wild-type mice.

|  |  |  |
| --- | --- | --- |
| **Canonical Pathways** | **-log(p-value)** | **z-score** |
| Sirtuin Signaling Pathway | 4.61 | -2.828 |
| Oxidative Phosphorylation | 3.39 | 3.162 |
| Glycolysis I | 3.03 | 2.449 |
| Toll-like Receptor Signaling | 2.91 | -1.633 |
| iNOS Signaling | 2.68 | -2.236 |
| Estrogen Biosynthesis | 2.43 | -1.633 |
| LPS/IL-1 Mediated Inhibition of RXR Function | 2.36 | -2 |
| Bupropion Degradation | 2.26 | -2 |
| Spliceosomal Cycle | 1.87 | -2.236 |
| Regulation Of The Epithelial Mesenchymal Transition By Growth Factors Pathway | 1.84 | -1.897 |
| Acetone Degradation I (to Methylglyoxal) | 1.44 | -2 |

**Table S3**

**Table S3A - Liver.** Expression of genes associated with disease and cellular functions, activation of “anemia” and “organ degeneration” in liver tissue of *Acss2*-/- compared to wild-type mice.

|  |  |
| --- | --- |
| **Symbol** | **Expr Log Ratio** |
| C9 | 1.14 |
| GBA | -1.16 |
| GPX4 | -1.16 |
| MFGE8 | -1.17 |
| PIGA | -1.12 |
| PITPNM2 | -1.14 |
| POLR3H | -1.09 |
| REEP6 | 1.2 |
| SLC25A38 | -1.19 |
| ZFP36L1 | -1.47 |

**Table S3B - Liver.** Expression of genes associated with disease and cellular functions, activation of “growth failure” in liver tissue of *Acss2*-/- compared to wild-type mice.

|  |  |
| --- | --- |
| **Symbol** | **Expr Log Ratio** |
| BNIP3L | -1.21 |
| FLT1 | -1.12 |
| GCK | -1.89 |
| ITPR1 | -1.2 |
| SHMT2 | 1.12 |
| TFRC | -1.45 |

**Table S3C - Liver.** Expression of genes associated with disease and cellular functions, activation of “organismal death” in liver tissue of *Acss2*-/- compared to wild-type mice**.**

|  |  |
| --- | --- |
| **Symbol** | **Expr Log Ratio** |
| BAG1 | -1.22 |
| BNIP3L | -1.21 |
| FDXR | -1.08 |
| HSD17B7 | -1.34 |
| ITPR1 | -1.2 |
| PRKACA | 1.1 |
| Rpl29 (includes others) | -1.54 |
| STIP1 | -1.21 |
| TBX3 | 1.17 |

**Table S3D – Liver:** Expression of genes associated with disease and cellular functions, inhibition of “infection by RNA virus” in liver tissue of *Acss2*-/- compared to wild-type mice.

|  |  |
| --- | --- |
| **Symbol** | **Expr Log Ratio** |
| ATG5 | 1.09 |
| ATMIN | -1.09 |
| FGD6 | -1.16 |
| SAMD9L | 1.41 |
| WASF1 | -1.11 |

**Table S4**

**Table S4A – Liver:** Expression of genes associated with **Network 1**: “amino acid metabolism, carbohydrate metabolism, small molecule biochemistry”, in liver tissue of *Acss2*-/- compared to wild-type mice.

|  |  |
| --- | --- |
| **Symbol** | **Expr Log Ratio** |
| ANKRD54 | -1.08 |
| Apol9a/Apol9b | 1.24 |
| ATP1B3 | -1.13 |
| AVEN | -1.1 |
| BICD2 | -1.14 |
| COMMD9 | -1.09 |
| DMWD | -1.12 |
| DYNLRB1 | -1.32 |
| EGLN3 | -1.09 |
| EIF6 | -1.18 |
| FADS2 | -1.22 |
| FOXRED1 | -1.12 |
| GALK1 | -1.33 |
| GLDC | 1.16 |
| GPN2 | -1.59 |
| IFT52 | -1.3 |
| JOSD2 | -1.24 |
| KLHDC10 | -1.22 |
| MSH6 | -1.11 |
| NDUFA8 | 1.1 |
| NUCB1 | -1.15 |
| NUDT5 | 1.11 |
| PALS2 | 1.13 |
| PPAT | -1.17 |
| SCAND1 | 1.61 |
| SDE2 | -1.19 |
| SEL1L | -1.11 |
| SHMT2 | 1.12 |
| TCF25 | -1.23 |
| TKT | 1.07 |
| TRIP6 | -1.17 |
| UBE2Q1 | -1.11 |
| USH2A | -1.53 |

**Table S4B – Liver:** Expression of genes associated with **Network 2**: “cellular development, cellular growth and proliferation, connective tissue development and function”, in liver tissue of *Acss2*-/- compared to wild-type mice.

|  |  |
| --- | --- |
| **Symbol** | **Expr Log Ratio** |
| ARL1 | -1.15 |
| ASPSCR1 | -1.22 |
| BRMS1 | -1.12 |
| CDK5RAP3 | -1.17 |
| DAP3 | 1.13 |
| DDX1 | -1.15 |
| Fus | 1.19 |
| G3BP2 | 1.18 |
| GRB7 | -1.31 |
| HABP4 | -1.09 |
| HPN | 1.22 |
| ILVBL | -1.2 |
| ING4 | -1.11 |
| LZTR1 | -1.09 |
| MRPS7 | -1.31 |
| NUAK2 | -1.31 |
| OLIG1 | 1.16 |
| PLEKHG3 | -1.12 |
| POLD2 | -1.1 |
| PPP6C | -1.22 |
| PXMP2 | 1.25 |
| RBM42 | -1.12 |
| RIOK3 | -1.34 |
| SRPRA | -1.54 |
| TAX1BP3 | -1.19 |
| TIMM10 | -1.15 |
| TMED4 | -1.14 |
| TRIM8 | -1.15 |
| TSPAN33 | -1.13 |
| UBXN6 | -1.18 |
| WFDC2 | -2.02 |
| YOD1 | 1.14 |

**Table S5**

**Table S5A – Brain:** Expression of genes associated with disease and cellular functions, activated “cell viability of tumor cell lines” and “size of body” in brain tissue of *Acss2*-/- compared to wild-type mice.

|  |  |
| --- | --- |
| **Symbol** | **Expr Log Ratio** |
| ARRB1 | 1.11 |
| DLX1 | 1.09 |
| IGFBP4 | 1.24 |
| KCNC1 | 1.1 |
| KLF6 | 1.16 |
| LMNA | 1.13 |
| PER2 | -1.15 |
| RAB3A | 1.01 |
| RAB3D | 1.06 |
| THRSP | 1.09 |

**Table S5B – Brain:** Expression of genes associated with disease and cellular functions, activation of “DNA endogenous promoter” in brain tissue of *Acss2*-/- compared to wild-type mice.

|  |  |
| --- | --- |
| **Symbol** | **Expr Log Ratio** |
| CCND1 | -1.3 |
| DEK | 1.12 |
| DLX1 | 1.09 |
| LDB2 | 1.22 |
| NDN | -1.1 |

**Table S5C – Brain:** Expression of genes associated with disease and cellular functions, activation of “cell viability” and “organization of cytoskeleton” in brain tissue of *Acss2*-/- compared to wild-type mice.

|  |  |
| --- | --- |
| **Symbol** | **Expr Log Ratio** |
| APP | -1.05 |
| ARRB1 | 1.11 |
| CCND1 | -1.3 |
| DCX | 1.12 |
| DUSP1 | 2.01 |
| GNAO1 | 1.23 |
| HSPB6 | 1.36 |
| KLC1 | 1.15 |
| NTRK2 | 1.19 |
| PER2 | -1.15 |
| PIK3R2 | 1.05 |
| POLR1D | 1.1 |
| RAB3A | 1.01 |
| RPS6KL1 | 1.12 |
| SORL1 | 1.74 |
| TRAF3 | -1.23 |
| WTIP | 1.06 |

**Table S5D – Brain:** Expression of genes associated with disease and cellular functions, “inhibition of organismal death” in brain tissue of *Acss2*-/- compared to wild-type mice.

|  |  |
| --- | --- |
| **Symbol** | **Expr Log Ratio** |
| DLX1 | 1.09 |
| KCNC1 | 1.1 |
| NTRK2 | 1.19 |
| OTX1 | 1.09 |

**Table S6**

**Table S6A – Brain:** Expression of genes associated with **Network 1**: “connective tissue disorders, developmental disorder, hereditary disorder”, in brain tissue of *Acss2*-/- compared to wild-type mice.

|  |  |
| --- | --- |
| **Symbol** | **Expr Log Ratio** |
| ACTR3 | 1.17 |
| ACTR3B | 1.07 |
| AIP | 1.15 |
| CSTF1 | 1.22 |
| DCPS | 1.11 |
| DEK | 1.12 |
| EIF1B | -1.06 |
| FRMD6 | 1.26 |
| GALT | 1.22 |
| HBS1L | 1.08 |
| HSPB6 | 1.36 |
| IDH3B | -1.05 |
| KCNMA1 | 1.2 |
| KEAP1 | 1.1 |
| KLF6 | 1.16 |
| NOSIP | -1.24 |
| NUDC | 1.16 |
| NXT2 | -1.06 |
| PIH1D1 | 1.09 |
| POLL | 1.06 |
| POLR1C | 1.11 |
| POLR1D | 1.1 |
| PRDX1 | -1.04 |
| SRPK1 | 1.15 |
| STK4 | 1.35 |
| TRIP12 | 1.11 |
| UBE3A | 1.1 |
| UBTD2 | 1.15 |

**Table S6B – Brain:** Expression of genes associated with **Network 2:** “metabolic disease, neurological disease, organismal injury and abnormalities”, in brain tissue of *Acss2*-/- compared to wild-type mice.

|  |  |
| --- | --- |
| **Symbol** | **Expr Log Ratio** |
| ATP5F1C | -1.05 |
| ATP6V0A2 | 1.1 |
| Cd59a | 1.61 |
| COX10 | -1.07 |
| CTDSPL | 1.09 |
| ELMO2 | -1.23 |
| GHITM | 1.15 |
| GLRX2 | 1.12 |
| IGFBP7 | 1.16 |
| ISCU | -1.03 |
| LARS2 | -1.23 |
| MRPS12 | -1.78 |
| MRPS17 | -1.34 |
| NDUFA12 | -1.13 |
| NDUFA4 | -1.06 |
| NDUFA5 | -1.04 |
| NDUFA7 | -1.08 |
| NDUFB8 | -1.04 |
| NEO1 | 1.14 |
| PPOX | 1.05 |
| PRCP | 1.08 |
| SLC39A10 | 1.1 |
| SNX21 | 1.16 |
| STT3A | -1.13 |
| TBRG4 | 1.07 |
| VARS2 | 1.09 |
| WARS2 | 1.17 |

**Table S7**

**Table S7A – Adipose:** Expression of genes associated with disease and cellular functions, “inhibition of vasculogenesis” in adipose tissue of *Acss2*-/- compared to wild-type mice.

|  |  |
| --- | --- |
| **Symbol** | **Expr Log Ratio** |
| ADIPOQ | 1.08 |
| CAV1 | 1 |
| IL33 | -1.24 |
| JUN | -1.4 |
| PPARG | -1.22 |
| PPARGC1B | 1.38 |
| RHOB | -1.42 |
| TKT | 1.54 |
| VLDLR | 1.29 |

**Table S7B – Adipose:** Expression of genes associated with disease and cellular functions, inhibited “infection of embryonic cell lines, infection of epithelial cell lines, and infection of kidney cell lines” in adipose tissue of *Acss2*-/- compared to wild-type mice.

|  |  |
| --- | --- |
| **Symbol** | **Expr Log Ratio** |
| BMP1 | -1.15 |
| GANAB | -1.19 |
| IRF3 | -1.14 |
| REPIN1 | -1.2 |
| RHOB | -1.42 |
| RNPS1 | -1.23 |
| SF3A1 | -1.25 |
| TRAFD1 | -1.2 |
| ZYX | -1.38 |

**Table S7C – Adipose:** Expression of genes associated with disease and cellular functions, “activation of glycolysis” in adipose tissue of *Acss2*-/- compared to wild-type mice. (**Note:** see also Figure 1 in main text).

|  |  |
| --- | --- |
| **Symbol** | **Expr Log Ratio** |
| ADIPOQ | 1.08 |
| ALDOA | 1.45 |
| CAV1 | 1 |
| ENO1 | 1.39 |
| GAPDH | 1.22 |
| GPD1 | 1.7 |
| GSTP1 | 1.18 |
| IDH3A | 1.19 |
| MAPKAPK2 | -1.22 |
| MLXIPL | 1.19 |
| PDHA1 | 1.25 |
| PFKL | 1.4 |
| PFKP | 1.26 |
| PPARG | -1.22 |
| PPARGC1B | 1.38 |
| SLC2A3 | -1.68 |
| TPI1 | 1.19 |

**Table S8**

**Table S8A – Adipose:** Expression of genes associated with **Network 1:** “cellular assembly and organization, RNA damage and repair, RNA post-transcriptional modification”, in adipose tissue of *Acss2*-/- compared to wild-type mice.

|  |  |
| --- | --- |
| **Symbol** | **Expr Log Ratio** |
| ANLN | -1.47 |
| BRD2 | -1.24 |
| CAMK2N1 | -1.16 |
| CDC42EP3 | 1.22 |
| CDC5L | -1.29 |
| CHD4 | -1.21 |
| CNIH4 | 1.13 |
| CRYZL1 | -1.23 |
| DDX17 | -1.67 |
| DDX21 | -1.21 |
| DHX15 | -1.16 |
| DIDO1 | -1.32 |
| EEF1A1 | -1 |
| EFTUD2 | -1.13 |
| HDGF | 1.07 |
| HEXIM1 | -1.32 |
| KANK1 | -1.26 |
| MECR | 1.24 |
| MRPL12 | 1.2 |
| NOL6 | -1.29 |
| PCBP1 | -1.21 |
| PIP4K2B | -1.22 |
| PTPN6 | -1.14 |
| RNPS1 | -1.23 |
| RPL23 | 1.22 |
| RSL1D1 | -1.21 |
| SLC25A10 | 1.78 |
| SLC25A5 | 1.15 |
| SLC4A1AP | -1.23 |
| SRPK1 | -1.24 |
| SYF2 | -1.23 |
| THUMPD1 | -1.27 |
| TOP1 | -1.12 |
| UPF2 | -1.33 |
| ZCCHC8 | -1.14 |

**Table S8B – Adipose:** Expression of genes associated with **Network 2**: “connective tissue disorders, developmental disorder, hereditary disorder”, in adipose tissue of *Acss2*-/- compared to wild-type mice.

|  |  |
| --- | --- |
| **Symbol** | **Expr Log Ratio** |
| ACVR1C | 1.6 |
| ATP6AP2 | -1.13 |
| ATP6V0A2 | 1.21 |
| ATP6V0E2 | -1.26 |
| ATP6V1A | 1.41 |
| BICD2 | -1.23 |
| BSDC1 | -1.81 |
| C1orf198 | -1.3 |
| CHORDC1 | -1.31 |
| CORO1A | -1.24 |
| CORO1C | -1.31 |
| FHL1 | -1.28 |
| GMFG | 1.25 |
| IFT172 | -1.22 |
| IFT20 | 1.12 |
| IFT52 | -1.33 |
| IFT81 | -1.15 |
| JDP2 | -1.12 |
| LRRC41 | -1.15 |
| LUZP1 | 1.47 |
| MYADM | -1.26 |
| TMEM63B | 1.39 |
| USP16 | -1.14 |
| USP2 | -1.79 |
| USP22 | -1.28 |
| USP39 | -1.25 |
| WBP2 | 1.09 |
| ZMAT3 | -1.13 |
| ZNRF2 | -1.3 |