**Supporting information**

**Index of supplementary figures and tables:**

**Supplementary Figure 1**.Effect of 30% DR on the levels of cell cycle regulators and JNK in HCVcpTg mice.

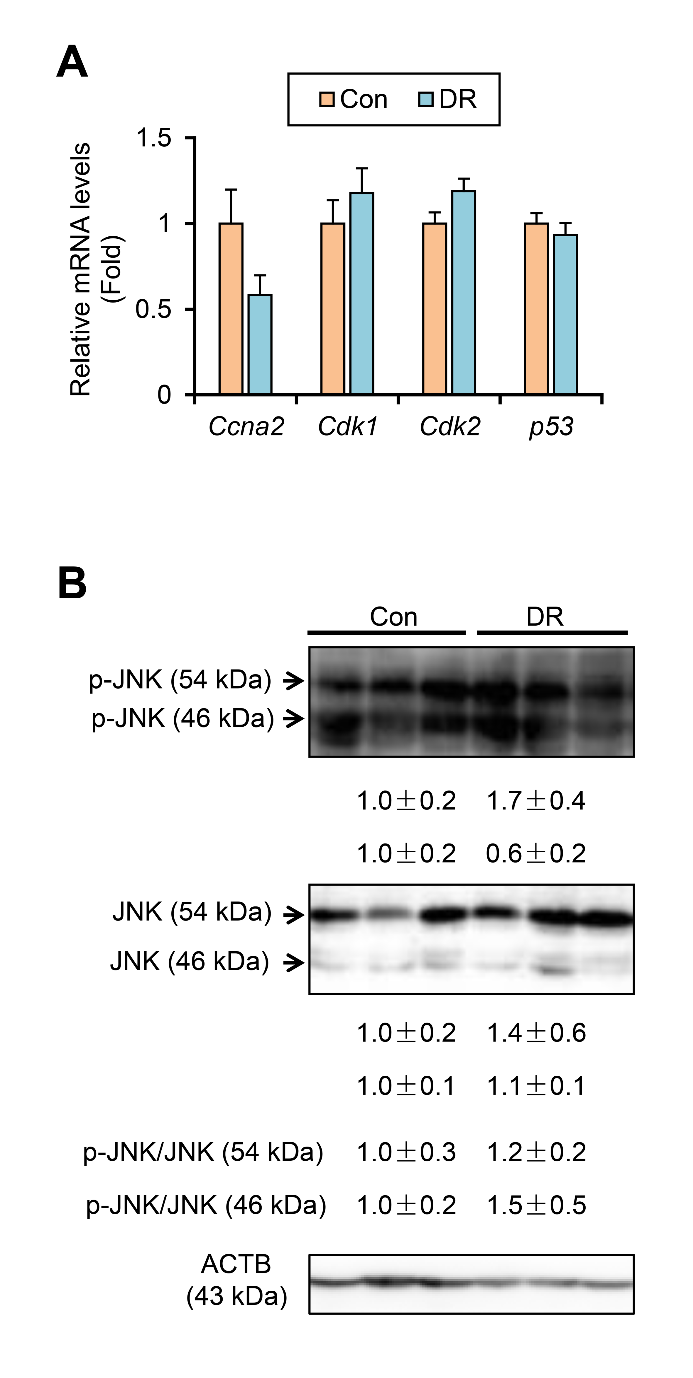
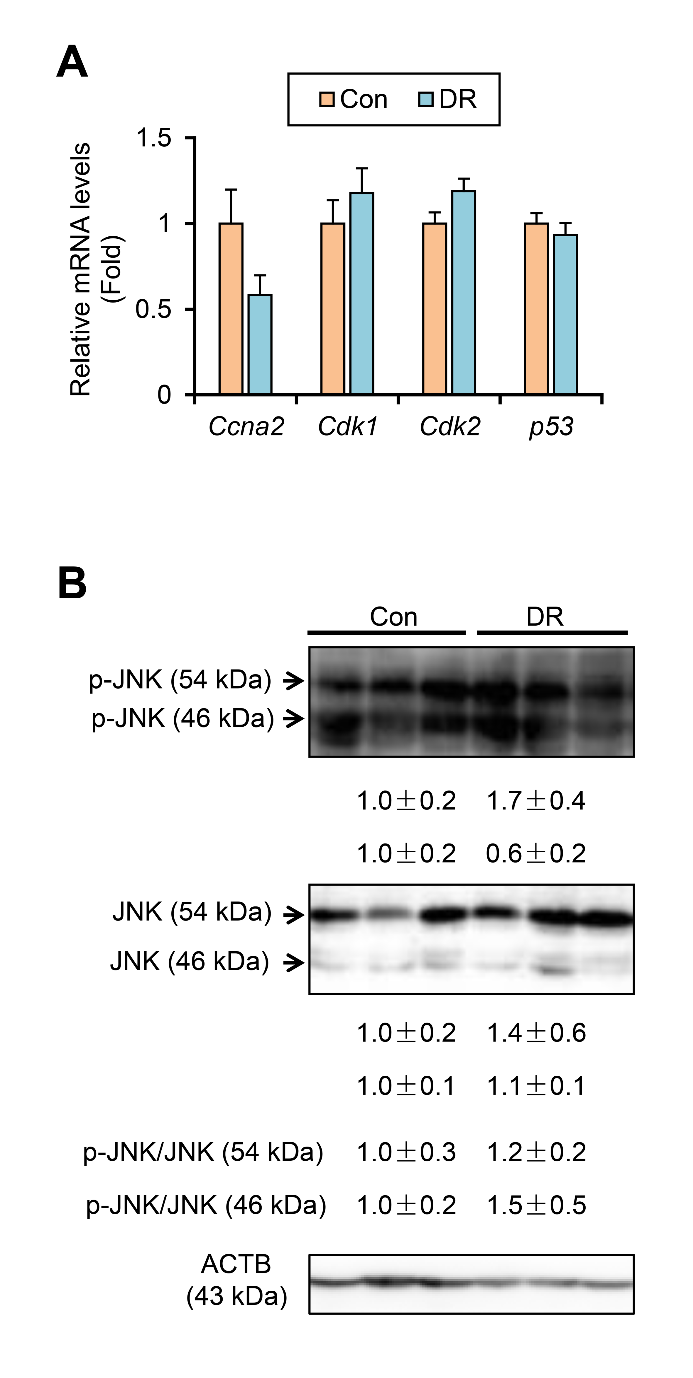
**Supplementary Figure 2**. 30% DR enhances FA mitochondrial β-oxidation without peroxisome proliferation and increased nuclear PPARα in HCVcpTg mice.

**Supplementary Figure 3.** 30% DR does not give any significant impact on hepatic fibrogenesis, epithelial-to-mesenchymal transition (EMT), or stemness in HCVcpTg mice.

**Supplementary Table 1.** Primer pairs used for qPCR.

**Supplementary Table 2.** Primary antibodies used for western blot.

**Supplementary Table 3.** Biochemical analysis of serum and liver.



**Supplementary Figure 1. Effect of 30% DR on the levels of cell cycle regulators and JNK in HCVcpTg mice.**

(**A**) Hepatic mRNA levels of genes encoding cyclin A2, cyclin-dependent kinase 1/2, and p53 were quantified by qPCR, normalized to 18S ribosomal RNA, and expressed as values relative to regularly-fed control HCVcpTg mice.

(**B**) Immunoblot analysis of p-JNK and JNK. Whole liver homogenates (45 μgprotein/lane) were separated 10% SDS-PAGE and the band of β-actin (ACTB) was used as a loading control. Band intensities were measured densitometrically, normalized to the loading control, and expressed as values relative to those of regularly-fed control HCVcpTg mice. Results were obtained from at leasttwo independent immunoblot experiments and representative blots were shown.

Data are expressed as mean ± SEM. \**P* < 0.05, \*\**P* < 0.01, and \*\*\**P* < 0.001 between regularly-fed control (Con) vs. 30% reduction in diet amount (DR).

**F:\Shinshu University\HCV core TG mice from 2014\SFA and DR\DR\To Frank\Corrected version\Liver Cancer\Liver Cancer\R1\Revised manuscript\To co-authors\Corrected by Frank\R1 FINAL\FigS2.tif**

**Supplementary Figure 2. 30% DR enhances FA mitochondrial β-oxidation without peroxisome proliferation and increased nuclear PPARα in HCVcpTg mice.**

(**A**) Hepatic mRNA levels of genes involved in FA uptake, carriage and activation (*Cd36*, *Fabp1*, and *Acsl1*), TG synthesis (*Dgat1/2*), and *de novo* cholesterol synthesis (*Hmgcs1*, *Hmcgr*, and *Fdft1*) were quantified by qPCR, normalized to 18S ribosomal RNA, and expressed as values relative to regularly-fed control HCVcpTg mice.

(**B**) Hepatic mRNA levels of genes involved in FA catabolism (*Ppara*, *Acadm*, *Acadl*, and *Acox1*), *de novo* FA synthesis (*Acaca* and *Scd1*), and TG secretion (*Mttp* and *Apob*). Similar assays were conducted to (**A**).

(**C-D**) Immunoblot analysis of nuclear PPARα, mitochondrial (MCAD and LCAD) and peroxisomal (PT and ACOX1) FA β-oxidizing enzymes, and peroxisomal membrane protein 70 (PMP70). Nuclear fractions (21 μg protein/lane) and whole liver lysates (28 μg protein/lane) were separated using 10% SDS-PAGE and the bands of histone H1 and β-actin (ACTB) were used as a loading control, respectively. The A and B bands were detected for ACOX1. Band intensities were measured densitometrically, normalized to the loading control, and expressed as values relative to those of regularly-fed control HCVcpTg mice. Results were obtained from two independent immunoblot experiments and representative blots were shown.

Data are expressed as mean ± SEM. \**P* < 0.05, \*\**P* < 0.01, and \*\*\**P* < 0.001 between regularly-fed control (Con) vs. 30% reduction in diet amount (DR).

**F:\Shinshu University\HCV core TG mice from 2014\SFA and DR\DR\To Frank\Corrected version\Liver Cancer\Liver Cancer\R1\Revised manuscript\To co-authors\Corrected by Frank\R1 FINAL\FigS3.tif**

**Supplementary Figure 3. 30% DR does not give any significant impact on hepatic fibrogenesis, epithelial-to-mesenchymal transition (EMT), or stemness in HCVcpTg mice.**

(**A**) Hepatic hydroxyproline contents.

(**B-D**) Hepatic mRNA levels of genes related to fibrogenesis (**B**), EMT (**C**), and stemness (**D**) were quantified by qPCR, normalized to 18S ribosomal RNA, and expressed as values relative to regularly-fed control HCVcpTg mice.

(**E**) Azan-Mallory staining.

Data are expressed as mean ± SEM. \**P* < 0.05 between regularly-fed control (Con) vs. 30% reduction in diet amount (DR).

**Supplementary Table 1. Primer pairs used for qPCR**

|  |  |  |
| --- | --- | --- |
| **Gene** | **Accenssion no.** | **Primer sequence (5'-3')** |
| *18S rRNA*  *Acaca*  *Acadl*  *Acadm*  *Acox1*  *Acsl1*  *Acta2*  *Afp*  *Aldh1a1*  *Apob*  *Arg1*  *Asc*  *Casp1*  *Cat*  *Ccl2*  *Ccna2*  *Ccnb1*  *Ccnd1*  *Cd14*  *Cd36*  *Cd44*  *Cd68*  *Cd133*  *Cdk1*  *Cdk2*  *Cdk4*  *Cdn1*  *Cldn1*  *Col1a1*  *Csf1*  *Ctgf*  *Cybb*  *Ddit3*  *Dgat1*  *Dgat2*  *Epcam*  *Fabp1*  *Fabp5*  *Fasn*  *Fdft1*  *Fgf21*  *Foxo3*  *Hmgcr*  *Hmgcs1*  *Hmox1*  *Hspa5*  *Igfbp7*  *Il1a*  *Il1b*  *Il6*  *Lcn2*  *Lgals3*  *Lgals3bp*  *Map1lc3b*  *Mmp1*  *Mpo*  *Mttp*  *Myd88*  *Nampt*  *Ncf1*  *Nfe2l2*  *Nlrp3*  *Nqo1*  *p16*  *p21*  *p53*  *Panx1*  *Pink1*  *Ppara*  *Ppargc1a*  *Saa1*  *Scd1*  *Serpine1*  *Sirt1*  *Sirt3*    *Socs3*  *Sod1*  *Sod2*  *Spp1*  *Sqle*  *Sqstm1*  *Tff3*  *Tgfb1*  *Thrsp*  *Tlr2*  *Tlr4*  *Tnf*  *Vim* | NR\_003278  NM\_133360  NM\_007381  NM\_007382  NM\_015729  NM\_007981  NM\_007392  NM\_007423  NM\_013467  NM\_009693  NM\_007482  NM\_023258  NM\_009807  NM\_009804  NM\_11333  NM\_009828  NM\_172301  NM\_007631  NM\_009841  NM\_007643  NM\_009851  NM\_001291058  NM\_008935  NM\_007659  NM\_183417  NM\_009870  NM\_009864    NM\_016674  NM\_007742  NM\_007778  NM\_010217  NM\_007807  NM\_007837  NM\_010046  NM\_026384  NM\_008532  NM\_017399  NM\_010634  NM\_007988  NM\_010191  NM\_020013  NM\_019740  NM\_008255  NM\_145942  NM\_010442  NM\_022310  NM\_008048  NM\_010554    NM\_008361  NM\_031168  NM\_008491  NM\_010705  NM\_011150  NM\_025735  NM\_008607  NM\_010824  NM\_008642  NM\_010851  NM\_021524  NM\_010876  NM\_010902  NM\_145827  NM\_008706  NM\_001040654  NM\_007669  NM\_011640.3  NM\_019482  NM\_026880  NM\_011144  NM\_008904  NM\_009117  NM\_009127  NM\_008871  NM\_019812  NM\_001370314  NM\_007707  NM\_011434  NM\_013671  NM\_009263  NM\_009270  NM\_011018  NM\_011575    NM\_011577  NM\_001113417.1  NM\_021297  NM\_011905  NM\_013693  NM\_011701 | F 5'-CACGGACAGGATTGACAGATTG-3'  R 5'-CAGACAAATCGCTCCACCAA-3'  F 5'-GGGCACAGACCGTGGTAGTT-3'  R 5'-CAGGATCAGCTGGGATACTGAGT-3'  F 5'- TTTCCGGGAGAGTGTAAGGA-3'  R 5'- ACTTCTCCAGCTTTCTCCCA-3'  F 5'-TGCTTTTGATAGAACCAGACCTACAGT-3'  R 5'-CTTGGTGCTCCACTAGCAGCTT-3'  F 5'-TGGTATGGTGTCGTACTTGAATGAC-3'  R 5'-AATTTCTACCAATCTGGCTGCAC-3'  F 5'-TCCTACGGCAGTGATCTGGTG-3'  R 5'-GGTTGCCTGTAGTTCCACTTGTG-3'  F 5'-ACTGGGACGACATGGAAAAG-3'  R 5'-GTTCAGTGGTGCCTCTGTCA-3'  F 5'-AGTTTCCAGAACCTGCCGAG-3'  R 5'-ACCTTGTCGTACTGAGCAGC-3'  F 5'-TGGACCAGTGCAACAAATCAT-3'  R 5'-ACATCATATAGCAGTTAACCCACAC-3'  F 5'-TCACCCCCGGGATCAAG-3'  R 5'-TCCAAGGACACAGAGGGCTTT-3'  F 5'-ACAAGACAGGGCTCCTTTCAG-3'  R 5'-GGCTTATGGTTACCCTCCCG-3'  F 5'-GAAGCTGCTGACAGTGCAAC-3'  R 5'-GCCACAGCTCCAGACTCTTC-3'  F 5'-TACCTGGCAGGAATTCTGGA-3'  R 5'-AGTCCTGGAAATGTGCCATC-3'  F 5'-CGACCAGGGCATCAAAAACTT-3'  R 5'-AACGTCCAGGACGGGTAATTG-3'  F 5'-AGGTCCCTGTCATGCTTCTG-3'  R 5'-GGGATCATCTTGCTGGTGAA-3'  F 5'-CGGAGCAAGAAAACCACTGA-3'  R 5'-CGTTCACTGGCTTGTCTTCTAAG-3'  F 5'-AACTGCTCTTGGAGACATTGGT-3'  R 5'-GCGTTTTTGCTTCCCTTTTC-3'  F 5'-CCAGAGGCGGATGAGAACAA-3'  R 5'-ATGGAGGGTGGGTTGGAAA-3'  F 5'-CTCTGTCCTTAAAGCGGCTTAC-3'  R 5'-GTTGCGGAGGTTCAAGATGTT-3'  F 5'-CCAAATGAAGATGAGCATAGGACAT-3'  R 5’-GTTGACCTGCAGTCGTTTTGC-3’  F 5’-CAGAGGCGACTAGATCCCTC-3’  R 5’-GAGTCACAGTGCGGGAACTC-3’  F 5'-GAGGTTGTGACGGTACCCAT-3’  R 5'-ACATTGTATTCCACCGCCAT-3’  F 5’-TGGTCCAGCCGAATGACTTC-3’  R 5’-AGAGGGCAATCTCCTTGGAATC-3’  F 5'-GAACACCTTTCCCAAGTGGAA-3'  R 5'-CCATTTTGCCAGAGATTCGT-3'  F 5'-TGCACCAGGACCTCAAGAAAT-3'  R 5'-TGAAGGACACGGTGAGAATGG-3'  F 5'-CCTGAGGACATACCTGGACAAAG-3'  R 5'-CCGCTTAGAAACTGACGCATT-3'  F 5’-CCCATCAATGCCAGGTATG-3’  R 5’-AAAGTAGGACACCTCCCAGAAG-3’  F 5’-ACATGTTCAGCTTTGTGGACC-3’  R 5’-TAGGCCATTGTGTATGCAGC-3’  F 5’-CCAGGATGAGGACAGACAGG-3’  R 5’-GGTAGTGGTGGATGTTCCCA-3’  F 5’-GGATTTTAAACTGATAGCCTCAAACTC-3’  R 5’-GCAGTATCTCCTTTGTTTTGAATCAC-3’  F 5’-GAAAACTCCTTGGGTCAGCACT-3’  R 5’-ATTTCGACACACTGGCAGCA-3’  F 5’-CAGCGACAGAGCCAGAATAA-3’  R 5’-GACCAGGTTCTGCTTTCAGG-3’  F 5'-CTGCTACGACGAGTTCTTGAGA-3'  R 5'-GATAGTAGGGACCATCCACTGTTG-3'  F 5'-GCTTCGCGAGTACCTGATGT-3'  R 5'-CACCACGATGATGATAGCATTG-3'  F 5’-CCGCGGCTCAGAGAGACT-3’  R 5’-AGGAAGTACACTGGCATTCACC-3’  F 5'-GCAGAGCCAGGAGAACTTTGAG-3'  R 5'-TTTGATTTTCTTCCCTTCATGCA-3'  F 5’-ATCCTGGAACGAGAACACGATCT-3’  R 5’-AGAGACGTGTCACTCCTGGACTT-3’  F 5’-TGGCCAAGCCAGACTGTATC-3  R 5’-AGGTGCAGACCGTCTCAGT-3  F 5'-CCGGAACCAGAGTGTGTTTAACT-3'  R 5'-CCTTCCGAATCTTCACTACTCCTT-3'  F 5'-CCTCTAGGTTTCTTTGCCAACAG-3'  R 5'-AAGCTGCAGGCCTCAGGAT-3'  F 5'-GCCATGGGGCTGCTGTC-3'  R 5'-AGTCATAGGCATGCTGCATGTG-3'  F 5'-GAAGGAGCCGAGCTGGAG-3'  R 5'-CTGGTGCCTCTGCCATCTTC-3'  F 5'-TGACACCTGAGGTCAAGCAC-3'  R 5'-GGCAGTATCTTGCACCAGGC-3'  F 5'-TGTGGTTTGTGAAGCCGTCAT-3'  R 5'-CGTCAACCATAGCTTCCGTAGTT-3'  F 5'-GACCACCTATTCCTGCGTCG-3'  R 5'-CCTTCAGGAGTGAAGGCCAC-3'  F 5'-GACCACCTATTCCTGCGTCG-3’  R 5'-CCTTCAGGAGTGAAGGCCAC-3’  F 5’-AAGAGGCGGAAGGGTAAAGC-3’  R 5’-TATGGAAGGACCTTGCTCGC-3’  F 5’-CGCTTGAGTCGGCAAAGAAATC-3’  R 5’-GTGCAAGTCTCATGAAGTGAGC-3’  F 5'-TGAAGCAGCTATGGCAACTG-3'  R 5'-AGGTCAAAGGTTTGGAAGCA-3'  F 5'-TGATGCACTTGCAGAAAACA-3'  R 5'-ACCAGAGGAAATTTTCAATAGGC-3'  F 5'-AATGTCACCTCCATCCTGGT-3'  R 5'-ATTTCCCAGAGTGAACTGGC-3'  F 5'-GTACAGCTAGCGGAGCGG-3'  R 5'-CGGATATCCTTGAGGGTTTG-3'  F 5’-AGGAAAGGGACCGATCATGC-3’  R 5’-CCGTGGTATCGTTGGAGCAG-3’  F 5’-CAGCTTCGCCGACCG-3’  R 5’-TGGTCTGGGACCAGAAACTTG-3’  F 5’-TTCTGGTCTTCTGGCACACG-3  R 5’TTGTAGCCTTTGGAACTGCTTG-3  F 5’-CTCCTCACCAACCGCTCC-3’  R 5’-TGCTCTCGAACAAAGAGGGT-3’  F 5'-GAGCGGTCTGGATTTACAACG-3'  R 5'-GTAGGTAGTGACAGATGTGGCTTTTG-3'  F 5'-TCATGTTCTCCATACCCTTGGT-3'  R 5'-AAACTGCGAGTGGGGTCAG-3'  F 5’- AGAGCACAGTACCATAACGGC-3’  R 5’-TGGTGCCTCTGTACTTCTCG-3’  F 5'-GCCCAAAGATGGCAAGAATAAC-3'  R 5'-TAGTCAGCAATGGCCCGATAG-3'  F 5'-GGACATGGAGCAAGTTTGGC-3'  R 5'-CCAGCGAGGAGATCGATGAG-3'  F 5'-GCTCCAACCATTCTCTGACC-3'  R 5'-AAGTAAGGCCGGAATTCACC-3'  F 5'-ACGACAACGGTCCTTTCCAG-3'  R 5'-GCAGGATGCCACTCTGAATC-3'  F 5'-ATGGAGTCCGCTGCAGACAGAC-3'  R 5'-ACGTTGCCCATCATCATCACCTGA-3'  F 5'-TCTGAGCGGCCTGAAGAT-3'  R 5'-CTGCGCTTGGAGTGATAGAA-3'  F 5'-ACCACTTGATGGAGAGTATTTCAC-3'  R 5'-GTAGCATGGGCATCCTTTAAC-3'  F 5'-GATGGTCACATGTATTGCCG-3'  R 5'-CTGTCGCCAGGAGAAAGAAC-3'  F 5'-ATATCTCGGCAGGTTCCTCCA-3'  R 5'-ATGTTAGGGTGTGGGGCAAG-3'  F 5'-CCTCAGGGTACCACTACGGAGT-3'  R 5'-GCCGAATAGTTCGCCGAA-3'  F 5'-GACTCAGTGTCACCACCGAAATC-3'  R 5'-GACCTGTGTCGAGAAAAGGATCTT-3'  F 5'-TCAGACAAATACTTCCATGCT-3'  R 5'-AAAGGCCTCTCTTCCATCACT-3'  F 5'-AGATCTCCAGTTCTTACACGACCAC-3'  R 5'-CTTTCATTTCAGGACGGATGTCT-3'  F 5’-GTCTTTCCGACCAAGAGCAG-3’  R 5’-GGTTGTGCCGAACCACAAAG-3’  F 5’-TTGACCGATGGACTCCTCAC-3’  R 5’-AACAAAAGTATATGGACCTATCCGC-3’  F 5'-AGGTGGAGGAAGCAGTGAGA-3'  R 5'-GCTTGGGGTTGTGAAAGAAA-3'  F 5'-GCGGGCACCTTTCTTATCC-3'  R 5'-TCCCCGACTGGGTCTTGAC-3'  F 5'-AAGCGGTGAACCAGTTGTGTT-3'  R 5'-AGCCTTGTGTATTGTCCCCATACT-3'  F 5'-TCCCAGACCTGCCTTACGACTAT-3'  R 5'-GGTGGCGTTGAGATTGTTCA-3'  F 5'-CTCCTTGCGCCACAGAATG-3'  R 5'-TTGGAAGAGTTTCTTGCTTAAAGTCA-3'  F 5'-GCAAGCTTCCTTCCTCCTTC-3'  R 5'-CAACTGTCATTCCTCCACCA-3'  F 5'-GTGGGACAGCCAGAGGAACAG-3'  R 5'-TGAGGGGTCTAGAGAGCTTGG-3'  F 5'-AGAGCCCTCTGGCTAATGCT-3'  R 5'-GCACCATACATTGGCTTGG-3'  F 5'-GGAGAGCCCTGGATACCAAC-3'  R 5'-CAACCCAGGTCCTTCCTAAA-3'  F 5'-AGACCTGCGGATGATTGGA-3'  R 5'-CTAAGAACAGAGGCGGGAAGA-3'  F 5'-CATCACCGGTCAGAAAACAA-3'  R 5'-ACCAAGATCCAGAAGAGCCA-3'  F 5'-TGTTCTTCTCCTGCCTGACA-3  R 5’-TGTCATCAGGGACTTTGCTG-3’  F 5’-CCACCACGCTCTTCTGTCTAC-3’  R 5’- AGGGTCTGGGCCATAGAACT-3’  F 5’-ACAAGTCCAAGTTTGCTGACC-3’  R 5’-AAGGGCATCCACTTCACAGG-3’ |

F, forward sequence; R, reverse sequence.

*Acaca,* acetyl-Coenzyme A carboxylase alpha

*Acadl,* acyl-Coenzyme A dehydrogenase, long-chain

*Acadm,* acyl-Coenzyme A dehydrogenase, medium chain

*Acox1,* acyl-Coenzyme A oxidase 1, palmitoyl

*Acsl1,* acyl-CoA synthetase long-chain family member 1

*Acta2,* actin, alpha 2, smooth muscle, aorta

*Afp,* alpha fetoprotein

*Aldh1a1,* aldehyde dehydrogenase family 1, subfamily A1

*Apob,* apolipoprotein B

*Arg1,* arginase

*Asc,* PYD and CARD domain containing

*Casp1,* caspase 1

*Cat*, catalase

*Ccl2,* chemokine (C-C motif) ligand 2

*Ccna2,* cyclin A2

*Ccnb1,* cyclin B1

*Ccnd1,* cyclin D1

*Cd14,* CD14 antigen

*Cd36,* CD36 molecule

*Cd44,* CD44 antigen

*Cd68,* CD68 antigen

*Cd133,* prominin 1 (CD133 antigen)

*Cdk1,* cyclin-dependent kinase 1

*Cdk2,* cyclin-dependent kinase 2

*Cdk4,* cyclin-dependent kinase 4

*Cdh1,* cadherin 1

*Cldn1,* claudin 1

*Col1a1,* collagen, type I, alpha 1

*Csf1,* colony stimulating factor 1

*Ctgf,* connective tissue growth factor

*Cybb,* cytochrome b-245, beta polypeptide

*Ddit3,* DNA-damage inducible transcript 3

*Dgat1,* diacylglycerol O-acyltransferase 1

*Dgat2,* diacylglycerol O-acyltransferase 2

*Epcam,* epithelial cell adhesion molecule

*Fabp1,* fatty acid binding protein 1

*Fabp5*, fatty acid binding protein 5

*Fasn,* fatty acid synthase

*Fdft1,* farnesyl diphosphate farnesyl transferase 1

*Fgf21,* fibroblast growth factor 21

*Foxo3*, forkhead box O3

*Hmgcr,* 3-hydroxy-3-methylglutaryl-Coenzyme A reductase

*Hmgcs1,* 3-hydroxy-3-methylglutaryl-Coenzyme A synthase 1

*Hmox1,* heme oxygenase 1

*Hspa5,* heat shock protein 5

*Igfbp7,* insulin-like growth factor binding protein 7

*Il1a,* interleukin 1 alpha

*Il1b,* interleukin 1 beta

*Il6,* interleukin 6

*Lcn2,* lipocalin 2

*Lgals3,* lectin, galactose binding, soluble 3

*Lgals3bp,* lectin, galactoside-binding, soluble, 3 binding protein

*Map1lc3b*, microtubule-associated protein 1 light chain 3 beta

*Mmp1,* matrix metallopeptidase 1

*Mpo,* myeloperoxidase

*Mttp,* microsomal triglyceride transfer protein

*Myd88,* myeloid differentiation primary response gene 88

*Nampt,* nicotinamide phosphoribosyltransferase

*Ncf1,* neutrophil cytosolic factor 1

*Nfe2l2,* nuclear factor, erythroid derived 2, like 2

*Nlrp3,* NLR family, pyrin domain containing 3

*Nqo1,* NAD(P)H dehydrogenase, quinone 1

*p16,* cyclin dependent kinase inhibitor 2A

*p21,* cyclin-dependent kinase inhibitor 1A (P21)

*p53,* transformation related protein 53

*Panx1*, pannexin 1

*Pink1,* PTEN induced putative kinase 1

*Ppara,* peroxisome proliferator activated receptor alpha

*Ppargc1a,* peroxisome proliferative activated receptor, gamma, coactivator 1 alpha

*Saa1,* serum amyloid A 1

*Scd1,* stearoyl-Coenzyme A desaturase 1

*Serpine1,* serine (or cysteine) peptidase inhibitor, clade E, member 1

*Sirt1,* Sirtuin 1

*Sirt3,* Sirtuin 3

*Socs3,* suppressor of cytokine signaling 3

*Sod1,* superoxide dismutase 1, soluble

*Sod2,* superoxide dismutase 2, soluble

*Spp1,* secreted phosphoprotein 1

*Sqle,* squalene epoxidase

*Sqstm1,* sequestosome 1

*Tff3*, trefoil factor 3

*Tgfb1,* transforming growth factor, beta 1

*Thrsp,* thyroid hormone responsive

*Tlr2,* toll-like receptor 2

*Tlr4,* toll-like receptor 4

*Tnf,* tumor necrosis factor

*Vim*, vimentin

**Supplementary Table 2.** Primary antibodies used for western blot

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Protein name | Abbreviation | Manufacturer | Catalog no. | Dilution |
| Nuclear factor kappa B p65 component | p65 | Cell Signaling Technology (Danvers, MA) | #8242 | 1:1000 |
| Histone H1 | Histone H1 | Santa Cruz Biotechnology (Dallas, TX) | #sc-10806 | 1:200 |
| Caspase 1 | Casp1 | Santa Cruz Biotechnology  (Dallas, TX) | #sc-56036 | 1:200 |
| Actin cytoplasmic 1 | ACTB | Abcam  (Cambridge, MA) | #8227 | 1:1000 |
| 4-Hydroxy-nonenal | 4-HNE | JalCA  (Shizuoka, Japan) | #MHN-020P | 1:100 |
| Superoxide dismutase  1 | SOD1 | Santa Cruz Biotechnology (Dallas, TX) | #sc-11407 | 1:200 |
| C/EBP homologous protein | CHOP | Cell Signaling Technology  (Danvers, MA) | #2895 | 1:1000 |
| Sequestosome 1 | p62 | Medical Biological Laboratories Co  (Nagoya, Japan) | #PM045MS | 1:1000 |
| Nuclear factor erythroid 2-related factor 2 | NRF2 | Medical Biological Laboratories Co. (Nagoya, Japan) | #M200-3MS | 1:1000 |
| Microtubule-associate  protein 1 light chain 3 | LC3 | Medical Biological Laboratories Co. (Nagoya, Japan) | #PM036MS | 1:1000 |
| Autophagy-related 5 | ATG5 | Medical Biological Laboratories Co  (Nagoya, Japan) | #PM050MS | 1:500 |
| Cyclin B1 | CCNB1 | Santa Cruz Biotechnology (Dallas, TX) | #sc-752 | 1:1000 |
| Cyclin D1 | CCND1 | Santa Cruz Biotechnology (Dallas, TX) | #sc-717 | 1:150 |
| Cyclin-dependent  kinase inhibitor 1A | CDKN1A  (p21) | Santa Cruz Biotechnology (Dallas, TX) | #sc-756 | 1:200 |
| Phosphorylated signal transducer and activator of transcription 3 | p-STAT3 | Cell Signaling Technology (Danvers, MA) | #9131 | 1:1000 |
| Signal transducer and activator of transcription 3 | STAT3 | Cell Signaling Technology (Danvers, MA) | #4904 | 1:2000 |
| Phosphorylated signal transducer and activator of transcription 5 | p-STAT5 | Cell Signaling Technology (Danvers, MA) | #4322 | 1:1000 |
| Signal transducer and activator of transcription 5 | STAT5 | Cell Signaling Technology (Danvers, MA) | #94205 | 1:1000 |
| Phosphorylated  extracellular-regulated  protein kinase 1/2 | p-ERK1/2 | Cell Signaling Technology (Danvers, MA) | #4370 | 1:2000 |
| Extracellular-regulated  protein kinase 1/2 | ERK1/2 | Upstate Cell Signaling Solutions (Lake Placid,NY) | #06-182 | 1:1000 |
| Insulin receptor substrate 1 | IRS-1 | Cell Signaling Technology (Danvers, MA) | #2382 | 1:1000 |
| Insulin receptor substrate 2 | IRS-2 | Cell Signaling Technology (Danvers, MA) | #4502 | 1:1000 |
| Phosphorylated phosphatidylinositol 3-kinase | p-PI3K | Cell Signaling Technology (Danvers, MA) | #4228 | 1:1000 |
| Phosphatidylinositol 3-kinase | PI3K | Cell Signaling Technology (Danvers, MA) | #4257 | 1:1000 |
| Phosphorylated serine/threonine kinase | p-AKT | Cell Signaling Technology (Danvers, MA) | #2965 | 1:1000 |
| Serine/threonine kinase | AKT | Cell Signaling Technology (Danvers, MA) | #4691 | 1:1000 |
| Phosphorylated AMP-activated protein kinase alpha | p-AMPKα | Cell Signaling Technology (Danvers, MA) | #9957 | 1:1000 |
| AMP-activated protein kinase alpha | AMPKα | Cell Signaling Technology (Danvers, MA) | #9957 | 1:1000 |
| Phosphorylated AMP-activated protein kinase beta 1 | p-AMPKβ1 | Cell Signaling Technology (Danvers, MA) | #9957 | 1:1000 |
| AMP-activated protein kinase beta 1 | AMPKβ1 | Cell Signaling Technology (Danvers, MA) | #9957 | 1:1000 |
| Sirtuin 3 | SIRT3 | Abcam  (Cambridge, MA) | #ab118334 | 1:1000 |
| Peroxisome proliferative activated receptor, gamma, coactivator 1 alpha | PGC1α | Santa Cruz Biotechnology (Dallas, TX) | #sc-13067 | 1:200 |
| Cyclin-dependent kinase inhibitor 2A | CDKN2A  (p16) | Santa Cruz Biotechnology (Dallas, TX) | #sc-759 | 1:1000 |
| Phosphorylated c-Jun N-terminal kinase | p-JNK | Santa Cruz Biotechnology (Dallas, TX) | #sc-6254 | 1:1000 |
| c-Jun N-terminal kinase | JNK | Santa Cruz Biotechnology (Dallas, TX) | #sc-571 | 1:1000 |
| Peroxisome proliferator-activated receptor alpha | PPARα | Santa Cruz Biotechnology (Dallas, TX) | #sc-9000 | 1:200 |

The other antibodies used were described previously (Aoyama et al., J Biol Chem 1998).

**Supplementary Table 3.** Biochemical analysis of serum and liver

**Serum**

|  |  |  |  |
| --- | --- | --- | --- |
| **Item** | **Control diet group**  (n=8) | **Diet restriction group**  (n=10) | ***P* value** |
| Total cholesterol (mg/dL) | 7.8 ± 1.3 | 10.0 ± 1.4 | 0.2712 |
| Triglyceride (mg/dL) | 139 ± 13.8 | 110 ± 11.4 | 0.1370 |
| NEFA (mEq/L) | 0.6 ± 0.1 | 0.78 ± 0.1 | 0.1297 |

Values are expressed as mean ± SEM.

**Liver**

|  |  |  |  |
| --- | --- | --- | --- |
| **Item** | **Control diet group**  (n=8) | **Diet restriction group**  (n=10) | ***P* value** |
| Total cholesterol (ug/g) | 513 ± 73.4 | 587 ± 77.8 | 0.5027 |
| Triglyceride (mg/g) | 6.1 ± 0.7 | 6.6 ± 0.8 | 0.6186 |
| Phosphatidylcholine  (mg/g) | 10.2 ± 0.6 | 7.8 ± 0.2 | 0.0020 |
| NEFA (uEq/g) | 18.8 ± 7.2 | 45.5 ± 4.7 | 0.0077 |

Values are expressed as mean ± SEM.