Supporting Information

Supplementary Materials and Methods

Animal models

Mice were housed in pathogen-free conditions in a temperature-controlled environment at 22-24°C with a 12-hour/12-hour light/dark cycle. To establish a NASH mouse model, male C57BL/6J mice (8-10 weeks of age) were subjected to continuous HFD (protein, 20%; fat, 60%; carbohydrates, 20%; D12492; HUAFUKANG Bioscience Co., Ltd., Beijing, China) feeding or HFHC diet (protein, 14%; fat, 42%; carbohydrates, 44%; cholesterol, 0.2%; TP26304; TrophicDiet, Nantong, Jiangsu Province, China) feeding for 24 or 16 weeks; the mice in the control group were fed a normal chow (NC) diet (protein, 18.3%; fat, 10.2%; carbohydrates, 71.5%; 1025; HUAFUKANG Bioscience Co., Ltd., Beijing, China). The drugs were freshly dissolved in normal saline 0.9%, Cordycepin (Cordy) were daily administered through oral gavage in a constant volume of 100 mg/kg or 200 mg/kg (normal saline 0.9% for control groups) for 8 weeks. 24-week HFD-fed mice were administered Compound C at the 15^{th} week for one week and then co-treated with cordycepin for an additional 8 weeks. During the experiments, body weight was assayed at different time points. All animal protocols were approved by the Animal Care and Use Committee of Renmin Hospital of Wuhan University.

Cell culture and treatment

The human hepatocyte L02 cell line was purchased from the China Center for Type Culture Collection, Wuhan, China. L02 cells and mouse primary hepatocytes were cultured in Dulbecco's modified Eagle's medium (DMEM) supplemented with 10% FBS (F05-001-B160216; Bio-One Biotechnology, Guangzhou, China) and 1% penicillin-streptomycin (15140-122; Gibco) in a 5% CO_2 incubator. To mimic the hepatic steatosis model *in vivo*, L02 cells and mouse primary hepatocytes were treated with cell culture medium containing the indicated concentrations of palmitic acid (PA,

P0500; Sigma-Aldrich, St. Louis, MO, USA) and oleic acid (OA, O-1008; Sigma-Aldrich, St. Louis, MO, USA) for 12-16 h; 0.5% fatty acid-free BSA (BAH66-0100; Equitech Bio, Kerrville, TX, USA) was used as a control. PA and OA were used at concentrations of 0.5 and 1 mM in L02 cells and 0.2 and 0.4 mM in primary hepatocytes, respectively.

The CRISPR/Cas9 system was used to construct cell lines with specific gene deletions. sgRNAs targeting the human PRKAA1, PRKAA2 genes were designed, which were cloned into the lentiCRISPRv2 plasmid (#98290, Addgene). The sgRNA-expressing plasmid, together with lentivirus packaging plasmids pMD2.G (#12259, Addgene) and psPAX2 (#12260, Addgene) were transfected into HEK293T cells at a ratio of 2:1:1. After transfection for 48h, the supernatants were collected and filtered through a 0.22 μm-filter. Then, the L02 cells were transduced with lentiviral supernatants in the presence of polybrene (2 μg/mL). The lentiviruses targeting PRKAA1 and PRKAA2 were combined and added into a single dish of L02 cells to generate AMPKα1/α2 double knockout cells. To select positive candidates puromycin (2μg/mL) was added. To facilitate the growth of cell clones single cells were placed in 96-well plates. Then, the positive clones were screened by western blotting using the indicated antibodies and further confirmed by sequencing. The sgRNA target sequences and genotyping primers are listed in **Supplementary Table 1**.

Histopathological analysis

Liver samples were fixed in 10% formalin. Hematoxylin and eosin (H&E) staining and Oil Red O (O0625; Sigma-Aldrich, St. Louis, MO, USA) staining was performed on paraffin-embedded and optimum cutting temperature (OCT) compound-embedded frozen liver sections. Picrosirius red (PSR, 26357-02; Hede Biotechnology Co., Ltd., Beijing, China) staining was carried out to visualize the degree of liver fibrosis. Histological images of section tissues were captured with a light microscope (Olympus, Tokyo, Japan).

The following histologic data were analyzed: diagnosis rendered by the Pathology Committee (i.e. “not steatohepatitis”, “borderline, zone 3 pattern”, “definite

steatohepatitis"); the aggregate NAS; the score of each component of the NAS [steatosis (0-3), lobular inflammation (0-3) and ballooning (0-2)]. In addition, portal chronic inflammation and steatosis location were included.

Immunofluorescence staining

For liver tissues, paraffin sections were labeled with an anti-CD11b (BM3925，1:100 dilution; Boster Biological Technology Co.Ltd, Wuhan, China) primary antibody overnight at 4°C and then incubated with a fluorophore-conjugated secondary antibody. Nuclei were stained with DAPI. Immunofluorescence images were obtained by fluorescence microscopy (DX51, Olympus).

Primary cell isolation

Primary hepatocytes were isolated from 8-week-old male C57BL/6 mice using collagenase perfusion and gradient centrifugation, as previously described (22). Briefly, mice were anesthetized and perfused with Liver Perfusion Medium (17701-038, Thermo Fisher Scientific, Waltham, MA, USA) twice through the portal vein followed by Liver Digestion Medium (17701-034, Thermo Fisher Scientific, Waltham, MA, USA). Then, the liver of each mouse was excised and filtered through a 70 μm cell strainer, and the hepatocytes were separated via centrifugation at 50 ×g twice and cultured with DMEM containing 10% FBS and 1% penicillin-streptomycin at 37°C.

Cellular Oil Red O staining

L02 cells and murine primary hepatocytes were treated with 0.5/1 mM PA/OA or 0.2/0.4 mM PA/OA, and then the cells were fixed with 4% paraformaldehyde and subsequently stained with 60% Oil Red O solution (O1391, diluted with water; Sigma-Aldrich, St. Louis, MO, USA) for 1-5 min. The lipid stains were obtained under a light microscope (Olympus, Tokyo, Japan).

Triglyceride and total cholesterol extraction and quantification

Triglycerides (TG) and total cholesterol (TC) were extracted from L02 cells and primary hepatocytes as described previously (22). Briefly, cells were suspended in 600 μl of PBS and vortexed with 3 ml of a chloroform:methanol (2:1) solution. After centrifugation for approximately 10 min, the lower phase was washed with water,

evaporated, and then dissolved in isopropanol. Commercial kits were used to measure cellular TG (290-63701, Wako, Tokyo, Japan) and TC (290-65801, Wako, Tokyo, Japan) levels according to the manufacturer's instructions.

Serum assays

Serum TG, TC, alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels were measured by using an ADVIA 2400 Chemistry System analyzer (Siemens, Tarrytown, NY, USA) according to the manufacturer's instructions.

Quantitative PCR analysis

Total RNA was extracted with TRIzol reagent (T9424, Sigma-Aldrich, St. Louis, MO, USA), and reverse-transcribed into cDNA by using a Transcriptor First-Strand cDNA Synthesis Kit (Roche) according to the manufacturer's instructions. SYBR Green (#04896866001, Roche) was used to quantify the PCR-amplification products. qPCR assays were performed on a real-time PCR system (LightCycler 480 Instrument II, Roche Diagnostics, Inc., Basel, BS, Switzerland) according to a standard procedure. The relative gene expression levels were normalized to the levels of the β-actin housekeeping gene. The primer sequences used are listed in **Supplementary Table 2**.

Western blot analysis

Tissues and cells were lysed in RIPA lysis buffer (65 mM Tris-HCl, 150 mM NaCl, 1 mM EDTA, 1% Nonidet P-40, 0.5% sodium deoxycholate and 0.1% SDS) containing protease inhibitor (04693132001, Roche, Basel, BS, Switzerland) and phosphatase inhibitor (4906837001, Roche, Basel, BS, Switzerland). Total proteins were extracted by centrifugation and quantified with a BCA kit (23225, Thermo, Waltham, MA, USA). Equal-quality protein samples were separated by 10% SDS-PAGE, transferred to PVDF membranes (IPVH00010; Millipore, Billerica, MA, USA), blocked with 5% skim milk in TBST, immunoblotted with the indicated primary antibodies overnight at 4°C and then incubated with suitable HRP-coupled secondary antibodies. Finally, the signals were visualized with an enhanced chemiluminescence (ECL) kit (170-5061, Bio-Rad, Hercules, CA, USA), and the signals were detected with a ChemiDoc MP Imaging System (Bio-Rad, Hercules, CA, USA). The antibodies used are listed in

Supplementary Table 3.

Compound C pretreatment

To verify the specificity of cordycepin in AMPK activation, we tested the effect of the AMPK inhibitor Compound C (Sigma-Aldrich) on the AMPK-activating effects of cordycepin in hepatocytes. Cells were grown to 70%-80% confluence and incubated in 0.02% BSA/DMEM for 24 h. Next, cells were treated with cordycepin (50 μM) or vehicle in the absence or present of Compound C (2 μM) for 12 h.

RNA-seq analysis

Total RNA was extracted using TRIzol reagent (T9424, Sigma-Aldrich, St. Louis, MO, USA), and the quality of the RNA was evaluated via agarose electrophoresis and with an RNA 6000 Nano kit (#5067-1511, Agilent, CA, USA). For the RNA-seq assays, cDNA libraries were constructed using an MGIEasy RNA Library Prep Kit (1000006384, MGI, Shenzhen, China) according to the manufacturer's instructions. Then, the gene expression profiles were determined on a BGISEQ-500 instrument (MGI, Shenzhen, China) by sequencing. The reads were mapped to Ensembl human (hg38/GRCh38) and mouse (mm10/GRCm38) reference genomes by HISAT2 software. Fragments Per Kilobase of exon model per Million mapped fragments (FPKM) value of each indentified gene were calculated by StringTie. Differential expressed genes (DEGs) were identified by DESeq2 with two standards: (1) fold change larger than 1.5 and (2) adjusted *P* values less than 0.05. The data have been submitted to Sequence ReadArchive (SRA) database with PRJNA number PRJNA684925 and PRJNA684926.

KEGG pathway enrichment analysis

KEGG (Kyoto Encyclopedia of Genes and Genomes) pathway enrichment analysis was performed using Fisher's exact test with our in-house R script, and the KEGG pathway annotations of all genes in the selected genome were download from KEGG database. The pathway with a *P* value <0.05 was defined as significantly enriched pathway.

Gene Set Enrichment Analysis

Gene Set Enrichment Analysis (GSEA) was implemented on the Java GSEA

platform. For each KEGG biological pathway, genes involved in were defined as a gene set, and then a ranked list and a ‘gene set’ permutation type of the gene set were generated. Gene sets with *P* values <0.05 and FDR values < 0.25 were considered statistically significant.

Phosphoproteomic analysis

Liver tissues from HFHC-fed mice treated with cordycepin (200 mg/kg) were analyzed by label-free phosphoproteomic assay. The cells were lysed with SDT buffer (4% SDS, 100 mM dithiothreitol [DTT], and 150 mM Tris-HCl, pH 8.0). Then, 400 mg of protein was reduced with 10 mM DTT at 37°C for 2.5 h. Subsequently, the samples were alkylated with iodoacetamide (50 mM) for 30 min in the dark. The proteins were then digested in 1.5 M urea buffer containing trypsin (1 mg/100 mg protein) for 18 h at 37°C. The digests were desalted using Sep-Pak C18 cartridges (#WAT051910, Waters, MA, USA), dried in vacuo, and stored at 80°C for further use.

The phosphopeptides were enriched using TiO_2 beads, and subjected to liquid chromatography (LC)-tandem mass spectrometry (MS/MS) analysis using a Proxeon EASY-nLC 1000 (Thermo Scientific, Shanghai Applied Protein Technology Co., Ltd., Shanghai, China). The peptides were first trapped (Thermo EASY column SC001 traps, 3 μm, 150 mm × 20 mm [RP-C18], Thermo Fisher Scientific) at a maximum pressure of 800 bar with 100% solvent A (0.1% formic acid and 2% acetonitrile in water) before being separated on an analytical column (EASY column SC200, 150 mm 3 100 mm [RP-C18], Thermo Fisher Scientific). The peptides were chromatographically separated with the following 120 min gradient program at a flow rate of 300 nL/min: 0-110 min, 0%-55% solvent B (0.1% formic acid and 84% acetonitrile in water); 110-115 min, 55%-100% solvent B; and 115-120 min, 100% solvent B. The eluents were analyzed on a Q Exactive mass spectrometer (Thermo Finnigan, Odense, Denmark) with scanning from m/z 300 to m/z 1800 at a resolution of 70,000 at m/z 400. Label-free quantification was performed to compare the abundances of phosphopeptides between the control and treatment samples, the Student's t-test was used to identify significant changes between controls and treatments. Phosphopeptides with *P* value < 0.05 were

considered as statistical significant-expressed phosphopeptides.

Proteomic analysis

Proteomic analysis was performed by data-dependent acquisition (DDA) MS assay. Equal aliquots of the samples in this experiment were pooled into one sample for DDA library generation and quality control. All fractions for DDA library generation were injected into a Thermo Scientific Q Exactive HF mass spectrometer connected to an Easy-nLC 1200 chromatography system (Thermo Scientific). Each sample peptide was analyzed in data-independent acquisition (DIA) mode. The DIA cycle contained a full MS selected ion monitoring (SIM) scan, and 30 DIA scans were performed covering a mass range of 350-1650 m/z with the following settings: SIM full-scan resolution, 60,000 at 200 m/z; automatic gain control (AGC), 3e6; maximum ion trap (IT) time, 50 ms; profile mode; DIA scan resolution, 30,000; AGC target, 3e6; maximum IT, auto; and normalized collision energy, 30 eV. The runtime was 120 min with a linear gradient of buffer B (80% acetonitrile and 0.1% formic acid) at a flow rate of 250 nL/min. Quality control samples (pools of equal aliquots of all the samples in the experiment) were injected in DIA mode at the beginning of the MS study and after every 5 injections throughout the experiment and were used to monitor MS performance. Label-free quantification was performed to compare the abundances of peptides between the control and treatment samples, the Student's t-test was used to identify significant changes between controls and treatments. Peptides with P value < 0.05 were considered as differentially-expressed peptides.

Statistical analysis

All data are presented as the mean ± SD and were analyzed using appropriate statistical methods with SPSS software. Student’s t-test was used to analyze differences between 2 groups, while one-way ANOVA followed by Bonferroni’s post hoc test (for data showing homogeneity of variance) or Tamhane’s T2 (M) post hoc test (for data showing heteroscedasticity) was applied for multiple comparisons. A P value of less than 0.05 was considered to indicate statistical significance. The statistical methods used and the corresponding P values for the data shown in each figure panel are included

in the figure legends.

Supplementary Tables

Supplementary Table 1 Oligonucleotide sequences for the generation of gene knockout L02 cell lines.

Gene	Target sequence	Genotyping primers (5'-3')
PRKAA1	sg-1: TACTCAATCGACAGAAGATT	F: CAGCCTAGGAAGAAACTTTTC
	sg-2: GTTGGCAAACATGAATTGAC	R: ACTCCTGACCTCAAGTGATCT
PRKAA2	sg-1: CATACCGAAATCGGCTATCT	F: CTTAATGTGCTCCACAGGCAGA
	sg-2: AATGCCAAGATAGCCGATTT	R: CTTTGCTGATGAATGCAGGAGGT

Supplementary Table 2 Primer sequences for qPCR

Gene	Sequence (5'-3')	
Human *FASN*	F:	ACAGCGGGGAATGGGTACT
	R:	GACTGGTACAACGAGCGGAT
Human *ACACA*	F:	TCACACCTGAAGACCTTAAAGCC
	R:	AGCCCACACTGCTTGTACTG
Human *SCD1*	F:	TCATAATTCCCGACGTGGCT
	R:	CCCAGAAATACCAGGGCACA
Human *PPARG*	F:	TACTGTCGGTTTCAGAAATGCC
	R:	GTCAGCGGACTCTGGATTCAG
Human *PPARA*	F:	GTCATCACGGACACGCTTTCA
	R:	CGGTCGCACTTGTCATACAC
Human *IL-6*	F:	GAGTAGTGAGGAACAAGCCAGA
	R:	AAGCTGCGCAGAATGAGATGA
Human *CCL5*	F:	TCATTGCTACTGCCCTCTGC
	R:	TACTCCTTGATGTGGGCACG
Human *CXCL10*	F:	GTGGCATTCAAGGAGTACCTC

	R:	TGATGGCCTTCGATTCTGGATT
Human *TNF-α*	F:	TGGCGTGGAGCTGAGAGATA
	R:	TGATGGCAGAGAGGAGGTTG
Human *IL-1β*	F:	TCGCCAGTGAAATGATGGCT
	R:	TGGAAGGAGCACTTCATCTGTT
Human *ACTB*	F:	CATGTACGTTGCTATCCAGGC
	R:	CTCCTTAATGTCACGCACGAT
Mouse *Fasn*	F:	CTGCGGAAACTTCAGGAAATG
	R:	GGTTCGGAATGCTATCCAGG
Mouse *Scd1*	F:	TCTTCCTTATCATTGCCAACACCA
	R:	GCGTTGAGCACCAGAGTGTATCG
Mouse *Accα*	F:	GGCCAGTGCTATGCTGAGAT
	R:	AGGGTCAAGTGCTGCTCCA
Mouse *Cd36*	F:	GACTGGGACCATTGGTGATGA
	R:	AAGGCCATCTCTACCATGCC
Mouse *Pparγ*	F:	ATTCTGGCCCACCAACTTCGG
	R:	TGGAAGCCTGATGCTTTATCCCCA
Mouse *Pparα*	F:	TATTCGGCTGAAGCTGGTGTAC
	R:	CTGGCATTTGTTCCGGTTCT
Mouse *Cpt1α*	F:	AGGACCCTGAGGCATCTATT
	R:	ATGACCTCCTGGCATTCTCC
Mouse *Srebp*	F:	CACTTCTGGAGACATCGCAAAC
	R:	ATGGTAGACAACAGCCGCATC
Mouse *Fabp1*	F:	TGGTCCGCAATGAGTTCACCCT
	R:	CCAGCTTGACGACTGCCTTGACTT
Mouse *Hmgcr*	F:	ATCATGTGCTGCTTCGGCTGCAT
	R:	AAATTGGACGACCCTCACGGCT
Mouse *Ccl2*	F:	TACAAGAGGATCACCAGCAGC
	R:	ACCTTAGGGCAGATGCAGTT

Mouse *Ccl5*	F:	TGCTGCTTTGCCTACCTCTC
	R:	TCTTCTCTGGGTTGGCACAC
Mouse *Cxcl10*	F:	ATGACGGGCCAGTGAGAATG
	R:	ATGATCTCAACACGTGGGCA
Mouse *Cxcl2*	F:	GCGCCCAGACAGAAGTCATA
	R:	CAGTTAGCCTTGCCTTTGTTCA
Mouse *Il-6*	F:	TAGTCCTTCCTACCCCAATTTCC
	R:	TTGGTCCTTAGCCACTCCTTC
Mouse *Il-1β*	F:	CCGTGGACCTTCCAGGATGA
	R:	GGGAACGTCACACACCAGCA
Mouse *Tnfα*	F:	CATCTTCTCAAAATTCGAGTGACAA
	R:	TGGGAGTAGACAAGGTACAACCC
Mouse *Col1a1*	F:	TGCTAACGTGGTTCGTGACCGT
	R:	ACATCTTGAGGTCGCGGCATGT
Mouse *Col3a1*	F:	ACGTAAGCACTGGTGGACAG
	R:	CCGGCTGGAAAGAAGTCTGA
Mouse *Ctgf*	F:	TGACCCCTGCGACCCACA
	R:	TACACCGACCCACCGAAGACACAG
Mouse *α-Sma*	F:	CCCAGACATCAGGGAGTAATGG
	R:	TCTATCGGATACTTCAGCGTCA
Mouse *Ctgf*	F:	TGACCCCTGCGACCCACA
	R:	TACACCGACCCACCGAAGACACAG
Mouse *Tgfb*	F:	ATTTGGAGCCTGGACACACA
	R:	GAGCGCACAATCATGTTGGA
Mouse *Timp1*	F:	GAGACCACCTTATACCAGCGTT
	R:	TACGCCAGGGAACCAAGAAG
Mouse *Actb*	F:	GTGACGTTGACATCCGTAAAGA
	R:	GCCGGACTCATCGTACTCC

Supplementary Table 3 Antibody information

Antibody	Cat No.	Manufacturer
p-AMPKa	2535	CST
AMPKa	2603	CST
p-ACC	3661	CST
ACC	3676	CST
GAPDH	600041Ig	Proteintech
p-Smad3	9520	CST
Smad3	9513	CST
p-Smad2	3108	CST
Smad2	BS1425	Bioworld
p-IKKβ	2694	CST
IKKβ	A0714	ABclonal
p-p65	3033	CST
p65	8242	CST
FASN	3189	CST
PPARγ	2435	CST

Supplementary Figures Legends

Supplementary Figure 1. Effects of cordycepin on lipid accumulation and inflammation in primary hepatocytes. (A) Representative Oil Red O staining showing the degrees of lipid accumulation in primary hepatocytes treated with DMSO, 50 μM cordycepin (Cordy) or 100 μM Cordy in response to BSA or PO (0.2 mM PA and 0.4 mM OA) stimulation for 12 h. (B) TG and TC levels in primary hepatocytes in the indicated groups stimulated with BSA or PO (0.5 mM PA and 1.0 mM OA) for 12 h. n = 3 per group. * indicates a significant difference between the DMSO-BSA group and the DMSO-PO group; $^{**}P < 0.01$. # indicates a significant difference between the DMSO-PO group and the Cordy-PO group; $^{\#}P < 0.05$, $^{\#\#}P < 0.01$. (C) Relative mRNA levels of the indicated lipid metabolism-related genes (*Fasn, Scd1, Accα* and *Srebpf*) and inflammatory factors (*IL-1β, IL-6, Tnfα, Ccl5* and *Cxcl10*) in primary hepatocytes treated with PA (0.5 mM) for 12 h. n = 4 per group. * indicates a significant difference between the DMSO-BSA group and the DMSO-PA group; $^{**}P < 0.01$. # indicates a significant difference between the DMSO-PA group and the Cordy-PA group; $^{\#}P < 0.05$, $^{\#\#}P < 0.01$.

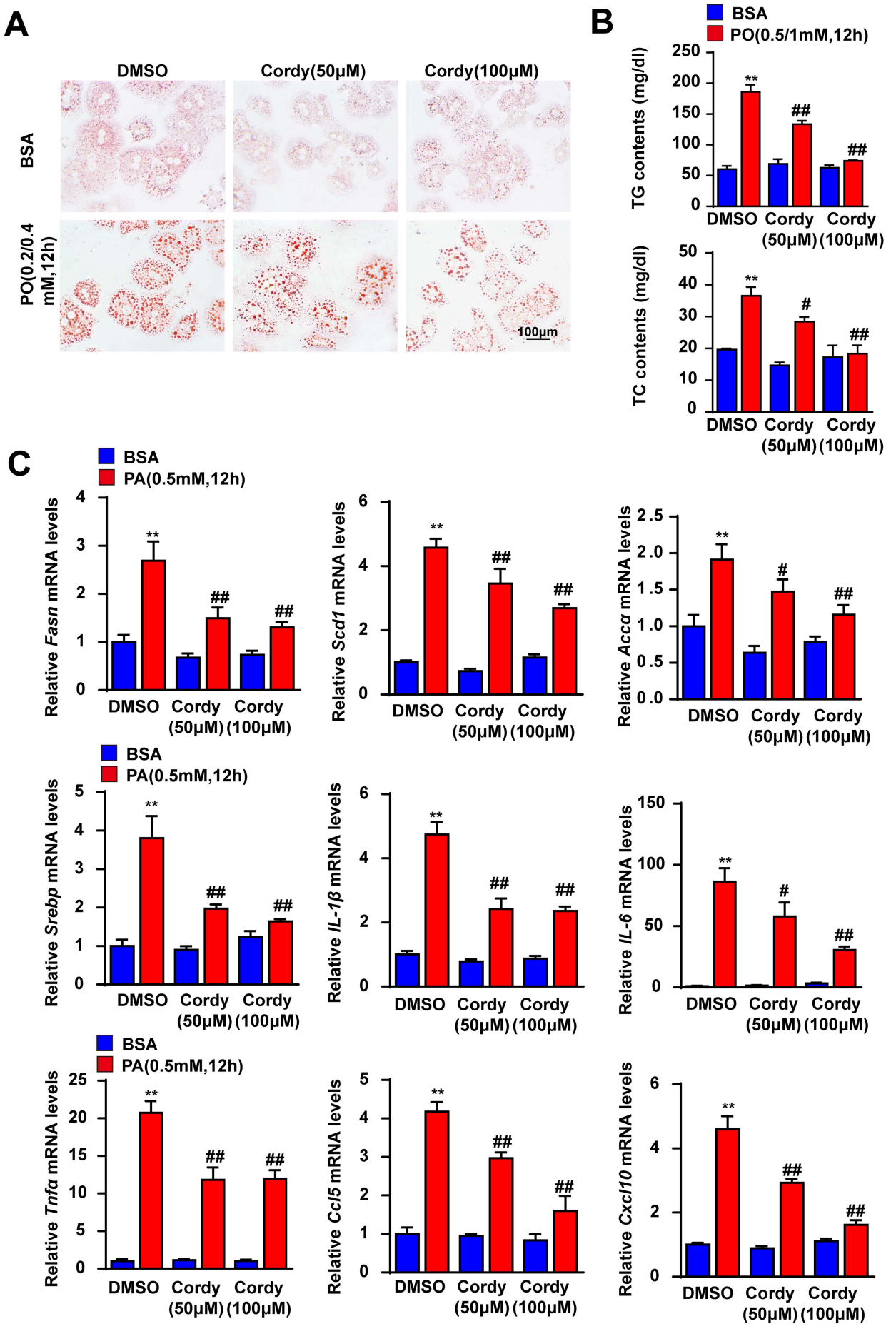
Supplementary Figure 2. Effects of cordycepin on metabolic parameters of mice fed by HFD. (A) Schedule of the animal experiment. Mice were fed NC or a HFD for 24 weeks, and cordycepin (Cordy) was administered once daily from week 16 to week 24 by gavage. n =10 per group. (B) Fasting body weights of the mice. n =10 per group. (C, D) White adipose weights and white adipose weight ratios of the mice. n =10 per group. (E) Serum lipid (TG and TC) levels. n =10 per group. The data are presented as the mean ± SD. * indicates a significant difference between the control-NC group and the control-HFD group; $^{*}P < 0.05$, $^{**}P < 0.01$. n.s. indicates that there was no significant difference between the control-HFD group and the Cordy-HFD group; $P > 0.05$. # indicates a significant difference between the control-HFD group and the Cordy-HFD group; $^{\#\#}P < 0.01$.

Supplementary Figure 3. Effects of cordycepin on metabolic parameters of mice

fed by HFHC diets. (A) Schedule of the animal experiment. Mice were fed NC or a HFHC diet for 16 weeks, and cordycepin (Cordy) was administered once daily from week 8 to week 16 by gavage. (B) Fasting body weights of the mice. n=10 per group. (C) White adipose weights and white adipose weight ratios of the mice. n=10 per group. (D) Serum lipid (TG and TC) levels. n=10 per group. The data are presented as the mean ± SD. * indicates a significant difference between the control group and the Cordy group; $^{*}P < 0.05$, $^{**}P < 0.01$. n.s. indicates that there was no significant difference between the control-HFHC group and the Cordy-HFHC group; $P > 0.05$.

Supplementary Figure 4. Cordycepin protected against lipid deposition in hepatocytes dependent on AMPK. (A) The phosphorylation of AMPKα and ACC in wild type and AMPK-KO cells treated by cordycepin (Cordy) was measured by immunoblotting analyses in the absence or presence of PA for 12h. (B) Representative Oil Red O staining showing the degrees of lipid accumulation in Wild type and AMPK-KO hepatocytes treated with DMSO, 50 μM cordycepin (Cordy) in response to PO (0.2 mM PA and 0.4 mM OA) stimulation for 12 h.

Supplementary Figure 5. AMPK is required for cordycepin in the treatment of NASH in mice. (A) Experimental scheme for HFD-fed mice treated with vehicle or cordycepin (Cordy) in the absence or presence of Compound C (CC). (B) Body weights of HFD-fed mice treated with vehicle or Cordy from 0 to 24 weeks. n = 10 per group. (C) White adipose weights and white adipose weight-to-body weight ratios in the indicated groups. n = 10 per group. (D) Serum lipid levels. n = 10 per group. The data are presented as the mean ± SD. n.s. indicates that there was no significant difference between the PBS-control-HFD group and the PBS-Cordy-HFD group; $P > 0.05$. * indicates a significant difference between the PBS-control-HFD group and the PBS-Cordy-HFD group; $^{*}P < 0.05$. n.s. indicates a significant difference between the CC-control-HFD group and the CC-Cordy-HFD group.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TC contents (mg/dl)
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PA(0.5mM,12h)
Relative Fasn mRNA levels
Relative Scd1 mRNA levels
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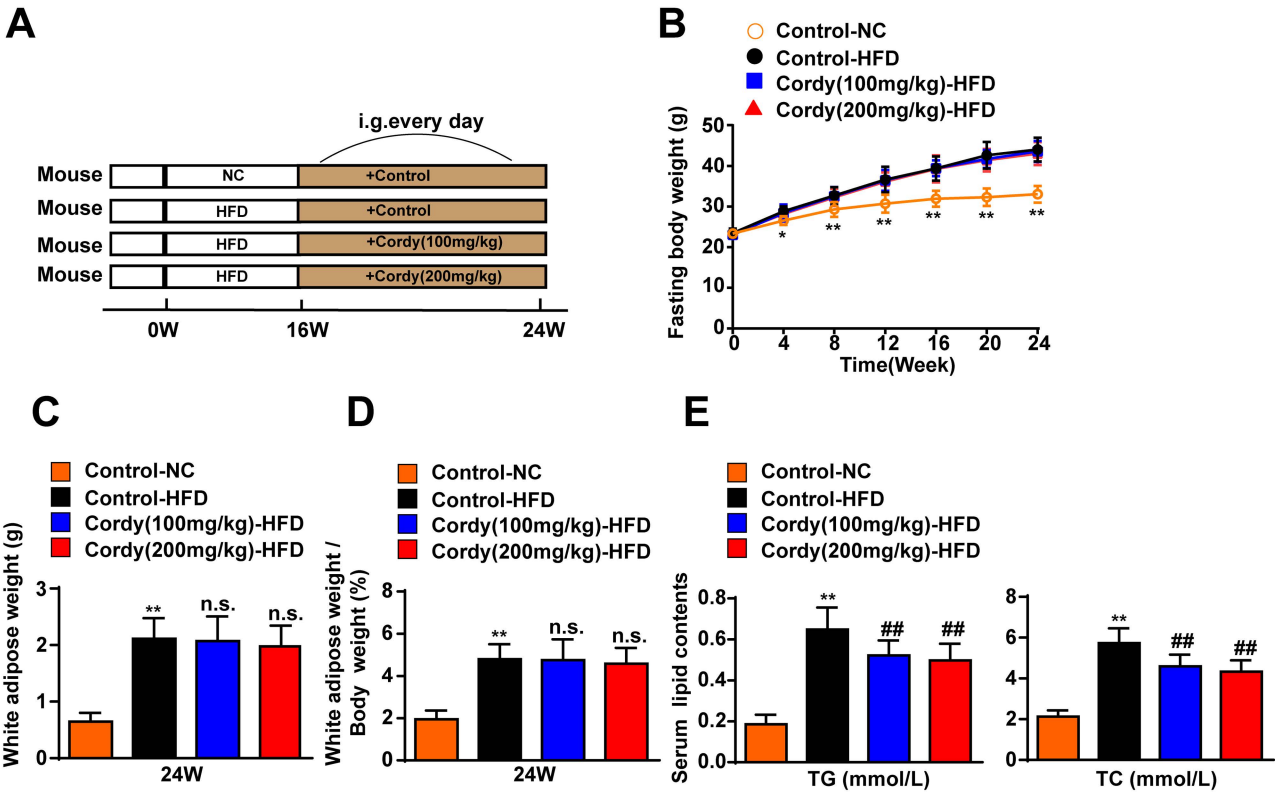
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Control-HFD
Cordy(100mg/kg)-HFD
Cordy(200mg/kg)-HFD
Fasting body weight (g)
Time(Week)
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TG (mmol/L)
TC (mmol/L)
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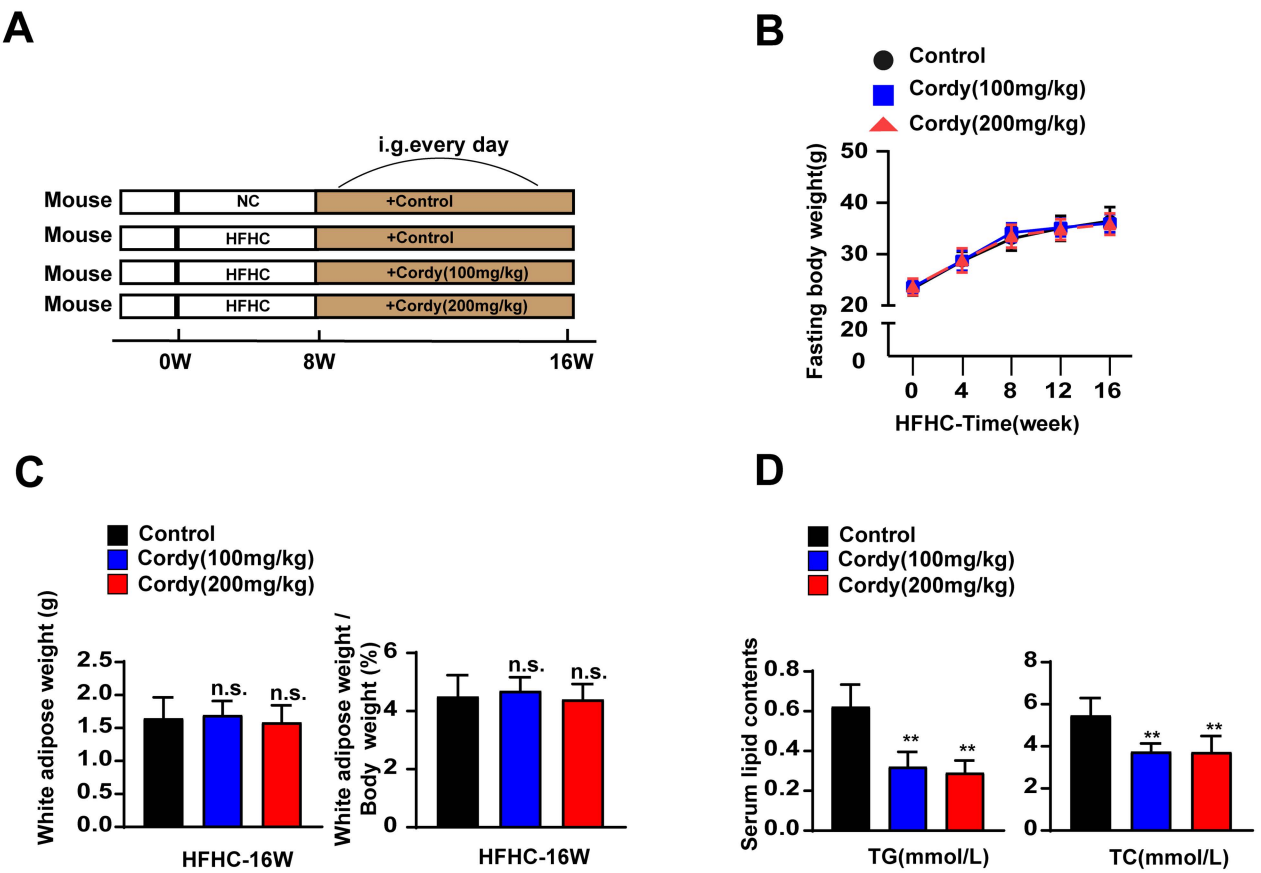
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8W
16W
B
Control
Cordy(100mg/kg)
Cordy(200mg/kg)
Fasting body weight(g)
50
40
30
20
20
0
0
4
8
12
16
HFHC-Time(week)
C
Control
Cordy(100mg/kg)
Cordy(200mg/kg)
White adipose weight (g)
2.5
2.0
1.5
1.0
0.5
0.0
n.s.
n.s.
HFHC-16W
White adipose weight / Body weight (%)
6
4
2
0
n.s.
n.s.
HFHC-16W
D
Control
Cordy(100mg/kg)
Cordy(200mg/kg)
Serum lipid contents
0.8
0.6
0.4
0.2
0.0
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TG(mmol/L)
8
6
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2
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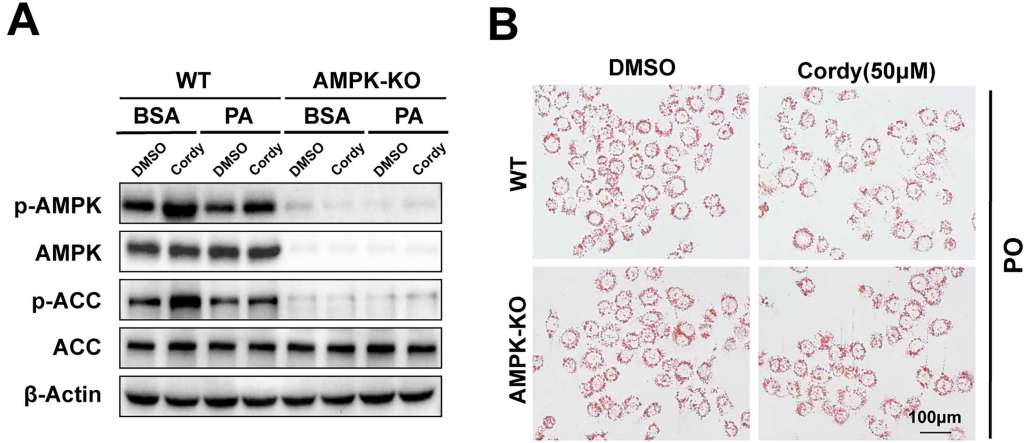
TC(mmol/L)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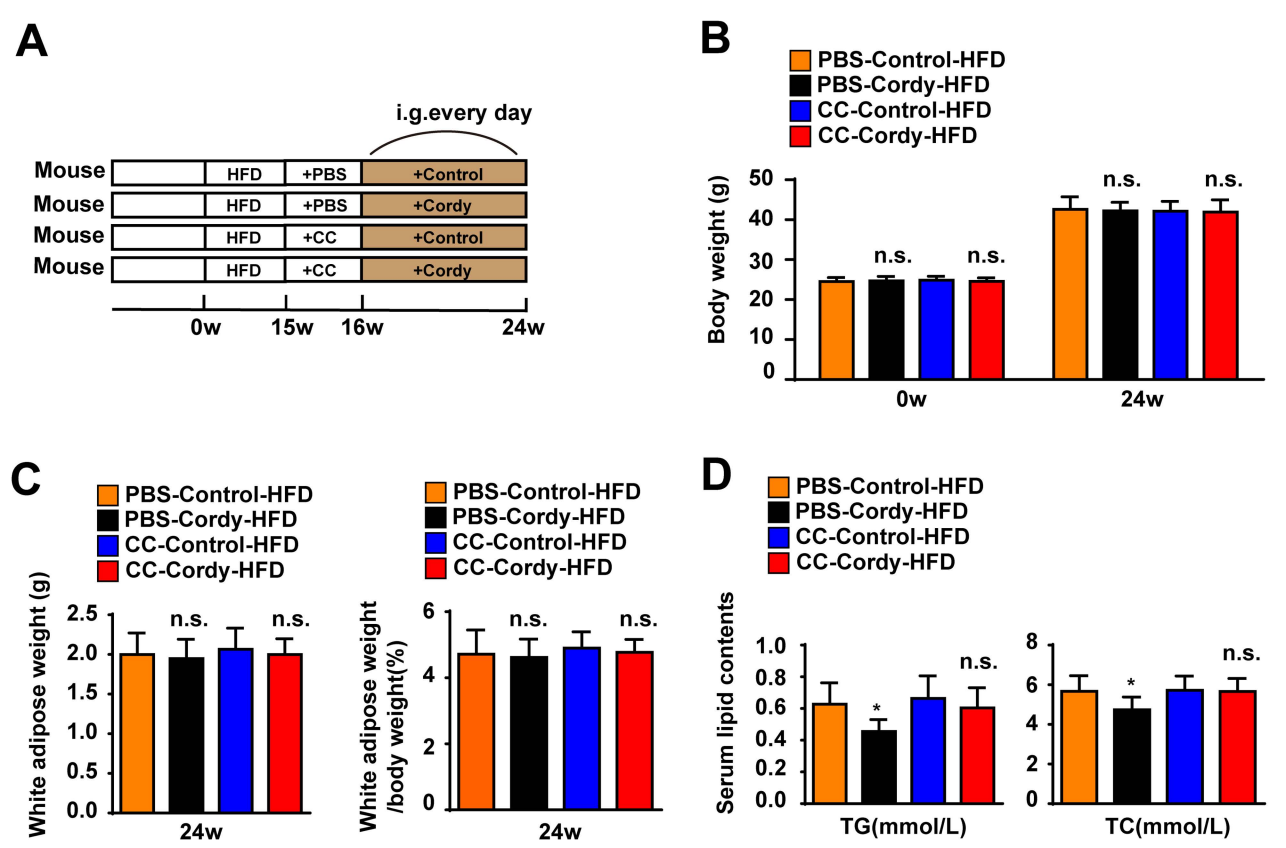
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+Control
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+Cordy
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+CC
+Cordy
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CC-Control-HFD
CC-Cordy-HFD
Body weight (g)
50
40
30
20
10
0
n.s.
n.s.
n.s.
n.s.
0w
24w
C
PBS-Control-HFD
PBS-Cordy-HFD
CC-Control-HFD
CC-Cordy-HFD
White adipose weight (g)
2.5
2.0
1.5
1.0
0.5
0.0
n.s.
n.s.
24w
PBS-Control-HFD
PBS-Cordy-HFD
CC-Control-HFD
CC-Cordy-HFD
White adipose weight /body weight(%)
6
4
2
0
n.s.
n.s.
24w
D
PBS-Control-HFD
PBS-Cordy-HFD
CC-Control-HFD
CC-Cordy-HFD
Serum lipid contents
1.0
0.8
0.6
0.4
0.2
0.0
*
n.s.
TG(mmol/L)
8
6
4
2
0
*
n.s.
TC(mmol/L)