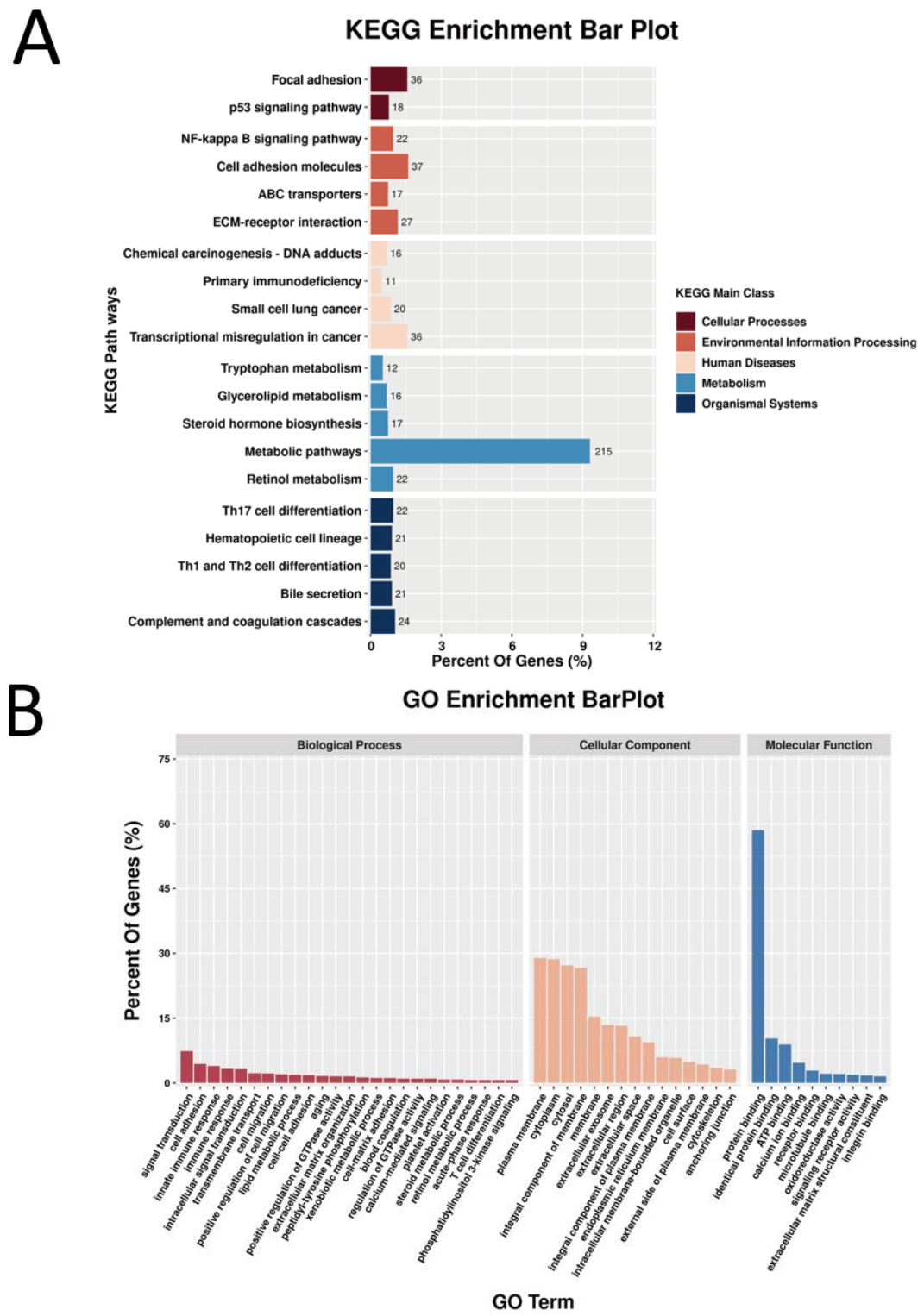
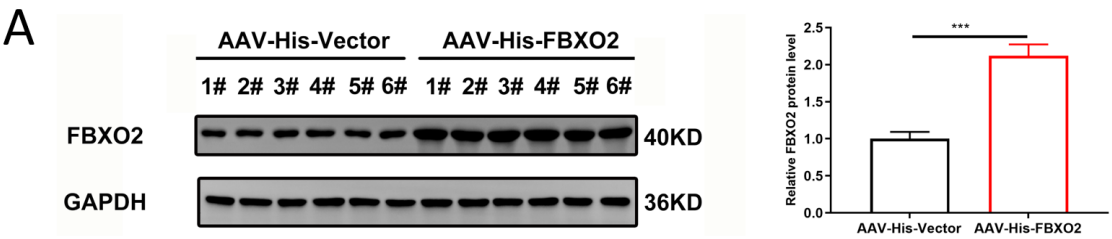
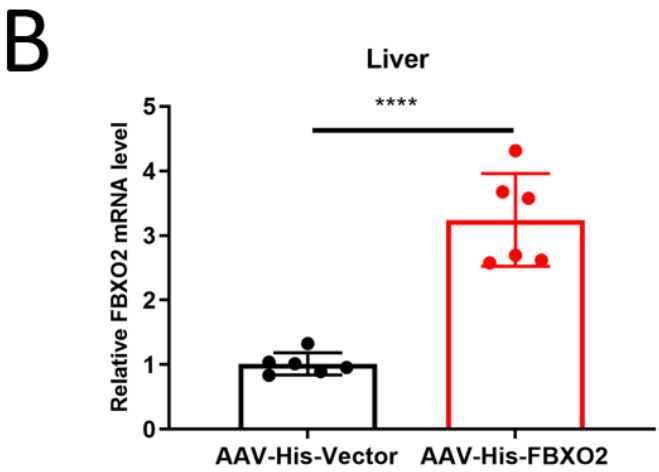
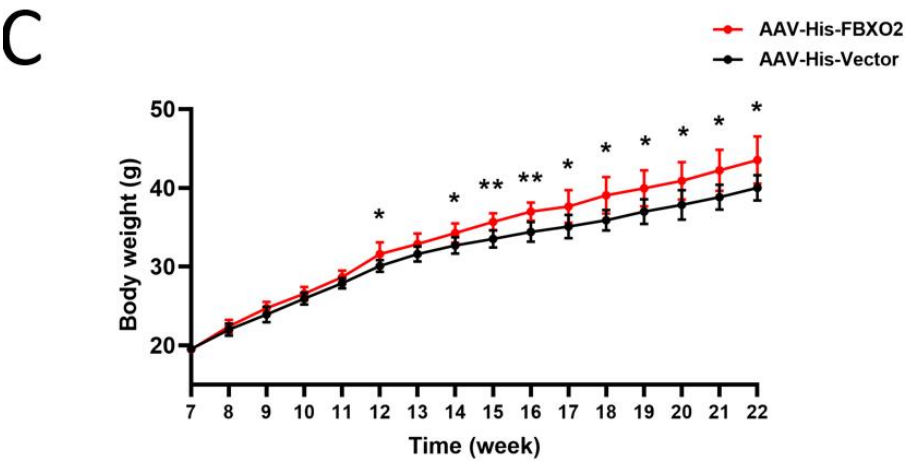
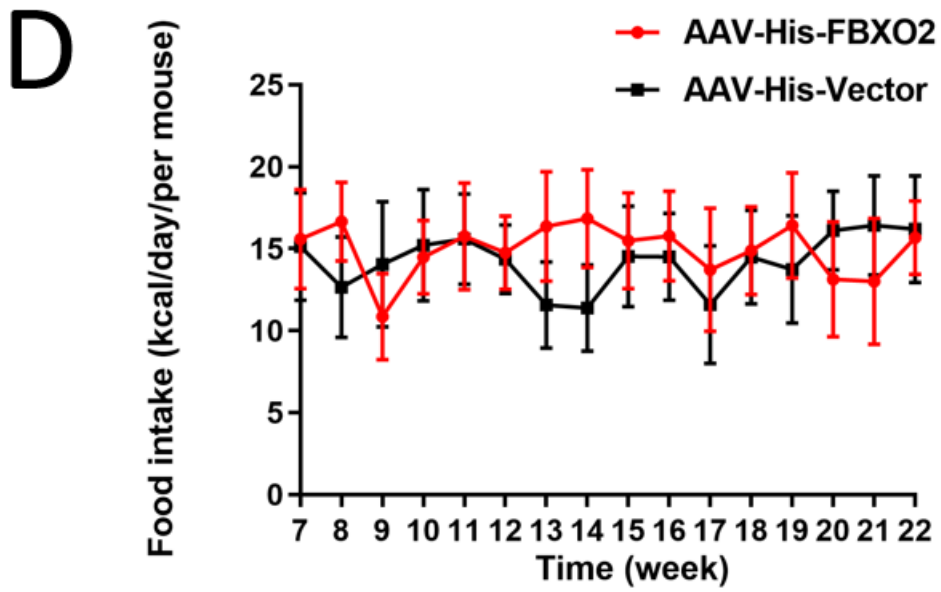


Supplementary Figure 1 Whole genome sequencing (WGS) analysis of liver tissue from patients with non-alcoholic fatty liver disease (NAFLD) and healthy controls. **A:** Barplot of the Kyoto Encyclopedia of Genes and Genomes (KEGG) enrichment analysis results; **B:** Barplot of the Gene Ontology (GO) enrich analysis results.

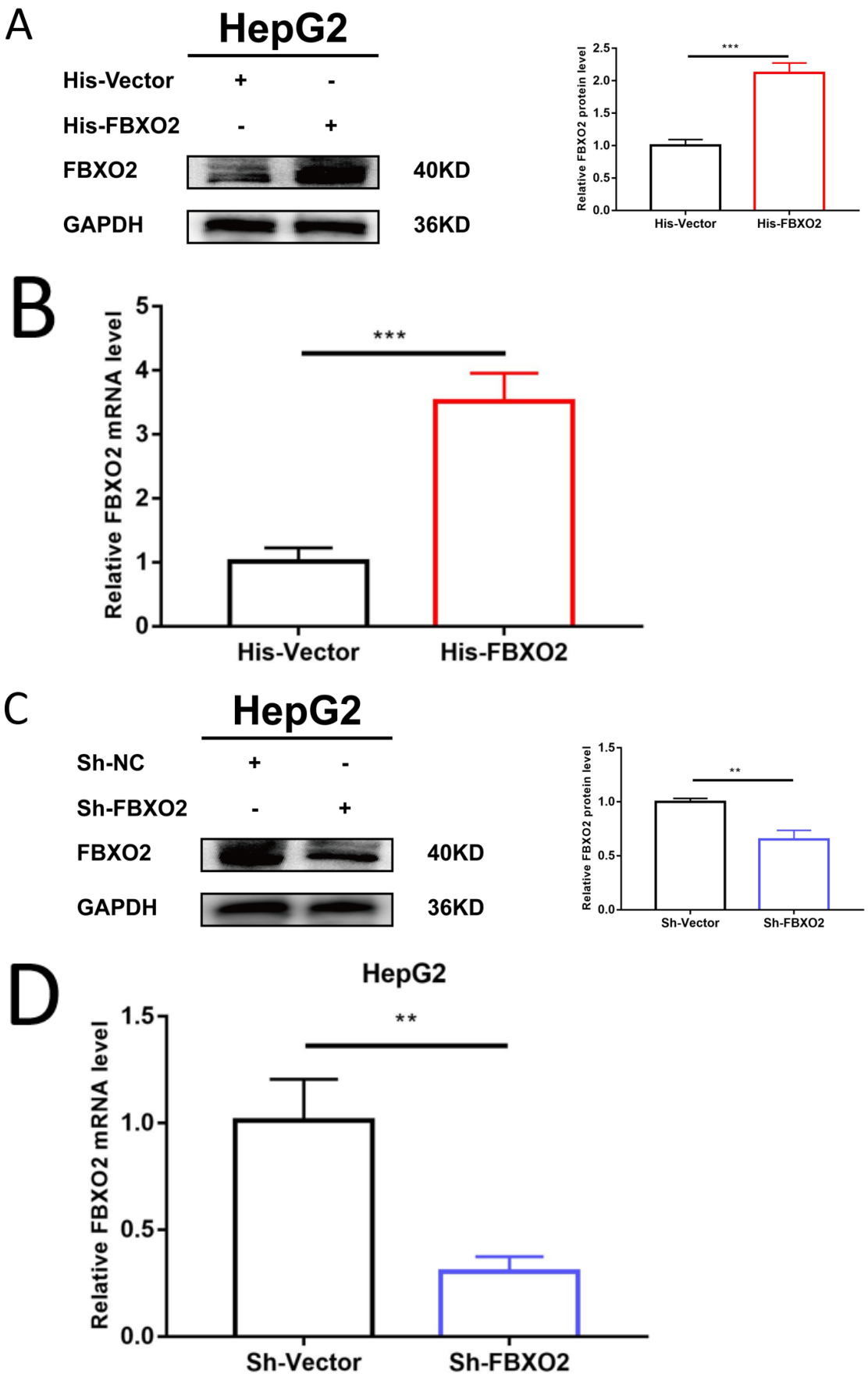

A
AAV-His-Vector
AAV-His-FBXO2
1# 2# 3# 4# 5# 6# 1# 2# 3# 4# 5# 6#
FBXO2
40KD
GAPDH
36KD
Relative FBXO2 protein level
***
AAV-His-Vector
AAV-His-FBXO2


B
Liver
****
Relative FBXO2 mRNA level
AAV-His-Vector
AAV-His-FBXO2


C
AAV-His-FBXO2
AAV-His-Vector
Body weight (g)
Time (week)

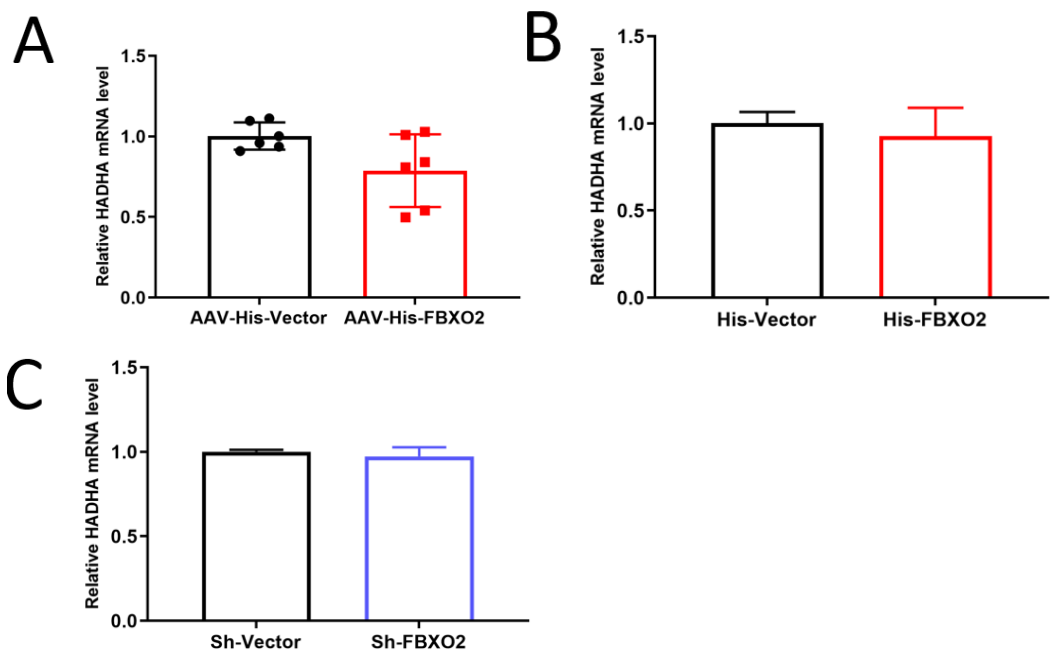

D
AAV-His-FBXO2
AAV-His-Vector
Food intake (kcal/day/per mouse)
Time (week)

Supplementary Figure 2 A: Western blot results and **B:** qRT-PCR analysis of the relative mRNA expression of F-box only protein 2 (FBXO2) in adeno-associated virus (AAV)-His-vector and AAV-His-FBXO2 mice after high-fat diet (HFD) feeding for 16 wk (n = 6 per group, ****p < 0.0001); **C-D:** Records for body weight and food intake (Kcal/day/per mice) of AAV-His-vector mice and AAV-His-FBXO2 mice after HFD feeding for 16 wk (n = 6 per group, *p < 0.05, **p < 0.01).



Supplementary Figure 3 A-B: We transfected His-F-box only protein 2

(FBXO2) plasmids into HepG2 cells to overexpress FBXO2, then HepG2 cells were treated with OA for 24 h. **A:** Western blot results and **B:** qRT-PCR analysis of the relative mRNA expression of FBXO2 in HepG2 cells. (***p < 0.001); **C-D:** We transfected Sh-FBXO2 plasmids into HepG2 cells to knockdown FBXO2 expression, then HepG2 cells were treated with OA for 24 h.**C:** Western blot results and **D:** qPCR analysis of the relative mRNA expression of FBXO2 in HepG2 cells. (**p < 0.01); **E:** We transfected His-FBXO2 and Myc-the hydroxyl CoA dehydrogenase alpha subunit (HADHA) plasmids into HepG2 cells to overexpress FBXO2 and HADHA, respectively, then HepG2 cells were treated with OA for 24 h. The western blot results of FBXO2 and HADHA protein expression in HepG2 cells were shown. (**p < 0.01, ***p < 0.001).



Supplementary Figure 4 A: qRT-PCR analysis of the relative mRNA expression of the hydroxyl CoA dehydrogenase alpha subunit (HADHA) in liver tissues from adeno-associated virus (AAV)-His-vector and AAV-His-F-box only protein 2 (FBXO2) mice after high-fat diet (HFD) feeding for 16 wk (n = 6 per group); **B:** We transfected His-FBXO2 plasmids into HepG2 cells to overexpress FBXO2, then HepG2 cells were treated with OA for 24 h. qRT-PCR analysis of the relative mRNA expression of HADHA in HepG2 cellswas shown; **C:** We transfected Sh-FBXO2 plasmids into HepG2 cells to knockdown FBXO2, then HepG2 cells were treated with OA for 24 h. qRT-PCR analysis of the relative mRNA expression of HADHA in HepG2 cells.

Supplementary Table 1 Information of normal chow diet (ND)and high-fat diet (HFD) mice

	ND (n=8)	HFD (n=8)	t -value	p-value
Body weight, g	24.39±1.18	43.16±2.26	20.850	<0.001
T-Cho, mmol/L	1.69±0.45	6.33±0.97	12.231	<0.001
TG, mmol/L	0.44±0.21	1.63±0.61	5.227	<0.001
FPG, mmol/L	6.54±1.16	8.39±1.43	2.841	0.013
NASH score	0	5.88±0.99	-	-

Data are presented as the mean ± standard deviation. $p < 0.05$ was considered statistically significant.

T-Cho:Total cholesterol; **TG**: triglycerides; **FPG**: fasting plasma glucose.

Name	Company	Product Number	Soruce	MW(kDa)	Dilution
GAPDH	Proteintech	60004-1-lg	Mouse	36	1:5000
FBXO2	Proteintech	14590-1-AP	Rabbit	40	1:1000
HADHA	Proteintech	10758-1-AP	Rabbit	83	1:1000
His tag	Proteintech	66005-1-Ig	Rabbit	-	1:8000
Myc tag	Proteintech	16286-1-AP	Rabbit	-	1:5000
HA tag	Proteintech	51062-2-AP	Rabbit		1:5000

Supplementary Table 2 Antibodies used for western blotting

GAPDH: glyceraldehyde-3-phosphate dehydrogenase; **FBXO2**: F-box protein 2; **HADHA**: the hydroxyl CoA dehydrogenase alpha subunit.

Supplementary Table 3 Primer sequences for qRT-PCR

Gene name	Species	Sequences (5′ to 3′)	
GAPDH	Human	Forward Primer	GGAGCGAGATCCCTCCAAAAT
		Reverse Primer	GGCTGTTGTCATACTTCTCATGG
FBXO2	Human	Forward Primer	GTGTCGCAAAGCACAGGTC
		Reverse Primer	CGGACAGTAGCTTAACGGTGAG
ACOX1	Human	Forward Primer	ACTCGCAGCCAGCGTTATG
		Reverse Primer	AGGGTCAGCGATGCCAAAC
ECH1	Human	Forward Primer	ATAGTGGCTTCTCGCAGACTC
		Reverse Primer	CAGTGAGGCGAAGGCTAATAC
MCAD	Human	Forward Primer	ACAGGGGTTCAGACTGCTATT
		Reverse Primer	TCCTCCGTTGGTTATCCACAT
PPARA	Human	Forward Primer	ATGGTGGACACGGAAAGCC
		Reverse Primer	CGATGGATTGCGAAATCTCTTGG
FASN	Human	Forward Primer	AAGGACCTGTCTAGGTTTGATGC
		Reverse Primer	TGGCTTCATAGGTGACTTCCA
PPARG	Human	Forward Primer	GGGATCAGCTCCGTGGATCT
		Reverse Primer	TGCACTTTGGTACTCTTGAAGTT
CD36	Human	Forward Primer	GGCTGTGACCGGAACTGTG

		Reverse Primer	AGGTCTCCAACTGGCATTAGAA
FABP1	Human	Forward Primer	ATGAGTTTCTCCGGCAAGTACC
		Reverse Primer	CTCTTCCGGCAGACCGATTG
HADHA	Human	Forward Primer	ATATGCCGCAATTTTACAGGGT
		Reverse Primer	ACCTGCAATAAAGCAGCCTGG
Gapdh	Mouse	Forward Primer	TAACTTCCTCACTCGAAGCCA
		Reverse Primer	AGTTCCATGACCCATCTCTGTC
Fbxo2	Mouse	Forward Primer	ATGGGGTGGAATTTACCCAAGA
		Reverse Primer	GACCCGAGTACCAGTCCTTCA
Acox1	Mouse	Forward Primer	TAACTTCCTCACTCGAAGCCA
		Reverse Primer	AGTTCCATGACCCATCTCTGTC
Cpt1a	Mouse	Forward Primer	CTCCGCCTGAGCCATGAAG
		Reverse Primer	CACCAGTGATGATGCCATTCT
Ech1	Mouse	Forward Primer	GCTACCGCGATGACAGTTTC
		Reverse Primer	TCAGAGATCGAAGGCTGATGTT
Ehhadh	Mouse	Forward Primer	ATGGCTGAGTATCTGAGGCTG
		Reverse Primer	GGTCCAAACTAGCTTTCTGGAG
Srebp1	Mouse	Forward Primer	TGACCCGGCTATTCCGTGA
		Reverse Primer	CTGGGCTGAGCAATACAGTTC
Acly	Mouse	Forward	ACCCTTTCACTGGGGATCACA

		Primer	
		Reverse Primer	GACAGGGATCAGGATTTCCTTG
		Forward Primer	
Dgat1	Mouse		TCCGTCCAGGGTGGTAGTG
		Reverse Primer	TGAACAAAGAATCTTGCAGACG A
Mcad	Mouse	Forward Primer	AGGGTTTAGTTTTGAGTTGACGG
		Reverse Primer	CCCCGCTTTTGTCATATTCCG
Ppara	Mouse	Forward Primer	AGAGCCCCATCTGTCCTCTC
		Reverse Primer	ACTGGTAGTCTGCAAAACCAAA
		Forward	
Hadha	Mouse	Primer	CTGACAGGATGCCTAGCCG
		Reverse Primer	CGCAGGTAATCCCAGAAGC
		Forward	
Fasn	Mouse	Primer	GGAGGTGGTGATAGCCGGTAT
		Reverse Primer	TGGGTAATCCATAGAGCCCAG
		Forward	
Pparg	Mouse	Primer	TCGCTGATGCACTGCCTATG
		Reverse Primer	GAGAGGTCCACAGAGCTGATT
		Forward	
Apoa1	Mouse	Primer	GGCACGTATGGCAGCAAGAT
		Reverse Primer	CCAAGGAGGAGGATTCAAACTG
		Forward	
Apoae	Mouse	Primer	CTGACAGGATGCCTAGCCG
		Reverse Primer	CGCAGGTAATCCCAGAAGC
Apoab	Mouse	Forward Primer	AAGCACCTCCGAAAGTACGTG

		Reverse Primer	CT CCAGCT CTACCTTAuAGTT GA
Cd36	Mouse	Forward Primer	ATGGGCTGTGATCGGAACTG
		Reverse Primer	GTCTTCCCAATAAGCATGTCTCC
Fabp1	Mouse	Forward Primer	ATGAACTTCTCCGGCAAGTACC
		Reverse Primer	CTGACACCCCCTTGATGTCC

GAPDH: glyceraldehyde-3-phosphate dehydrogenase; **FBXO2**: F-box protein 2; **ACOX1**: acyl-CoA oxidase 1; **ECH1**: enoyl coenzyme A hydratase 1; **MCAD**: medium-chain acyl-coenzyme A dehydrogenase; **PPARA**: peroxisome proliferator-activated receptor alpha; **FASN**: fatty acid synthase; **PPARG**: peroxisome proliferator-activated receptor gamma; **CD36**: cluster of differentiation 36 ; **FABP1**: fatty acid binding protein-1; **HADHA**: the hydroxyl CoA dehydrogenase alpha subunit.

Supplementary material Sequences of the plasmids and lentiviruses used

	Sequence
His-FBXO2 NM_012168 CH895916 (WZ Bioscience Inc)	CGCCATGGACGGAGACGGTGACCCAGAGAGCGTGGGCC AGCCCgaggaggcaagccCGGAGGAGCAGCCAGAGGAGGCGA GTGCTGAGGAGGAGCGGCCGGAGGACCAGCAGGAGGAG GAGGCGGCGGCCGCCGCCGCGTACCTGGACGAGCTGCCC GAGCCGCTGCTGCTGCGCGTGCTGGCCGCACTGCCGGCC GCCGAGCTGGTGCAGGCCTGCCGCCTGGTGTGCCTGCGCT GGAAGGAGCTGGTGGACGGCGCCCCGCTGTGGCTGCTCA AGTGCCAGCAGGAGGGGCTGGTGcccgagggcggcgtGGAGGA GGAGCGCGACCACTGGCAGCAGTTCTACTTCCTGAGCAA GCGGCGCCGCAACCTTCTGCGTAACCCGTGTGGGGAAGA GGACTTGGAAGGCTGGTGTGACGTGGAGCATGGTGGGGA CGGCTGGAGGGTGGAGGAGCTGCCTGGAGACAGTGGGG TGGAGTTCACCCACGATGAGAGCGTCAAGAAGTACTTCG CCTCCTCCTTTGAGTGGTGTCGCAAAGCACAGGTCATTGA CCTGCAGGCTGAGGGCTACTGGGAGGAGCTGCTGGACAC GACTCAGCCGGCCATCGTGGTGAAGGACTGGTACTCGGG CCGCAGCGACGCTGGTTGCCTCTACGAGCTCACCGTTAA GCTACTGTCCGAGCACGAGAACGTGCTGGCTGAGTTCAG CAGCGGGCAGGTGGCAGTGCCCCAAGACAGTGACGGCG GGGGCTGGATGGAGATCTCCCACACCTTCACCGACTACG GGCCGGGCGTCCGCTTCGTCCGCTTCGAGCACGGGGGGC AGGACTCCGTCTACTGGAAGGGCTggttcggggcccgggtgacCA ACAGCAGCGTGTGgtagaaccca
Myc-HADHA BC009235 HG15019-NM	ATGGAGCAGAAACTCATCTCAGAAGAGGATCTGGGTGGA GGCGGTAGCGTGGCCTGCCGGGCGATTGGCATCCTCAGC CGCTTTTCTGCCTTCAGGATCCTCCGCTCCCGAGGTTATAT ATGCCGCAATTTTACAGGGTCTTCTGCTTTGCTGACCAGA ACCCATATTAACTATGGAGTCAAAGGGGATGTGGCAGTT

(SinoBiological)	GTTCGAATTAACTCTCCCAATTCAAAGGTAAATACACTGA GTAAAGAGCTACATTCAGAGTTCTCAGAAGTTATGAATG AAATCTGGGCTAGTGATCAAATCAGAAGTGCCGTCCTTA TCTCATCAAAGCCAGGCTGCTTTATTGCAGGTGCTGATAT CAACATGTTAGCCGCTTGCAAGACCCTTCAAGAAGTAAC ACAGCTATCACAAGAAGCACAGAGAATAGTTGAGAAAC TTGAAAAGTCCACAAAGCCTATTGTGGCTGCCATCAATG GATCCTGCCTGGGAGGAGGACTTGAGGTTGCCATTTCATG CCAATACAGAATAGCAACAAAAGACAGAAAAACAGTAT TAGGTACCCCTGAAGTTTTGCTGGGGGCCTTACCAGGAGC AGGAGGCACACAAAGGCTGCCCAAAATGGTGGGTGTGC CTGCTGCTTTGGACATGATGCTGACTGGTAGAAGCATTCG TGCAGACAGGGCAAAGAAAATGGGACTGGTTGACCAAC TGGTGGAACCCCTGGGACCAGGACTAAAACCTCCAGAGG AACGGACAATAGAATACCTAGAAGAAGTTGCAATTACTT TTGCCAAAGGACTAGCTGATAAGAAGATCTCTCCAAAGA GAGACAAGGGATTGGTGGAAAAATTGACAGCGTATGCC ATGACTATTCCATTTGTCAGGCAACAGGTTTACAAAAAA GTGGAAGAAAAAGTGCGAAAGCAGACTAAAGGCCTTTA TCCTGCACCTCTGAAAATAATTGATGTGGTAAAGACTGG AATTGAGCAAGGGAGTGATGCCGGTTATCTCTGTGAATCT CAGAAATTTGGAGAGCTTGTAATGACCAAAGAATCAAAG GCCTTGATGGGACTCTACCATGGTCAGGTCCTGTGCAAGA AGAATAAATTTGGAGCTCCACAGAAGGATGTTAAGCATC TGGCTATTCTTGGTGCAGGGCTGATGGGAGCAGGCATCG CCCAAGTCTCCGTGGATAAGGGGCTAAAGACTATACTTA AAGATGCCACCCTCACTGCGCTAGACCGAGGACAGCAAC AAGTGTTCAAAGGATTGAATGACAAAGTGAAGAAGAAA GCTCTAACATCATTTGAAAGGGATTCCATCTTCAGCAACT

	TGACTGGGCAGCTTGATTACCAAGGTTTTGAAAAGGCCG
Sh-FBXO2 (WZ	GACTGGTAGTCAACGTCGATTGAGGACATCAGACTAT GACTAAGCGTTATGAAGTAGAAGCGGTGATTCCAG
	ATCACTGTATCTTTGCCAGTAACACATCTGCTCTCCCAAT CAGTGAAATCGCTGCTGTCAGCAAAAGACCTGAGAAGGT GATTGGCATGCACTACTTCTCTCCCGTGGACAAGATGCAG CTGCTGGAGATTATCACGACCGAGAAAACTTCCAAAGAC ACCAGTGCTTCAGCTGTAGCAGTTGGTCTCAAGCAGGGG AAGGTCATCATTGTGGTTAAGGATGGACCTGGCTTCTATA CTACCAGGTGTCTTGCGCCCATGATGTCTGAAGTCATCCG AATCCTCCAGGAAGGAGTTGACCCGAAGAAGCTGGATTC CCTGACCACAAGCTTTGGCTTTCCTGTGGGTGCCGCCACA CTGGTGGATGAAGTTGGTGTGGATGTAGCGAAACATGTG GCGGAAGATCTGGGCAAAGTCTTTGGGGAGCGGTTTGGA GGTGGAAACCCAGAACTGCTGACACAGATGGTGTCCAAG GGCTTCCTAGGTCGTAAATCTGGGAAGGGCTTTTACATCT ATCAGGAGGGTGTGAAGAGGAAGGATTTGAATTCTGACA TGGATAGTATTTTAGCGAGTCTGAAGCTGCCTCCTAAGTC TGAAGTCTCATCAGACGAAGACATCCAGTTCCGCCTGGT GACAAGATTTGTGAATGAGGCAGTCATGTGCCTGCAAGA GGGGATCTTGGCCACACCTGCAGAGGGAGACATCGGAGC CGTCTTTGGGCTTGGCTTCCCGCCTTGTCTGGGAGGGCCTT TCCGCTTTGTGGATCTGTATGGCGCCCAGAAGATAGTGGA CCGGCTCAAGAAATATGAAGCTGCCTATGGAAAACAGTT CACCCCATGCCAGCTGCTAGCTGACCATGCTAACAGCCC TAACAAGAAGTTCTACCAGTAA

FBXO2: F-box only protein 2; **HADHA**: the hydroxyl CoA dehydrogenase alpha subunit.

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Green: Myc tag; **Yellow**: Linker