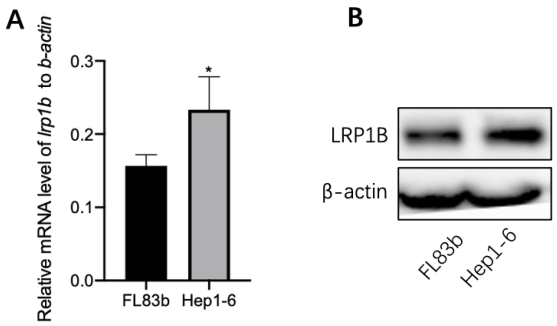
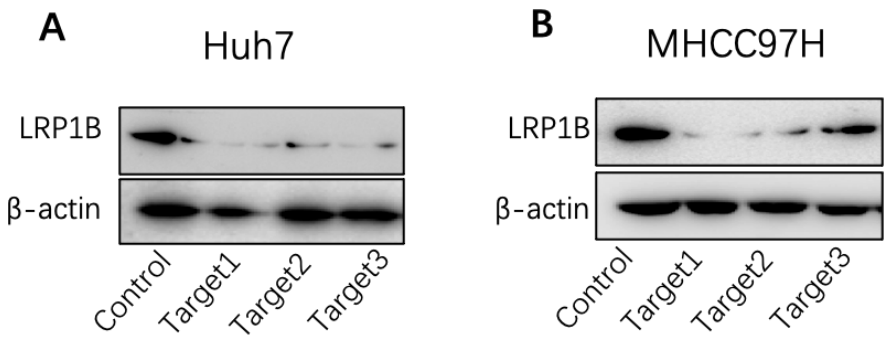
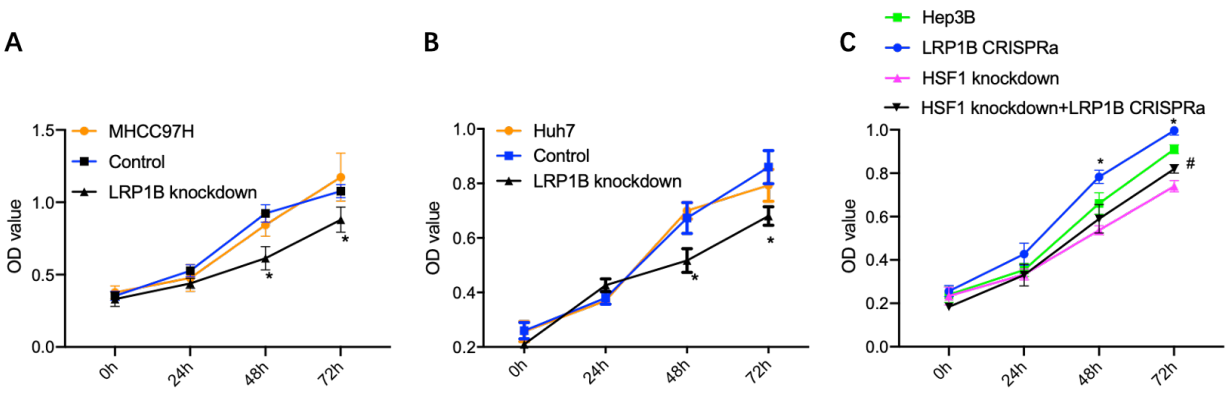


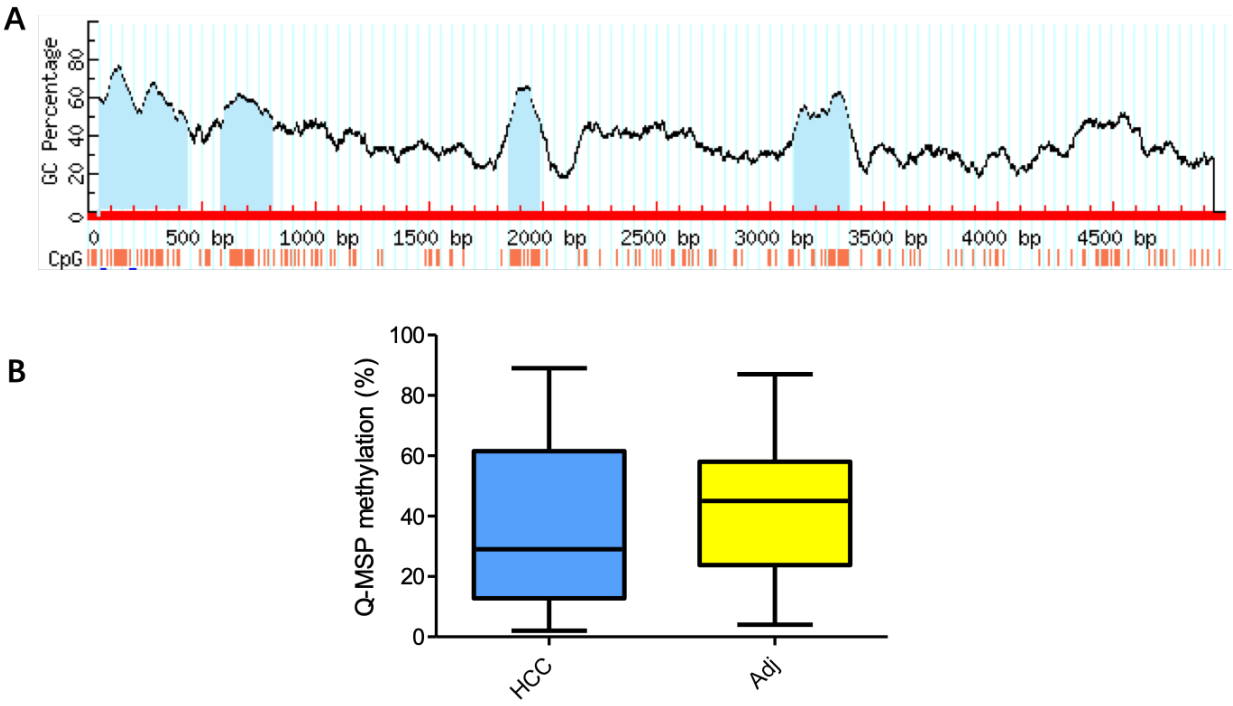
sFig.1 Relative expression of LRP1B in mouse Hep 1-6 cells as compared to hepatocyte mouse FL83b. A, mRNA level of lrp1b in cancerous cells Hep1-6 was higher than that in non-cancerous cells FL83b by quantitative PCR. *p<0.05. **B**, Relative high protein level of LRP1B in cancerous cells Hep 1-6 was also observed by using western blotting.



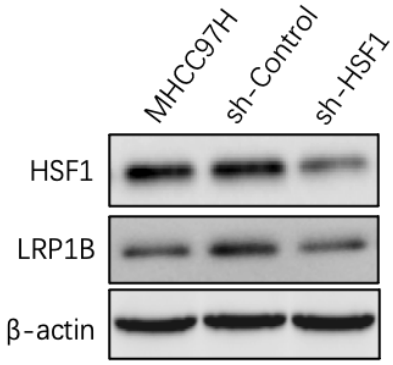
sFig.2 The knockdown efficiency of LRP1B is successful in Huh7 and MHCC97H cell lines. After lentivirus Lenti-LRP1B-V2-sg vector was transfected into Huh7 and MHCC97H cells, the expression of LRP1B was examined by western blotting. β-actin was regarded as an internal control. Target1: Lenti-LRP1B-V2-sg1; Target2: Lenti-LRP1B-V2-sg2; Target3: Lenti-LRP1B-V2-sg3. The figures were repeatedly measured for three times.



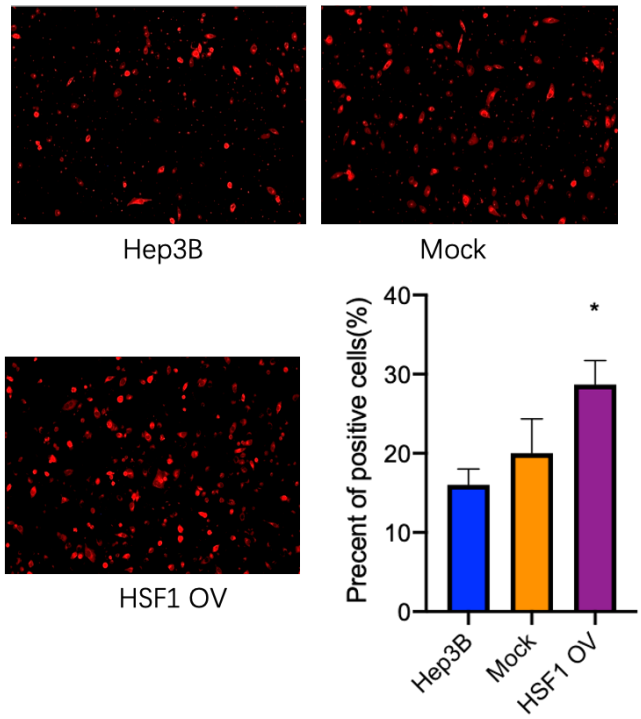
sFig.3 Effects of LRP1B downregulation and upregulation on growth of HCC cells. A,B, After LRP1B knockdown, the growth of MHCC97 (A) and Huh7 (B) cells at 0h, 24h, 48h and 72h was detected by performing a CCK-8 assay. Data represented the mean±standard deviation. *p<0.05.



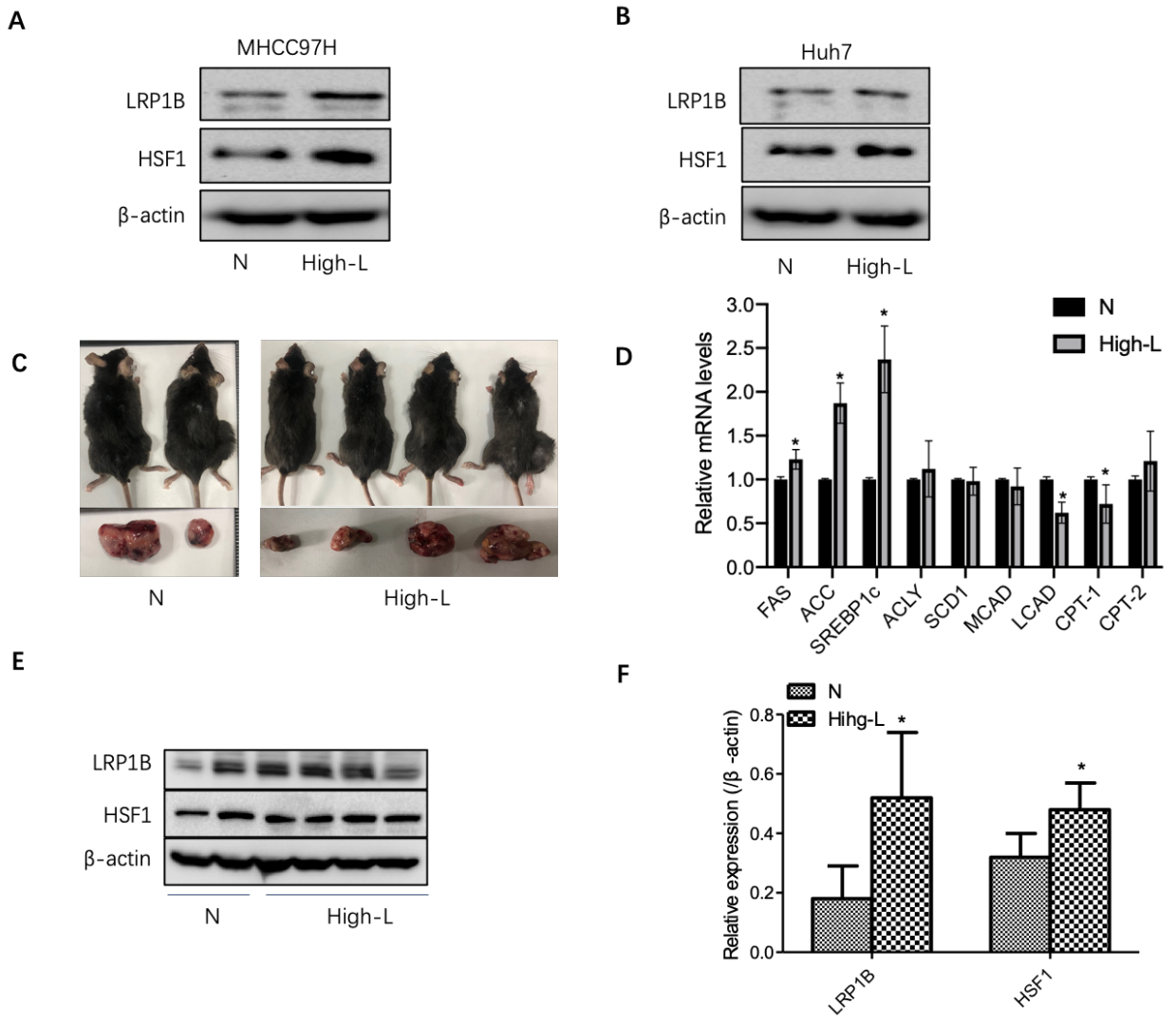
sFig.4 High expression of LRP1B in HCC have indirectly relation to DNA methylation of LRP1B gene. A, MethPrimer software (http://www.urogene.org/cgi-bin/methprimer/methprimer.cgi) predicted CPG island in the regulated region of LRP1B gene. The regions of light blue indicated four CPG islands. **B**, The methylation level of the LRP1B gene promoter was examined in HCC tissues and adjacent tissues by Quantitative Methylation-Specific PCR (Q-MSP). HCC: HCC tissues; Adj: adjacent tissues. Statistical significance was analyzed by two-tailed unpaired Student's t-test.



sFig.5 Effect of HSF1 knockdown on LRP1B expression in MHCC97H cells. Western blotting confirmed the efficiency of HSF1 knockdown in MHCC97H cells. HSF1 knockdown induced the decrease of LRP1B protein in MHCC97H cells, similar to that in Huh7 cells. β-actin was regarded as an internal control. Data represented the mean±standard deviation.



sFig.6 Effect of HSF1 overexpression on lipid content in HCC cells. Representative images of DiD staining in Hep3B cells with or without HSF1 overexpression. The red indicated the positive lipophilic cells. Scale bar=50μm, magnification×100. Histogram indicated the proportion of lipophilic cells in various Hep3B cells by using flow cytometry.



sFig.7 High-fat can upregulate the expressions of LRP1B and HSF1 in HCC cells and tissues. A, **B**, Representative images of western blotting analysis for LRP1B and HSF1 expressions in MHCC97H (A) and Huh7(B) cells with cultured high-fat medium (High-L) or normal medium (N). **C**, 10 four-week-old male C57BL/6J mice were purchased from the shanghai Institute of Material Medicine, Chinese Academy of Science and kept in specific pathogen-free conditions. All the care and experiments of animal were followed the institutional guidelines for the care and use of laboratory animals approved by the National Institutes of Health and the National Academy of Sciences. After each mouse was subcutaneously injected in the right flank with 200 μL 1×PBS containing 5×106 Hep1-6 cells, 5 experimental mice were fed with a high fat diet and 5 control mice with normal diet. Mice were killed at the 5th weeks, and subcutaneous tumor tissues were

collected for subsequent experiments. **D**, Relative mRNA levels of several key enzymes for fatty acid synthesis-FAS, ACC, SREBP1c, ACLY, SCD1 as well as important enzymes for β-oxidation of fatty acids-CPT-1, CPT-2, LCAD, MCAD in mouse homograft tumor tissues between normal control group and high-fat group were determined by quantitative PCR. *p<0.05. **E, F**, Western blotting analysis for LRP1B and HSF1 expressions in tumor tissues from the above results. β-actin was regarded as an internal control. N: normal; High-L: high-fat. *P <0.05. Data represented the mean ± standard deviation. Statistical significance was analyzed by two-tailed unpaired Student's t-test.

Supplementary Table.

Name	Primer sequences (5′-3′) for PCR
LRP1B (human)	F-AACAAAGACAATTAGAAGGCAGCCTATCATCAATG
	R-TTATGCTACTGTTTCTCTGATGCCAATTTC
lrp1b (murine)	F-TGGGGGTCTTTTAGAACCAAG
	R-TTGTTGGCCCAGAAGTTAGTG
b-actin (human)	F-GAGCCAGATCCCTCCAAAAT
	R-AAATGAGCCCCAGCCCTTCT
b-actin (murine)	F-CCCATCTATGAGGGTTACGC
	R-TTTAATGTCACGCACGATTTC
FAS(human)	F-GCTTTGCTGCCGTGTCCTTCTA
	R-TAGAAGGACACGGCAGCAAAGC
FAS(murine)	F-GAGGGTGTGCCATTCTGTCA
	R-GCTATTCTCTACCGCTGGGG
SREBP1c (human)	F-ACAGTGACTTCCCTGGCCTAT
	R-GCATGGACGGGTACATCTTCAA
SREBP1c (murine)	F-CTGCTGCTGACAGCTGTAAA
	R-AGCGCTTCTCAATGGCATTG
ACLY (human)	F-TCGGCCAAGGCAATTTCAGAG
	R-CGAGCATACTTGAACCGATTCT
ACLY (murine)	F-CTGGCTGAGAACGGTTTCCT
	R-AACGCTGTATGGCAGGTGAA
SCD1(human)	F-TCTAGCTCCTATACCACCACCA
	R-TCGTCTCCAACTTATCTCCTCC
SCD1(murine)	F-GTACCGCTGGCACATCAACT
	R-AACTCAGAAGCCCAAAGCTCA
MCAD(human)	F-GGCCGTGACCCGTGTATTAT
	R-CTGCAGCATCGCCCGAA
MCAD(murine)	F-TCAAGATCGCAATGGGTGCT
	R-GCTCCACTAGCAGCTTTCCA
LCAD(human)	F-CCGGAGAGATTCGGAGATGC
	R-TCAGAGGGGTGGGAATCTGA
LCAD(murine)	F-TCTATGGCACAAAGGCCCAG
	R-GGCTACATCGGATCCACTCG
CPT2(human)	F-TTGTGAGCCCCTCGGAAATC
	R-TCAGCTGGCCATGGTACTTG
CPT2(murine)	F-TGTGAGCGGAAGATCCCAAC
	R-GCTTTCCAACCCGATCTCCT

$ACC_{(human)}$	F-CATGCGGTCTATCCGTAGGT
	R-ACCTACGGATAGACCGCATG
$ACC_{(murine)}$	F-GTGGTACCTGGCTGCTAGTC
	R-GGCAGCCTCAGTTTCTTTGC
$CPT\text{-}1_{(human)}$	F-CAAGGACATGGGCAAGTTTT
	R-AAAACTTGCCCATGTCCTTG
$CPT\text{-}1_{(murine)}$	F-GACTCCGCTCGCTCATTCC
	R-GGCAGATCTGTTTGAGGGCT
shRNA	
shRNA-HSF1	5′-CCGGCAGGAGCAGCTCCTTGAGATTCAA GAGATCTCAAGGAGCTGCTCCTGTTTTTG-3′
sgRNA	
LRP1B-1-a	5′-CACCAATCCAACGGTTCTGTATGTC-3′
LRP1B-1-b	5′-AAACACATACAGAACCGTTGGATTC-3′
LRP1B-2-a	5′-CACCAACGTTTATACTGGACAGTAC-3′
LRP1B-2-b	5′-AAACTACTGTCCAGTATAAACGTTC-3′
LRP1B-3-a	5′-CACCAAAAAGACTTGTGGACCTCATC-3′
LRP1B-3-b	5′-AAACATGAGGTCCACAAGTCTTTTTC-3′