Supplementary Information

Table S1： The primers used in qPCR are listed in table.

Primers	Sequences (5' to 3')	Amplicon (bp)
CSFV-RT	CTAGCCATGCCCACAGTAGGA	286
	CTCCATGTGCCATGTACAGCA	
APOH-RT	CAGTTTCACTTGCAACCGGG	229
	TCCAAACATTGCGTGCTGTG	
ABCA1-RT	CGACAATGTGGAGAGGACGAA	169
	GCCAGTTTTCTTCTCCATACCC	
APOE-RT	CACCGAGGACCTGCAGAAG	223
	CAACTGGCTGCCCTGCTC	
DHCR24-RT	CGGCAAGTCCTCAAGTCCTC	132
	AGTCCCTGAGTACCCACAGT	
DHCR7-RT	TGTGGTTCGCTAACTCCCAC	121
	ATCATGGCGAAGGTGGAGAC	
FDFT1-RT	AGTTCTACAATCTGCTGCGCT	143
	CTGGATAACGGCTGCGAAAC	
HMGCS1-RT	GAGCCGTGCCAAGTTGCG	275
	CAGCAGCTACACCGTCGTATT	
HMGCR-RT	TCGCAGATGGCATGACTCGT	204
	CTGACCTGGACTGGAAACGG	
HSD17B7-RT	TGGACTTCACCTGTGCTTGG	133
	GAACACCGATGACAAGCTGC	
LIPG-RT	TCTATTGCTGTTTTGCGGCG	253
	ATGCCACTCATCGTCCATCC	
SREBP2-RT	AGGTCCCGTTACCTTCCTTCT	289
	GTCACCAGGCTTTGGACTTG	
IRF3-RT	ACACCCTCTGGTTCTGCATG	171
	GGCTGTTGGAAATGTGCAGG	
IRF7-RT	GACTTCGGCACCTTCTTCCA	134
	AGGACGAGGCTCTTCTCCTT	
CCL2-RT	AGAAGATCTCGATGCAGCGG	121
	TTCTGCTTGGGTTCTGCACA	
CXCL10-RT	CTCTCCAGAACTGTTCGCTGT	113
	TCAACATGTGGGCAAGATTGAC	
IFNB1-RT	TGGCATGTCAGAAGCTCCTG	163
	ATGCCGAAGATCTGCTGGAG	
MX1-RT	ATCTCCAGCCACATCCCTCT	146
	CTCTTGTCGCTGGTGTCACT	
MX2-RT	AACGGACCGTCTCCTGTTTC	100
	TGAATGGGATCTGGTTGGCC	
GAPDH-RT	ATCCTGGGCTACACTGAGGA	146
	TGTCGTACCAGGAAATGAGCT	

Table S2: The primary and secondary antibodies are listed in table.

Antibodies	Host	Dilutions	Supplier
CSFV Envelope glycoprotein E2 Antibody	Rabbit	1:1000	Bioss
LDLR Monoclonal antibody	Mouse	1:1000	Proteintech
Anti-PCSK9 Antibody	Rabbit	1:1000	BOSTER
Phospho-TBK1/NAK Antibody	Rabbit	1:1000	Beyotime
TBK1 Rabbit Polyclonal Antibody	Rabbit	1:1000	Beyotime
β-Actin Mouse Monoclonal Antibody	Mouse	1:1000	Beyotime
HRP-labeled Goat Anti-Mouse IgG(H+L)	Goat	1:1000	Beyotime
HRP-labeled Goat Anti-Rabbit IgG(H+L)	Goat	1:1000	Beyotime
Goat Anti-Rabbit IgG H&L (Alexa Fluor® 488)	Goat	1:1000	Abcam

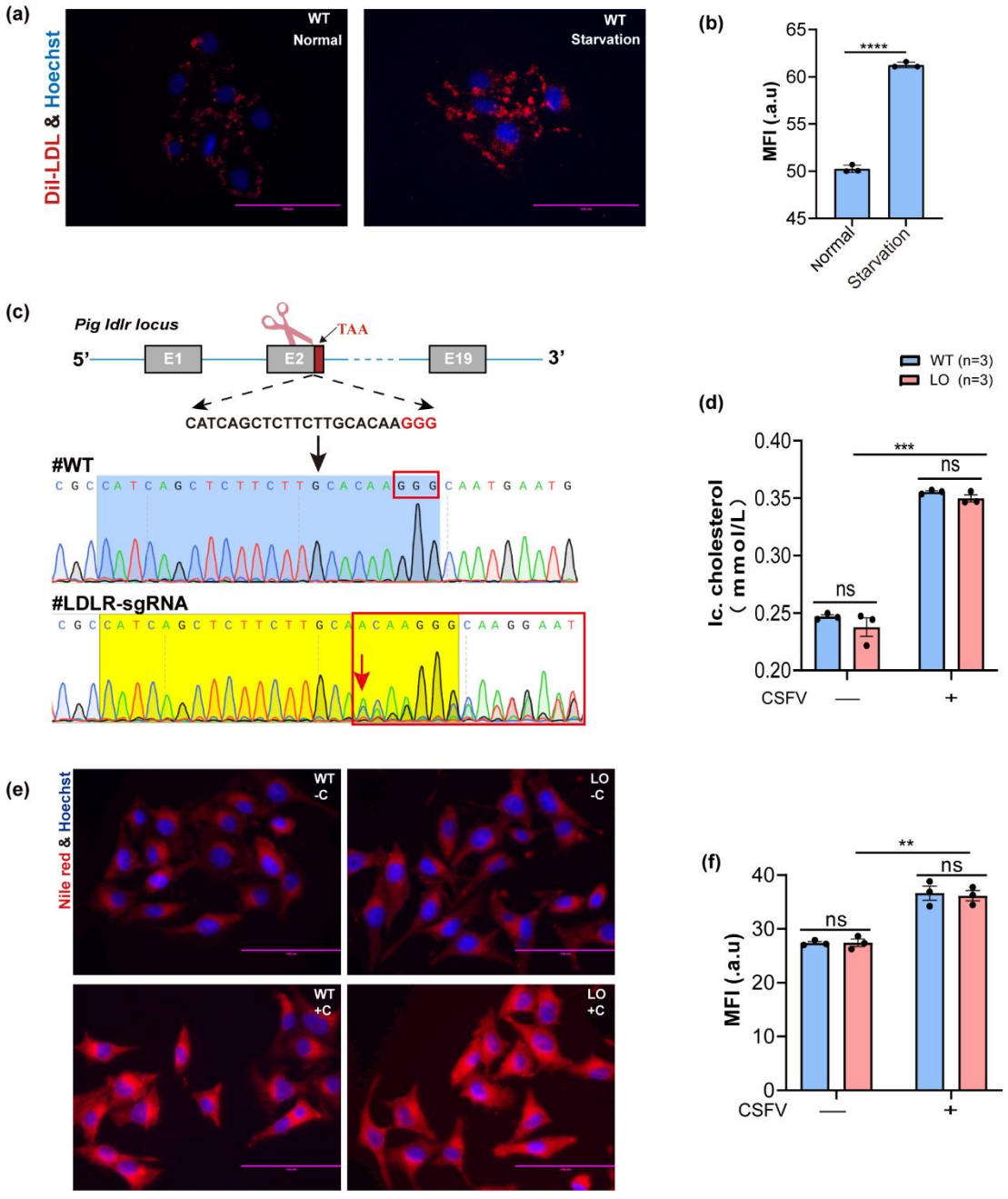

Figure S1. (a–b) Starvation treatment increased dil-LDL uptake, $n = 3$, $^{****}p < 0.0001$. **(c)** Construction and efficiency detection of LDLR-KO gene editing system. **(d–f)** The disruption of LDLR had no any effect on intracellular cholesterol levels, $n = 3$, $^{**}p < 0.01$, $^{***}p < 0.001$. **(WT, wild-type; LO, ldlr-ko; MFI, mean fluorescent intensity)**

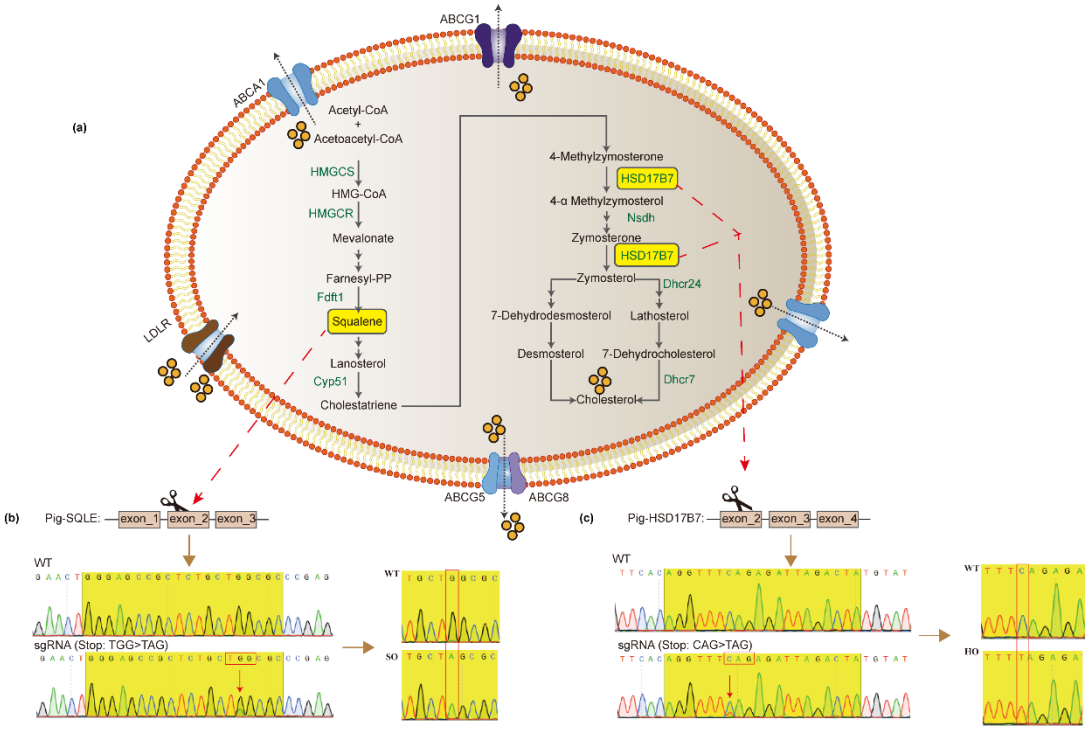

Figure S2. (a) Cholesterol biosynthesis schematic diagram. **(b–c)** Construction and efficiency detection of *SQLE* and *HSD17B7* gene editing system.

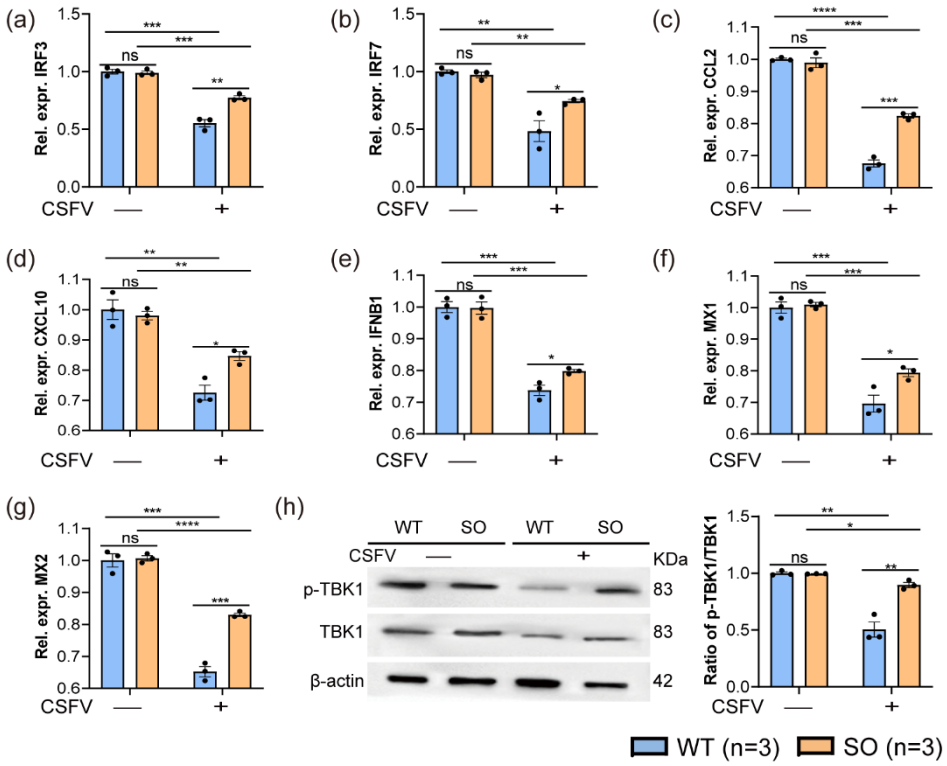

Figure S3. (a–h) The expression of ISGs and p-TBK1 was decreased in CSFV-infected PK-15 cells, and the disruption of cholesterol biosynthesis obviously enhanced type I IFN signaling, n = 3, *$p < 0.05$, **$p < 0.01$, ***$p < 0.001$, ****$p < 0.0001$. **(WT, wild-type; SO, sqle-ko; Rel. expr, relative expression)**