

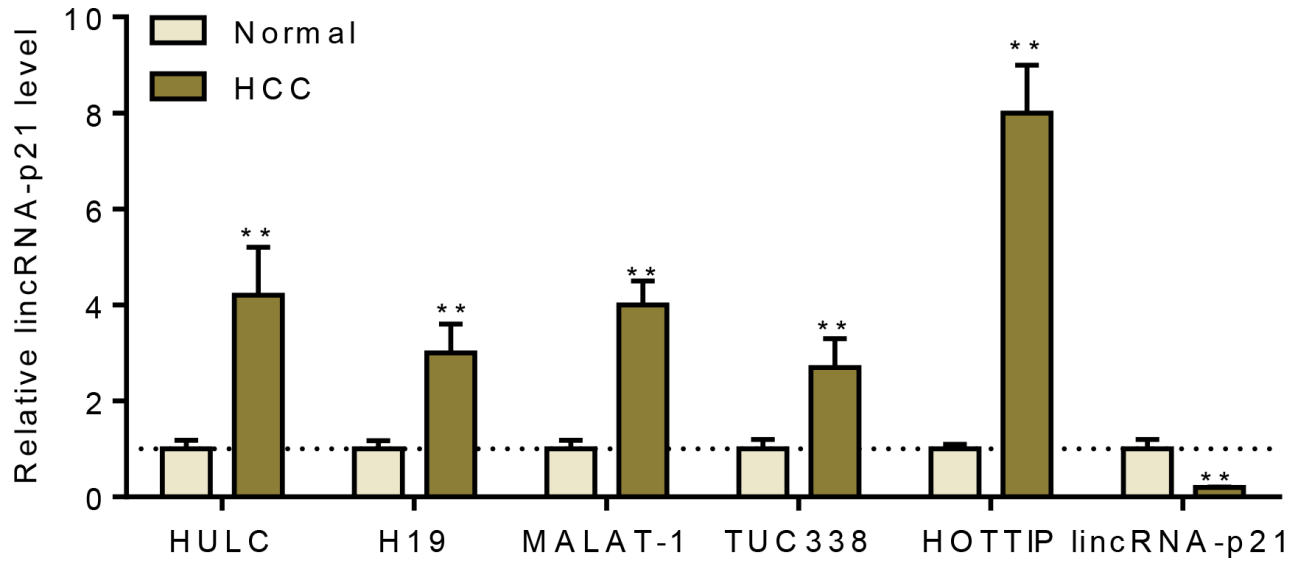
## SUPPLEMENTARY INFORMATION

### HUMAN LINCRNA-P21 SEQUENCE

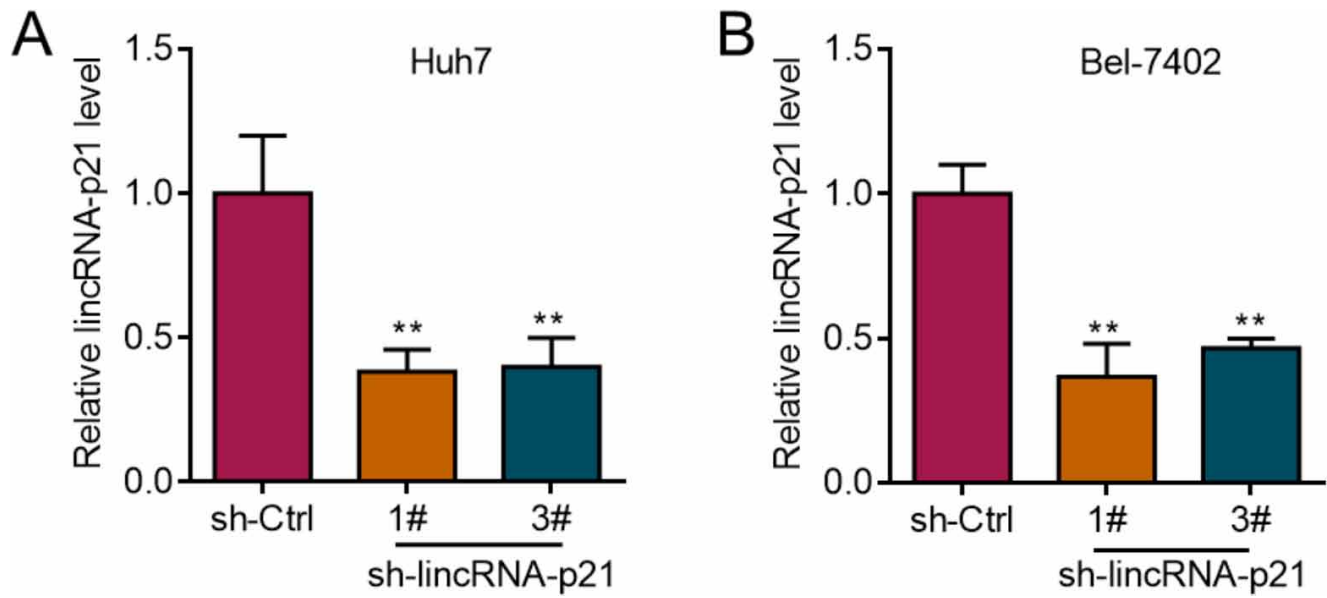
> lincRNA-p21

TGGCAGTCTGACCCACACTCCCCACGCCCCA  
 GGACCAAGTCGCCTGAGCCCCATAGCCACA  
 CTCTGCCGGCCTTGGCCGGGCTTGCCTTG  
 ATCATCTCCAGCTTTGCCAGGGGTGCAGA  
 AACCACCCACTCAGCGCTGGAAAAACCAG  
 TTATATCTCCAAAGACCCAGGGCAAGAA  
 TTGTG GACAACCTCAGCTGGCCTGGCCTG  
 TCCCACTCGC TTTCCATTTCCCCCACCCT  
 GAGACAGGATGCCA CTGTGTAGCCCAGT  
 GTAGTGAACACTTGG AATAC AAAATAA  
 AGATGGTGGAATGAGACATTCCGTCTC  
 CAGTTCCTAACATCAGAAGTGAGCACCT  
 GTGTGT CACCAGCAACATATTGGAGGCC  
 AGCTGCCTACAC CAATCAGAAACAGGG  
 ACCACAAAGTCTGCAGGG GTGAGATA  
 GGCCTTTTCAGTGTCTACGATTTCA  
 TCGATGGACATTACTGTGATTTCTCTT  
 CCTGCCCTG TATGTGCGGGTCTATCGCC  
 ATCTCGCCATCTCCGG CTCCTGTGTT  
 ATGAAGACAGTCTCATGCAGCCCA  
 GACCAATCTCAAATGACTAGGTAAACT  
 GAGGCT GGCCTTGAACCAGTCCCTCCT  
 GCCTCTATCTCCTG AGAGCTGGGTAAC  
 AGCTTCTGGAGCCTCACCCA GCTTCG  
 CTTTCACCACCCCAGCCAATCCTGTG  
 AC TCCTCTTCATAGCGAGAGCATTG  
 ACACCTTATGTTCTGAGTGTGAAAA  
 AAAAAAAAAAATCACATAGTA  
 CTTCCCTACTAGAACCTTGGCCGGG  
 TCAACTGAAG TGTGTGTGTTTGCTT  
 ACCAGTCTGCAGGTTTGCTT AAGTTT  
 GTTTATTTAGAGACCAGGTCTTGCT  
 CTG TTGCCTAAGCCAACTTGAAACT  
 CTCTGGGCTCCAA CAGTTCTCCTGCT  
 CCATCTTTCTAGAGCAGCTGG GACT  
 CTAGGCATGCTCCACTACAGCTGACT  
 GAAG CTTGAATGAATGAATGAATGA  
 ATGAGTTAC TACCTCTGAGGGACCCT  
 CCTCATGGCCTTCTCAA CTCTGTACT  
 TTAATTAGTTGCTTAGAGGTGTCTCC  
 ATGCCTCAGTTTCCCCATCTGTAAT  
 AGTAAACGA GTTCACAGGCGTGGT  
 CTGTGCTTGGAGCAAGAA CAAAAC  
 CATCCTGGCCTATACTCTCTAGGG  
 ACTC TACAGAGCCCATCCCTTTGG  
 CTATCAGACTGTTG AGATAAAGGTT  
 CCCCCAGGAATCGGAATCCCCTC  
 CGACAGGAGTCTCATGCTCAGAGA  
 AAAAAAAAAA GCTGAAGCCTGCTG  
 ACAGCCAGAGAGGGTACTT GTCTG  
 TCAGGGAAAAATTCTACACAGGAC  
 AGAC TGGAGCCCAGACTGGTCTGG  
 GTCAGTGACACAC GGCACAGCAC  
 ACGGTGGGACAACCTGGCTGTGC  
 ATCTCTCTCAAACCTCTTGTCA  
 CCCTTCTCACTG TGGCCACAGCGA  
 AGCGAATACATCTCTCTGCTTT  
 TCACTACGTAGCTCCATCATTGC  
 CCTTGGGGGGG GTAGCGAGGAAG  
 GTCACTGGGGCCCTGCCTCTG  
 ATAAGAAGAACGAGCAATTATGAT  
 TCCAGGAA CCGAGGGTGCTCTTG  
 CTGTTCAAGTGTCTCCAGCA  
 CCCCCGAGACCCAGGGCTGCCG  
 TCAAGGGTG TCAATAAACACGTAT  
 CGATTGAGCCAACAATGC

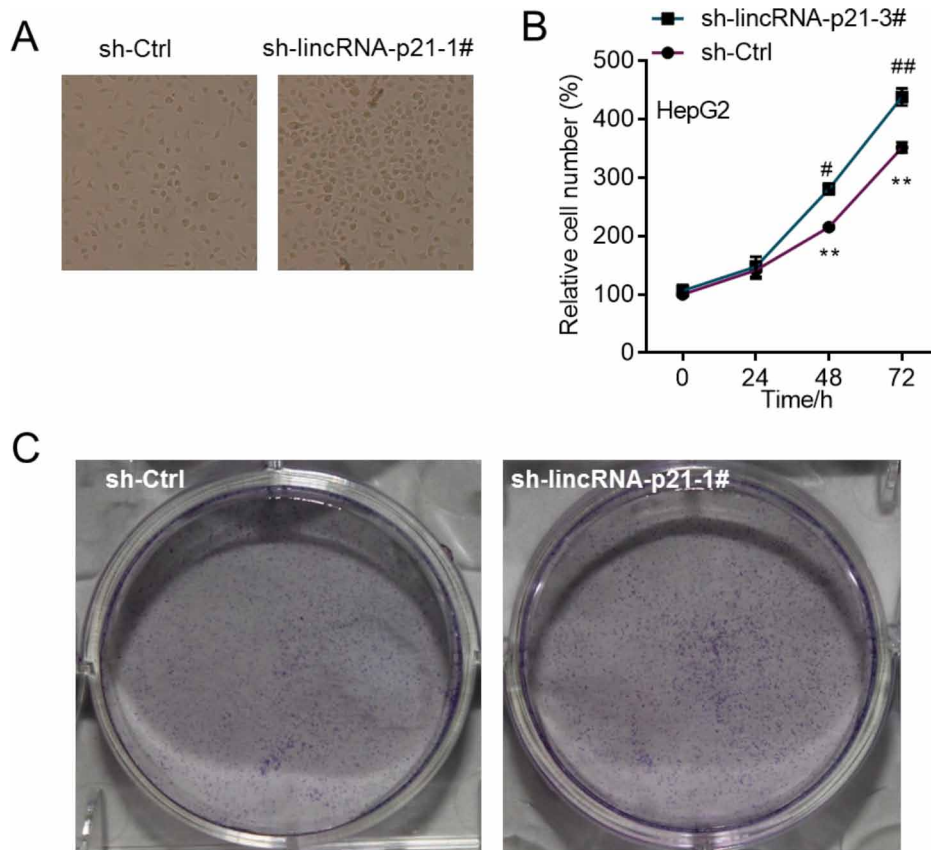
CAGAATTGGACCTGCAGAGGAGAAAATGGACAA  
 ACAAGACAGTGAGCCTGCAGGTGAGACCAGAA  
 CTGGAGCCAACAATCTACCTCTCTCTCCCA  
 ACCCTAGCAACGCCAGCAGCTCTCTGGGCG  
 AGGGGCA CAGTTGCTTCCAGTTGGCAGA  
 ACCAGTCTCCCA GCTTCCCTTCAGA  
 ACCCAGCACCTGCTGAGCCA CCGACCC  
 ACGGACTGTCTCTCTGGAAGGCAG CC  
 ACCGACCCACGGACTGTCTCTCTCTGGA  
 AAGG CAGTTCACCTCTGGGTTTCAAC  
 ACTGCCCTTTCC CCTTTCTTCTTAGCC  
 CTTAGGAATCCCTGAAA GCTTCCTGT  
 GCTTGTGGCTTCTGTGACTTCTCAA  
 CATCTCTTGTGCACACACACACACAC  
 ACACACACACACCAGCCTGTGTCTAAG  
 CAGTTCATC CTGTACAAATGTCTCTG  
 ATAAAATAACTGATTC CATTTCTGT  
 CACCTGCTGAGGCTCCAGCAGCTCT  
 GCCCTCAGACCTCTTAAAGCTGAGGCT  
 CAGAAG CACAGGGAGGCACGGGAAC  
 CTGGTCCCAGGCC CTGGCTTGTCTG  
 GAGCGAAGGAATCTATTGCTTCG  
 GCCACTCGGTCAGAATCCCTCGGAG  
 ATTGATGTG ATATGCACAGTGACAC  
 CCAATCGGGCTTGGAAAA CTGGG  
 CCAACAGTTAAGCCACACAAAGGAA  
 ACTA ACCACAGCTCCACTGGCAACT  
 GGCTCCTTGGCA AGTGCCAAAACA  
 AACAGCTGTGGTGCAGGCCTT CCCC  
 GGGCTGCCGGCTTCTGGACACTGGC  
 AGA GGCCGCTCAAGAAGGGAGTAC  
 CTGAGTAGGGTG TTGTTCA  
 GTTGGTAGAACGTTTGCTTGCCTT  
 CCA TGAAGCCCAGGGTTCTGTCTG  
 CACCTCATACTG TGATCCTAGCAGT  
 TGGGAAAAGACAGCAAGCAC CCG  
 GATCAGAAGTTCAAGACCACCTCC  
 CCTTTA TAAAGGGATCTGAGGCAG  
 CCTGGGACATCTGAA TGACAAATG  
 AAAAGAGCCGTGAGCTATCTGGTG  
 TTTTCTTCATGGAAGTCCAAGTCT  
 CCCCCTCATT CCTCCCAGGATTCT  
 CCGAATCTGGCTGTTGTCTT TTG  
 CGATATTTTAGAATATTCTAGCC  
 AGAGCGCA GAGTATAAAATACA  
 AGTCAAAGGCAATGAGCATA TG  
 TTAGATGGATGGAGGAGGGCC  
 TAAAAATGCT GGTGCTGGGGAG  
 GAAAAATGGCTCAGCAGTTAA  
 GAGCACCGGCTGCTTTTACAGAG  
 GACCTGCCTT CAGTTCACAGCA  
 ACCGCATGACGGCAACTCTGG  
 TTCCAGGAAATCCAATGCCCTCT  
 TCTGACCTCTA TAGGCACCCG  
 CAAGCACACAGTGCACAGACAA  
 TCATACACACGTGT.



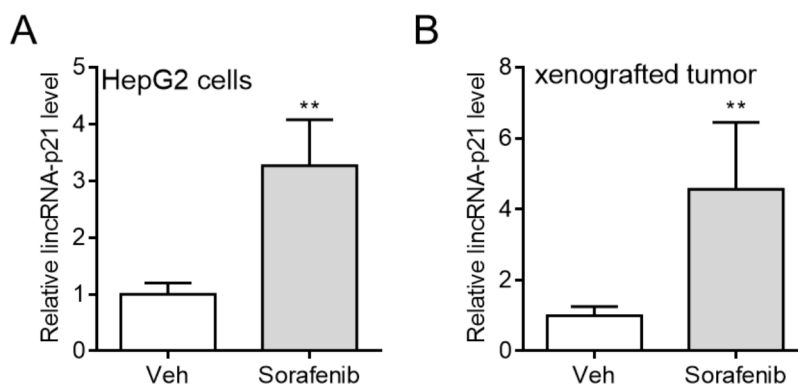
**Supplementary Figure S1: lincRNAs level in normal liver tissues and human hepatocellular carcinoma (HCC).**  
\*\* $p < 0.01$  vs. normal.  $N = 10$ .



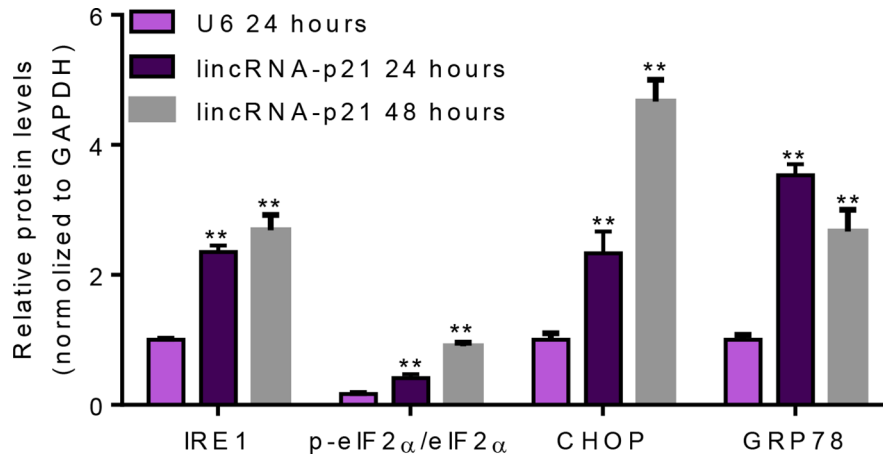
**Supplementary Figure S2: Lentivirus-mediated lincRNA-p21 knockdown in Huh7 and Bel-7402 cells.** Huh7 **A.** and Bel-7402 **B.** cells were infected with lentivirus carrying sh-Ctrl or sh-lincRNA-p21 for 48 hours. The level of lincRNA-p21 was analyzed with q-PCR. \*\* $p < 0.01$  vs. sh-Ctrl.



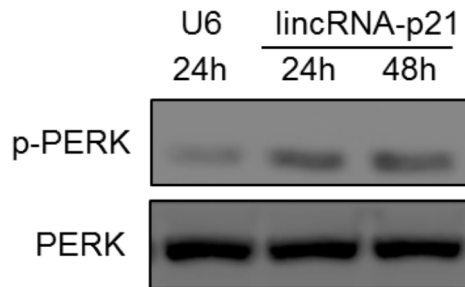
**Supplementary Figure S3: LincRNA-p21 knockdown promotes cell proliferation and colony formation in HepG2 cells.** **A.** Representative image showing lincRNA-p21 knockdown promotes HepG2 cell proliferation. The photographs were captured 48 hours post infection of lentivirus. **B.** LincRNA-p21 knockdown promotes HepG2 cell proliferation.  $**p < 0.01$  vs sh-Ctrl 0 day;  $\#p < 0.05$  and  $##p < 0.01$  vs sh-Ctrl of the corresponding time points. **C.** Representative photograph showing lincRNA-p21 knockdown promotes colony formation of HepG2 cells.



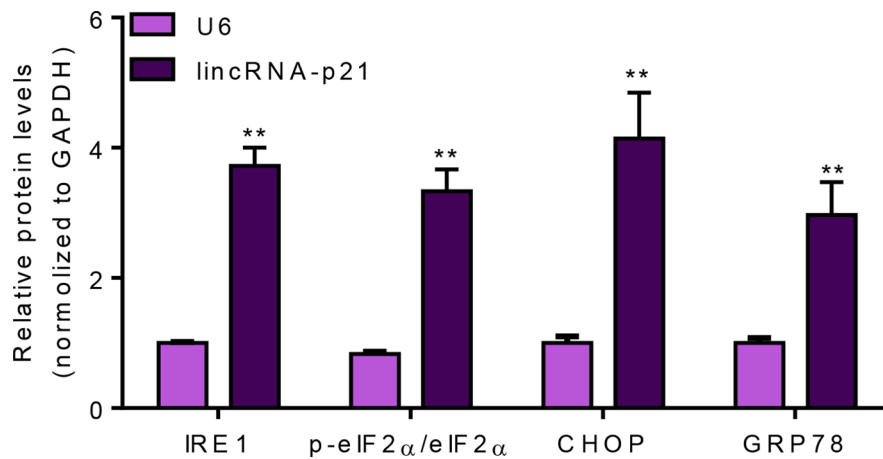
**Supplementary Figure S4: Sorafenib promotes lincRNA-p21 expression.** **A.** HepG2 cells were treated with 20  $\mu$ M sorafenib for 48 hours. LincRNA-p21 expression was analyzed with q-PCR.  $**p < 0.01$  vs control (Veh). **B.** Tumor xenograft experiment was performed. The mice were sacrificed four weeks after tumor implantation. Sorafenib (30 mg/kg/d) was administered in 100  $\mu$ L by intraperitoneal injection on day three after tumor implantation. LincRNA-p21 expression was analyzed with q-PCR.  $**p < 0.01$  vs control (Veh).  $N = 5$  in each groups.



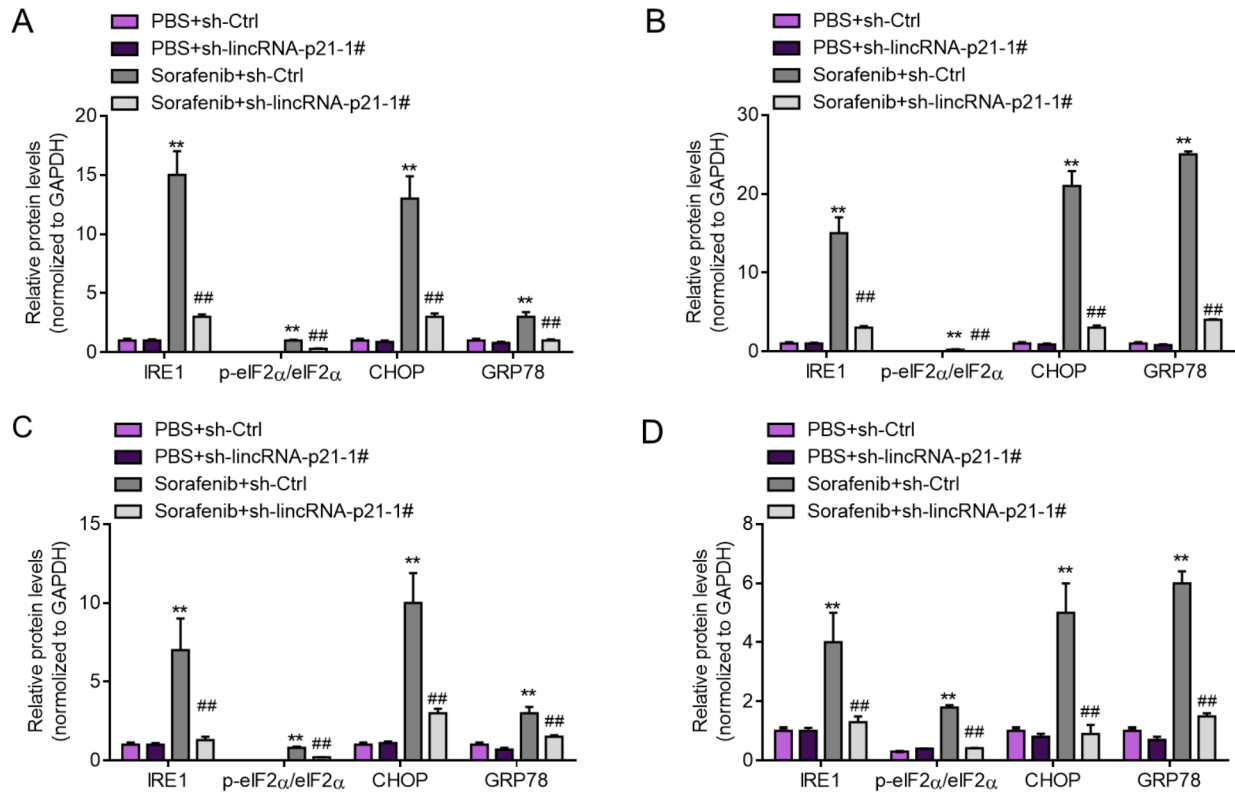
Supplementary Figure S5: Quantitative data related to Figure 6E.  $**p < 0.01$  vs. U6 24 hours.



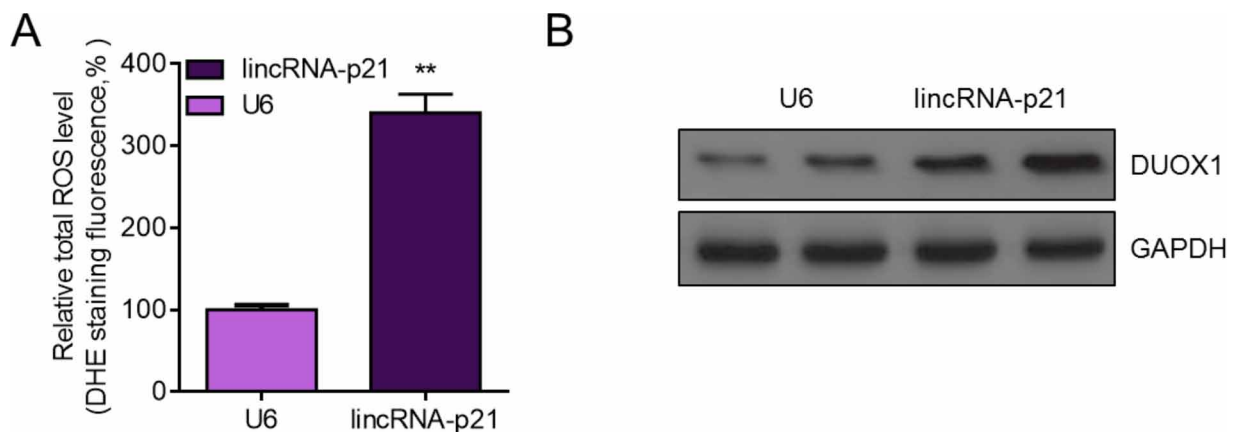
Supplementary Figure S6: lincRNA-p21 activates PERK (Protein kinase RNA-like endoplasmic reticulum kinase). HepG2 cells were infected with indicated lentivirus for indicated times.



Supplementary Figure S7: Quantitative data related to Figure 6G.  $**p < 0.01$  vs. U6 24 hours.



**Supplementary Figure S8: Quantitative data related to Figure 7D–7G.** A. Quantitative data related to Figure 7D.  $n = 5$ . B. Quantitative data related to Figure 7E. The experiments were repeated for three times. C. Quantitative data related to Figure 7F. The experiments were repeated for three times. D. Quantitative data related to Figure 7G. The experiments were repeated for three times. \*\* $p < 0.01$  vs. PBS+sh-Ctrl; ## $p < 0.01$  vs. Sorafenib+sh-Ctrl.



**Supplementary Figure S9: LincRNA-p21 regulates oxidative stress.** HepG2 cells were infected with indicated lentivirus for 24 hours. A. DHE staining was performed to test the total ROS level. Relative total ROS level is shown. B. Representative western blot showing lincRNA-p21 increases the level of DUOX1 (dual oxidase 1).

**Supplementary Table S1: Primers used for q-PCR**

Name	Sense (5'-3')	Antisense (5'-3')
lincRNA-p21	CCTGTCCCACTCGCTTTC	GGAAGTGGAGACGGAATGTC
IRE1	CAGTGGCCTTTGGTG GGTGTG	GTCTGGGTCTTCGCTGCT CTCCT
CHOP	CACCACTCTTGACCC TGCTTCTCT	GTTTCCTGGTTCTCCCTT GGTCTT
GRP78	TTCGGCACCTCGGTAACCT	GGACTGCGTGATCTCCCTCT
MDM2	TCGTGCGGTGAGGGTACTG	AACCACTTCTTGGAACCAGGT
BAX	CATATAACCCCGTCAACGCAG	GCAGCCGCCACAAACATAC
PUMA	GCCAGATTTGTGAGACAAGAGG	CAGGCACCTAATTGGGCTC
NOXA	CCAAGCCGTGACCAAGGAC	CGCCACATTGTGTAGCACCT
$\beta$ -actin	GACCTGACTGACTACCTCATGAAGAT	GTCACACTTCATGATGGAGTTGAAGG

**Supplementary Table S2: sh RNA sequences targeting human lincRNA-p21.**

Sh-RNA	Sequence (5'-3')
lincRNA-p21-1#	GGAGGACACAGGAGAGGCA
lincRNA-p21-2#	GCCACCACTCACCCTGG
lincRNA-p21-3#	GCATTGTTGCATCATCATG
lincRNA-p21-4#	CTGCAAGGCCGCATGATGA