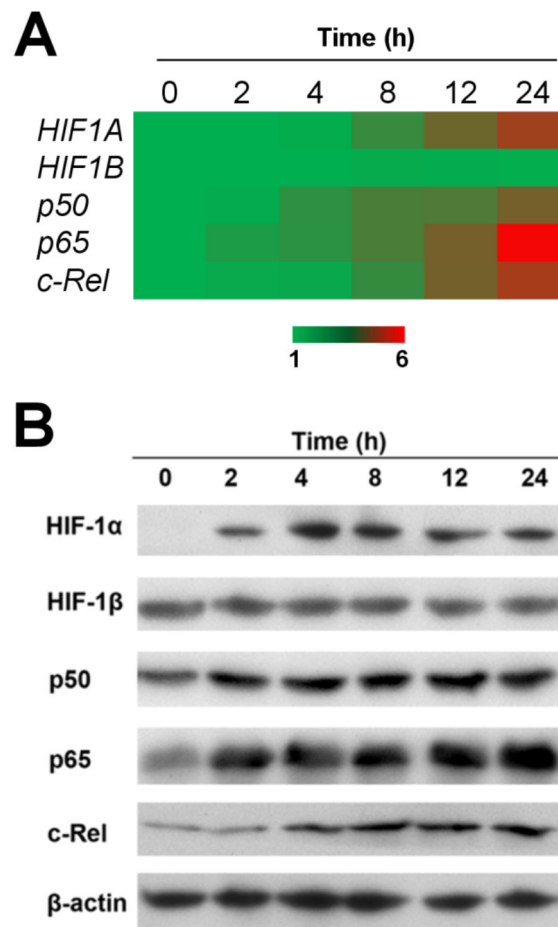
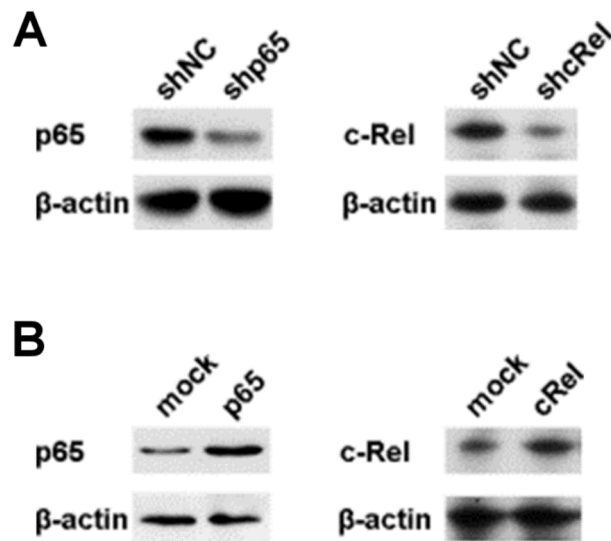


SUPPLEMENTARY FIGURES AND TABLES

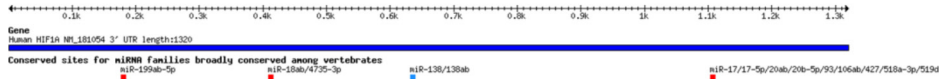


Supplementary Figure S1: Temporal expression of HIF-1 α in Huh7 cells under short-term and prolonged hypoxia. Huh7 cells were exposed to 1% O₂ for 0–24 h and assessed the mRNA (A) and protein (B) expressions of HIF-1 α , HIF-1 β , NF- κ B-p50, p65 and c-Rel. The results in (A) were expressed as the mean of n=4 independent experiments and expressed with heatmap.



Supplementary Figure S2: Knockdown and overexpression of NF- κ B in HepG2 cells. (A) HepG2 cells were transfected with shNC, shp65, or shcRel for 48 h. The protein expressions of p65, c-Rel and β -actin were determined with western-blot. (B) HepG2 cells were transfected with mock, p65, or cRel for 48 h. The protein expressions of p65, c-Rel and β -actin were determined with western-blot.

A

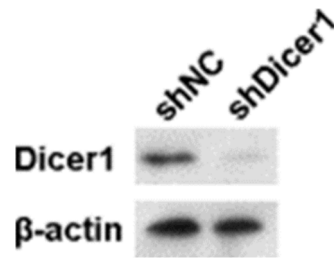


	predicted consequential pairing of target region (top) and miRNA (bottom)	seed match	site type contribution	3' pairing contribution	local AU contribution	position contribution	TA contribution	SPS contribution	context score	context score percentile	conserved branch length	P _{cr}
Position 177-183 of HIF1A 3' UTR	5' ...CAUCCUUUUUUUGSACACUUUU... 3' CUUGCCCAUCAGACUUGGACCC	7mer-m8	-0.120	0.021	0.007	-0.037	0.005	-0.032	-0.16	71	2.102	0.60
hsa-miR-199a-5p												
Position 177-183 of HIF1A 3' UTR	5' ...CAUCCUUUUUUUGSACACUUUU... 3' CUUGCCCAUCAGACUUGGACCC	7mer-m8	-0.120	0.030	0.007	-0.037	0.005	-0.032	-0.15	68	2.102	0.60
hsa-miR-199b-5p												
Position 409-415 of HIF1A 3' UTR	5' ...AUCAUUUUUUUUUUUUUUUUUUU... 3' UACAGAUUAAACUCUGGAAA	7mer-m8	-0.120	-0.016	-0.144	-0.004	-0.016	-0.032	-0.33	94	2.012	0.58
hsa-miR-4735-3p												
Position 409-415 of HIF1A 3' UTR	5' ...AUCAUUUUUUUUUUUUUUUUUUU... 3' GAUAGACUGGACUUCACUGGAAU	7mer-m8	-0.120	0.012	-0.144	-0.004	-0.016	-0.032	-0.30	93	2.012	0.58
hsa-miR-18a												
Position 409-415 of HIF1A 3' UTR	5' ...AUCAUUUUUUUUUUUUUUUUUUU... 3' GAUUGACUGGACUUCACUGGAAU	7mer-m8	-0.120	0.021	-0.144	-0.004	-0.016	-0.032	-0.30	92	2.012	0.58
hsa-miR-18b												
Position 632-638 of HIF1A 3' UTR	5' ...AAUUCUUUUUUUUUUUUUUUUUU... 3' GCGGACUUAAGUUUGUGGUGCA	7mer-1A	-0.074	0.001	-0.035	0.019	0.006	-0.066	-0.15	60	1.906	0.69
hsa-miR-138												
Position 1104-1110 of HIF1A 3' UTR	5' ...AAUUGUUUUUUUUUUUUUUUUUU... 3' GAUUGACUGGACUUCACUGGAAU	7mer-m8	-0.120	0.003	-0.075	-0.032	0.025	0.020	-0.18	90	1.735	0.62
hsa-miR-20b												
Position 1104-1110 of HIF1A 3' UTR	5' ...AAUUGUUUUUUUUUUUUUUUUUU... 3' GAUUGACUGGACUUCACUGGAAU	7mer-m8	-0.120	0.003	-0.075	-0.032	0.025	0.020	-0.18	90	1.735	0.62
hsa-miR-20a												
Position 1104-1110 of HIF1A 3' UTR	5' ...AAUUGUUUUUUUUUUUUUUUUUU... 3' GAUUGACUGGACUUCACUGGAAU	7mer-m8	-0.120	0.021	-0.075	-0.032	0.025	0.020	-0.16	88	1.735	0.62
hsa-miR-93												
Position 1104-1110 of HIF1A 3' UTR	5' ...AAUUGUUUUUUUUUUUUUUUUUU... 3' GAUUGACUGGACUUCACUGGAAU	7mer-m8	-0.120	0.021	-0.075	-0.032	0.025	0.020	-0.16	87	1.735	0.62
hsa-miR-17												
Position 1104-1110 of HIF1A 3' UTR	5' ...AAUUGUUUUUUUUUUUUUUUUUU... 3' GAUUGACUGGACUUCACUGGAAU	7mer-m8	-0.120	0.021	-0.075	-0.032	0.025	0.020	-0.16	87	1.735	0.62
hsa-miR-196a												
Position 1104-1110 of HIF1A 3' UTR	5' ...AAUUGUUUUUUUUUUUUUUUUUU... 3' GAUUGACUGGACUUCACUGGAAU	7mer-m8	-0.120	0.021	-0.075	-0.032	0.025	0.020	-0.16	87	1.735	0.62
hsa-miR-106b												
Position 1104-1110 of HIF1A 3' UTR	5' ...AAUUGUUUUUUUUUUUUUUUUUU... 3' GUGAGAUUUUUUUUUUUUUUUUU	7mer-m8	-0.120	0.040	-0.075	-0.032	0.025	0.020	-0.14	84	1.735	0.62
hsa-miR-519d												

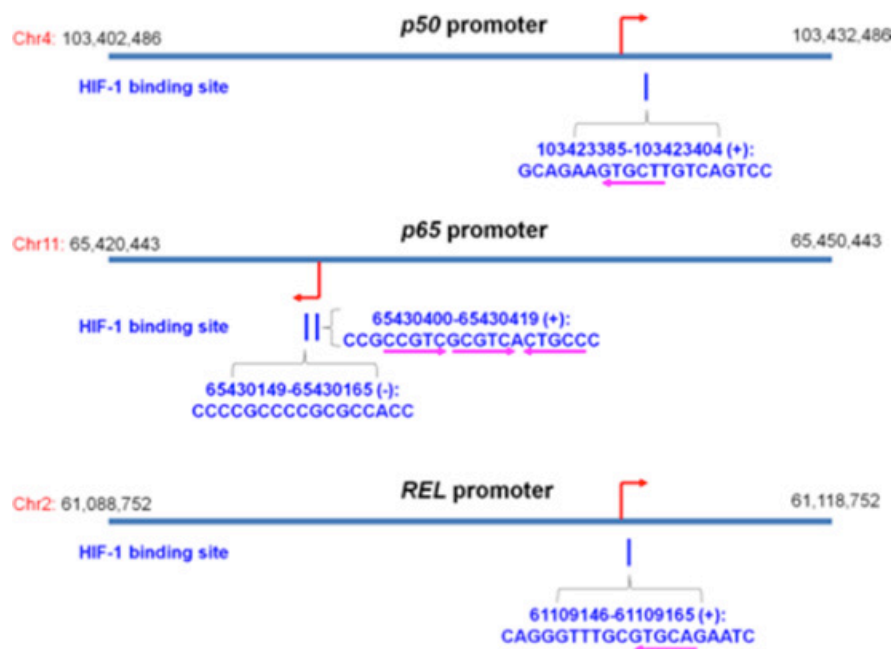
B

miRNA Symbol	Binding sequence	Distance from TSS
miR-199a-5p	tgGGGAActcctc (NF-κB p50/p65)	-4785
	GGAAAtccca (c-Rel)	-3030
	gtgtCACGTgacaac (HIF-1)	-1549
miR-17	GGAAAtccca (c-Rel)	-2483
		-3098
miR-18a	GGAAAtccca (c-Rel)	-2483
		-3098
miR-20a	GGAAAtccca (c-Rel)	-2483
		-3098
miR-93	GGAAAtccca (c-Rel)	-36
		-2167
miR-106b		-4313
	GGAAAtccca (c-Rel)	-263
		-2394
		-4540

Supplementary Figure S3: HIF-1 upstream and c-Rel downstream miRNAs. (A) Targetscan predicted binding of miRNAs with conserved 3'UTR sites of *HIF1A*. (B) miRGen predicted c-Rel downstream and HIF-1 upstream miRNAs.



Supplementary Figure S4: Knockdown of Dicer1 in HepG2 cells. HepG2 cells were transfected with shNC or shDicer1 for 48 h. The protein expressions of Dicer1 and β -actin were determined with western-blot.



Supplementary Figure S5: HIF-1 binding site on NF- κ B promoters. Vista predicted HIF-1 binding sites (blue) in the promoters of p50, p65, and c-Rel. Pink arrows show HRE sequences. Red arrow, transcription start site; +, positive strand.

Supplementary Table 1: Primers for target genes

Gene	Genebank ID	Forward	Reverse	Product Size
<i>ACTB</i>	NM_001101	catccgcaaagacctgtacg	cctgcttctgatccacatc	218
<i>HIF1A</i>	NM_001243084	tccaagaagccctaacgtgt	tgatcgctggctgctgtaa	180
<i>ARNT/HIF1B</i>	NM_001197325	aagccgtcttctcactga	tgctgccaaccattcagac	160
<i>p50</i>	NM_003998	aatgggtggagtctgggaagg	tctgacgttctctgact	226
<i>p65</i>	NM_001145138	acaagtggccattgtgtcc	acgttctctcaatccggt	169
<i>cRel</i>	NM_001291746	acctctgccttctcaagct	gatgacgcttccattccgac	213
<i>Dicer1</i>	NM_001195573	tggtccacgagtcacaatca	cagccaatcgtacacagctc	209

Qiagen Catlog No.

U6-2	MS00033740
miR-199a-5p	MS00006741
miR-18a	MS00031514
miR-20a	MS00003199
miR-93	MS00003346
miR-17	MS00029274
miR-106b	MS00003402

Supplementary Table 2: Plasmid vectors information

	Origene Catlog No.
shNC	TR30007
shp65	TL302038
shcRel	TL309876
shHIF1A	TG320380
shDicer1	TL308001
mock	PS100071
p65	RC220780L2
cRel	RC211878L2
	ABM Catlog No.
mock-miR	m003
miR-93	mh41079
miR-199a-5p	mh40255
miR-17	mh41055
miR-18a	mh41057