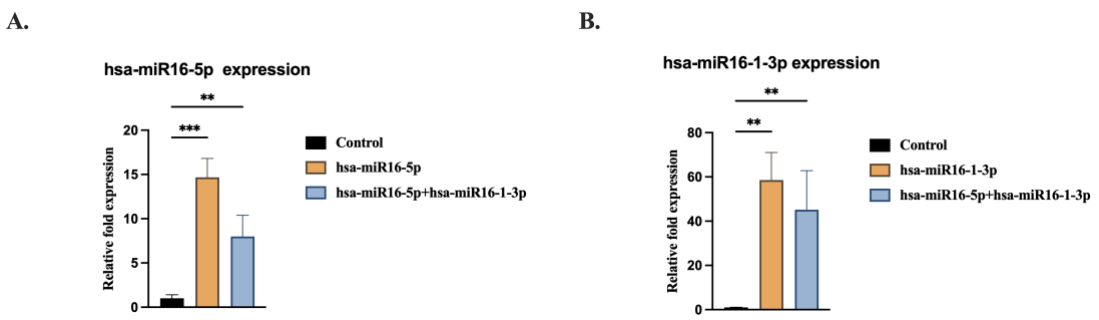
Supplementary Table 1. Nucleotide sequence of the wild-type HIF1A 3′UTR fragment used in the dual-luciferase reporter assay.

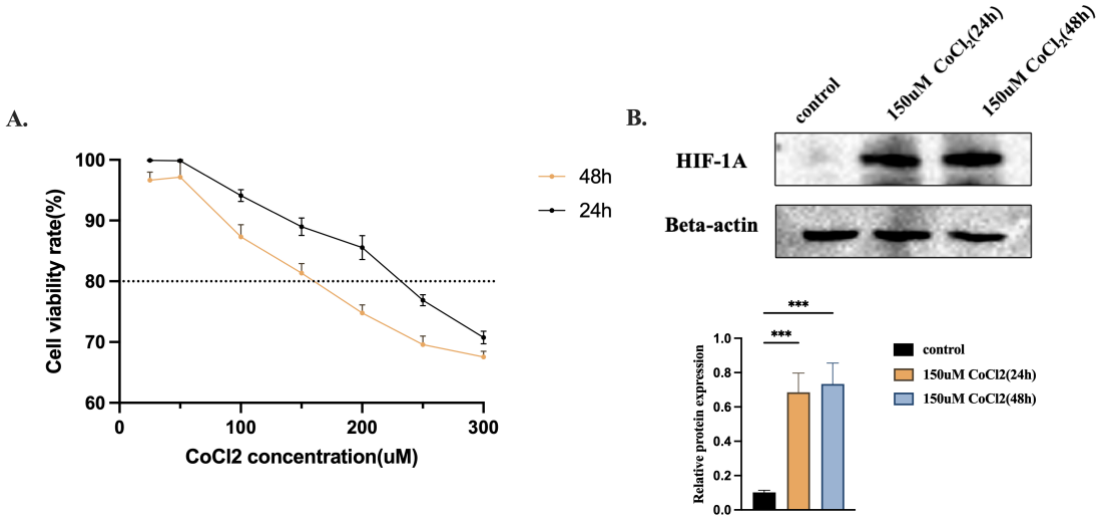
HIF1A-3'UTR-WT	aacctactgcagggtgaagaattactcagagctttggatcaagttaactgagctttttcttaatttcattccttttttttggacactggtggctcatta cctaaagcagtctatttatattttctacatctaattttagaagcctggctacAATACTGcacaaacttggttagttcaattttgatccccttttct acttaatttacattaatgctctttttagtatgttctttaatgctggatcacagacagctcattttctcagttttttggtatttaaaccattgcattgcagt agcatcatttta

Supplementary Table 2. List of oligonucleotides used in the article.

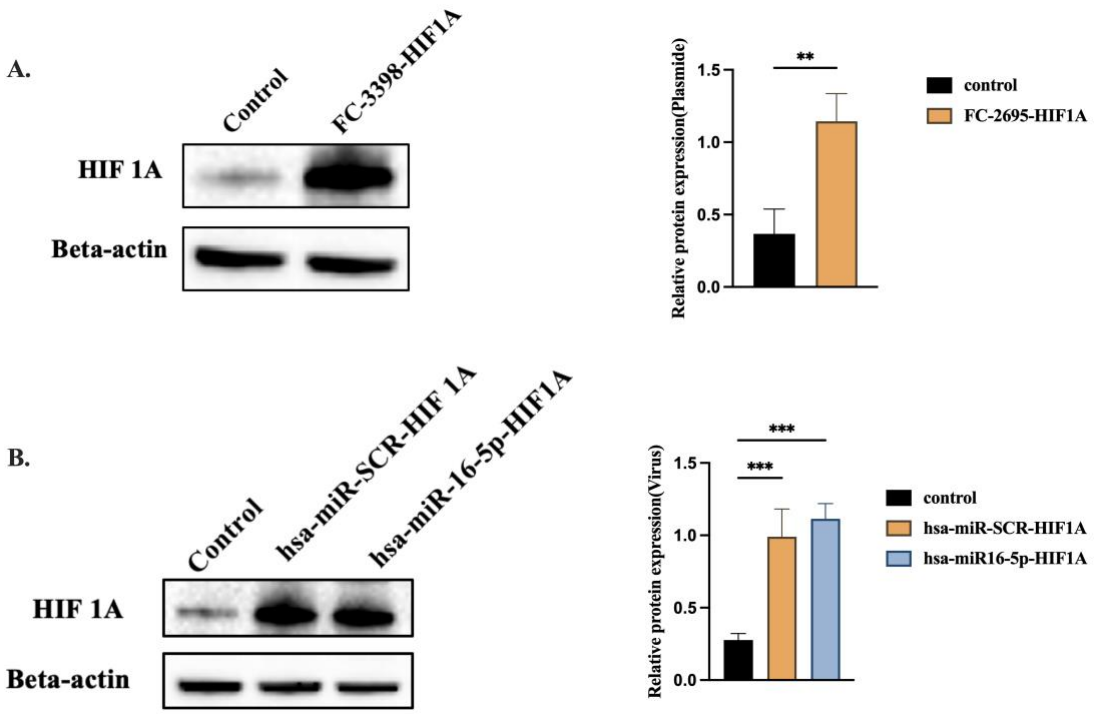
Oligonucleotide Name	Oligonucleotide Sequence
miR-16-F	aCCGGT*TAGCAGCACGTAAATATTGGCG*CTCGAG*CGCCAATATTTACGTGCTGCTA*TTTTTG
miR-16-R	AATTCAAAAATAGCAGCACGTAAATATTGGCGCTCGAGCGCCAATATTTACGTGCTGCTAAc
hsa-miR-16-1*-F	accggCCAGTATTAACTGTGCTGCTGActcgagTCAGCAGCACAGTTAATACTGGttttg
hsa-miR-16-1*-R	aattcaaaaaCCAGTATTAACTGTGCTGCTGActcgagTCAGCAGCACAGTTAATACTGGc
shScrambled-F	aCCGGT*CCTAAGGTTAAGTCGCCCTCG*CTCGAG*CGAGGGCGACTTAACCTTAGG*TTTTTG
shScrambled-R	AATTCAAAAA*CCTAAGGTTAAGTCGCCCTCG*CTCGAG*CGAGGGCGACTTAACCTTAGG*Ac
PLKO-Dir	tgtggaaaggacgaaacacc
PLKO-Rev	tctttcccctgcactgtacc
PLKO-15'	GACTATCATATGCTTACCGT



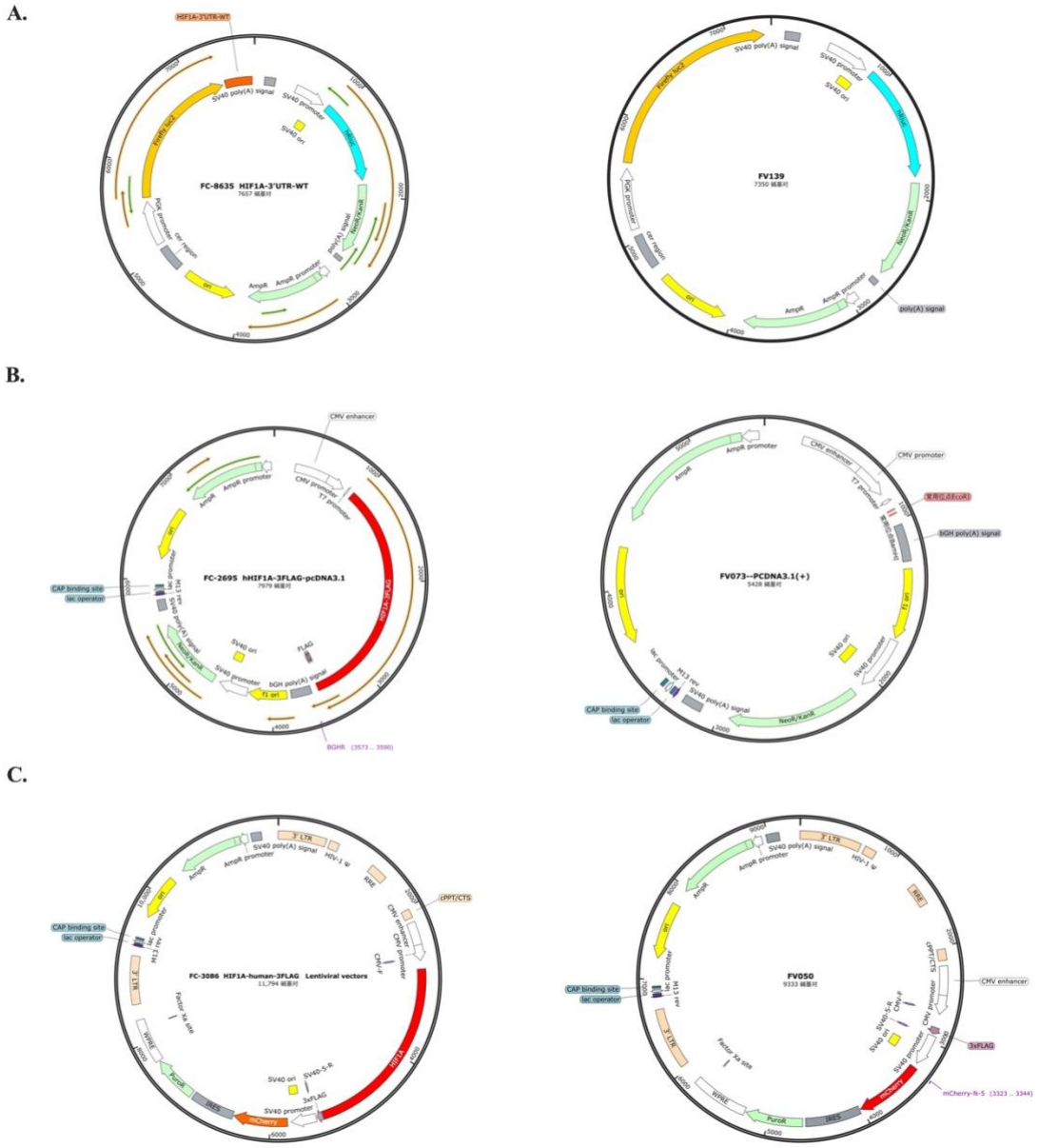
Supplementary Figure 1. Validation of stable miRNA-overexpressing A549 cell lines.
(A) Relative expression of miR-16-5p quantified by RT-qPCR in A549 control, A549-miR-16-5p, and A549-miR-16-5p + miR-16-1-3p cells. (B) Relative expression of miR-16-1-3p quantified by RT-qPCR in A549 control, A549-miR-16-1-3p, and A549-miR-16-5p + miR-16-1-3p cells. Data are presented as mean ± SD from three independent experiments; *p < 0.05, **p < 0.01, and ***p < 0.001 were considered statistically significant.



Supplementary Figure 2. Optimization of $CoCl_2$ concentration for hypoxia induction in A549 cells.
(A) Cell viability of A549 cells after 24 h and 48 h exposure to increasing concentrations of $CoCl_2$, as determined by MTT assay. (B) Western blot analysis showing HIF1A protein stabilization in A549 cells treated with graded $CoCl_2$ concentrations (24h,48h). β-actin served as a loading control. Quantitative analysis (right) demonstrated that treatment with 150 μM $CoCl_2$ for 24 h and 48h achieved strong HIF1A upregulation while maintaining > 80% cell viability, and this concentration was therefore used for all subsequent hypoxia-mimicking experiments. Data are presented as mean ± SD; *p < 0.05, **p < 0.01, and ***p < 0.001.



Supplementary Figure 3. Validation of HIF1A overexpression in stably transduced A549 cells.
(A) Western blot analysis confirming transient overexpression of HIF1A in A549 cells following plasmid transfection (FC-2695-HIF1A) compared with vector-transfected control cells. (B) Western blot validation of stable HIF1A overexpression in A549 cells generated by lentiviral transduction. Cells stably expressing HIF1A were established in the background of hsa-miR-SCR control cells (hsa-miR-SCR-HIF1A) or hsa-miR-16-5p–overexpressing cells (hsa-miR-16-5p-HIF1A). β-actin was used as the internal loading control. Quantified protein expression levels (right panels) are presented as mean ± SD from three independent experiments. Statistical significance is indicated as *$p < 0.05$, **$p < 0.01$, and ***$p < 0.001$.



Supplementary Figure 4. Plasmid maps of HIF1A constructs and corresponding control vectors used in this study. (A) Dual-luciferase reporter plasmid FC-8635 (HIF1A-3′UTR-WT), generated based on the Promega pmiR-GLO backbone (Cat. No. E1330), containing the full-length wild-type human HIF1A 3′ untranslated region cloned downstream of the firefly luciferase coding sequence. The corresponding empty vector FV-149 (pmiR-GLO without 3′UTR insert) was used as a negative control in luciferase reporter assays. (B) Transient overexpression plasmid FC-2695 (HIF1A-3×FLAG-pcDNA3.1) encoding full-length human HIF1A with a C-terminal 3×FLAG epitope tag, driven by the CMV promoter, for transient transfection experiments. The empty vector FV-073 (pcDNA3.1(+)) served as the corresponding control. (C) Lentiviral expression vector FC-3086 (HIF1A-3×FLAG) constructed on the PLVX-Puro backbone for generating stable HIF1A-overexpressing cell lines. The empty lentiviral vector FV-050 (PLVX-Puro) was used as the negative control in stable transduction experiments. All plasmids were purchased from Fubio Biotechnology Co., Ltd. (Suzhou, China). Vector backbones are derived from commercially available systems (Promega pmiR-GLO, pcDNA3.1, and PLVX-Puro), and plasmid maps are shown for reference.