

Mitochondria-specific targeting of noncanonical *EGR1* ntmRNA-coordinated mitophagy receptor BNIP3 homodimerization disrupts mitochondrial metabolism and suppresses hepatocellular carcinoma growth *in vitro* and *in vivo*

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Supplemental tables

Table S1. Oligonucleotides used for PCR and *EGR1* knockdown

Primer name	Sequences (5'-3')
EGR1	AGCAGCACCTTCAACCCTCAG GTAACCTGGTCTCCACCAGCA
U6	GTGCTCGCTTCGGCAGCACATATAC ATATGGAACGCTTCACGAATTTGCG
Cox2	ATGGCACATGCAGCGCAAGTAGGTC GTTAGGAAAAGGGCATAACAGGAC
β -actin	CAGGTCATCACCATTGGCAATGAGC CGGATGTCCACGTCACACTTCATGA
COX1	CGCTATCCCCACCGGCGTCAAAG GTCGTGTAGTACGATGTCTAGTG
MT-CYBT	GACAGACCTAGTTCAATGAATC ATAGGGCAAGGACGCCTCCTAG
MT-ND1	GCATACCCCCGATTCCGCTA TGAGGGGGAATGCTGGAGAT
MT-ND2	CATGCTAGCTTTTATTCCAGTTC GTTATGGTTCATTGTCCGGAGAGT
MT-ND3	CGAGTGCGGCTTCGACCCTA AGGGGTAAAAGGAGGGCAATTTC
U6 promoter	GCATATACGATACAAGGCTGTTA GGTGTTTCGTCCTTTCCACAAGAT
SMRE	TAATACGACTCACTATAGGGCCAATGGTGATCCTC ATGTGAGAGTACGGTCAAGCAG
SP3	TAATACGACTCACTATAGGGCCAATGGTGATCCTC GAACCGAAGCTCAGCTCAGC
SCTL	GACCGTACTCTCACATGTGGC CCCAATCGCAGCTACTTTATTTTCG
HA tag	GTCGTGACGCGGGATCCTCTAGACGCCACCATGTACCCATACGACGTC CCAGACTACGCT GCTGATGCCGTCGACCTTGGTCACTTTACCAGCGTAGTCTGGGACGTC GTA
shEGR1-1	CGTCCCCGGTTACTACCTCTTAT
shEGR1-2	ACTCTTGATGTGAAGATAATTTGCA
shCT	GCAGCAACTGGACACGTGATCTTAA
Cas13a gRNA	ATAAGAGGTAGTAACCGGGGACGGGTAA
Cas13a gCT	GTTGCAGTAGATCTTCGACTAGATCTAC
siEGR1	CGTCCCCGGTTACTACCTCTUU

siCtrl (sense)	UUCUCCGAACGUGUCACGUTT
siCtrl (antisense)	ACGUGACACGUUCGGAGAATT

Table S2. Antibodies

Antibodies	Company	Dilution	MW(kDa)
EGR1 (15F7) Rabbit mAb	Cell Signaling Technology	1:1000	75
OPA1 (D6U6N) Rabbit mAb	Cell Signaling Technology	1:1000	80-100
Mitofusin-1 (D6E2S) Rabbit mAb	Cell Signaling Technology	1:1000	82
Mitofusin-2 (D2D10) Rabbit mAb	Cell Signaling Technology	1:1000	80
Phospho-DRP1(Ser616) Rabbit mAb	Cell Signaling Technology	1:1000	78-82
Phospho-DRP1(Ser637) Rabbit mAb	Cell Signaling Technology	1:1000	78-82
LC3B (D11) XP® Rabbit mAb	Cell Signaling Technology	1:1000	14,16
Phospho-SQSTM1/p62 (Ser349) (E7M1A) Rabbit mAb	Cell Signaling Technology	1:1000	62
Optineurin (E4P8C) Rabbit mAb	Cell Signaling Technology	1:1000	75
NDP52 (D1E4A) Rabbit mAb	Cell Signaling Technology	1:1000	52,60
MFF(E5W4F) Rabbit mAb	Cell Signaling Technology	1:1000	25,27,30,35
HIF-1 α (D1S7W) XP® Rabbit mAb	Cell Signaling Technology	1:1000	120
BNIP3 (D7U1T) Rabbit mAb	Cell Signaling Technology	1:1000	22-28, 50-55
BNIP3L/Nix (D4R4B) Rabbit mAb	Cell Signaling Technology	1:1000	38,76
Parkin (Prk8) Mouse mAb	Cell Signaling Technology	1:1000	50
PINK1 (D8G3) Rabbit mAb	Cell Signaling Technology	1:1000	60,50
Bcl-2 (124) Mouse mAb	Cell Signaling Technology	1:1000	26
Cytochrome c (136F3) Rabbit mAb	Cell Signaling Technology	1:1000	14
Caspase-3(D3R6Y) Rabbit mAb	Cell Signaling Technology	1:1000	17, 19, 35
PARP Antibody 9542	Cell Signaling Technology	1:1000	89,116

	Technology			
Cleaved PARP(Asp214)	Cell	Signaling	1:1000	89
	Technology			
Cleaved Caspase-3(Asp175)	Cell	Signaling	1:1000	17,19
	Technology			
Bax	Cell	Signaling	1:1000	20
	Technology			
FUNDC1 Polyclonal Antibody	Thermo fisher		1:1000	18
Anti-MTCO1 antibody	Abcam		1:800	37
Recombinant Anti-TOMM20 antibody	Abcam		1:1000	16
COX IV (3E11) Rabbit mAb	Cell	Signaling	1:1000	17
	Technology			
Anti-beta Actin antibody	Abcam		1 µg/ml	42
Anti-mouse IgG, HRP-linked Antibody	Cell	Signaling	1:2000	/
	Technology			
Anti-rabbit IgG, HRP-linked Antibody	Cell	Signaling	1:2000	/
	Technology			

Supplemental figures

Figure S1. Mitochondria-specific RNA targeting using the LwaCas13a-mBN-MLS system.

- A** LwaCas13a-mBN-MLS targeting and control vectors. pU6: RNA polymerase III U6 promoter; gEGR1: Cas13a guiding RNAs that target the *EGR1* ntmRNA; T5: the TTTTT termination signal of RNA polymerase III; pEF1: the EF1-alpha promoter; HA: HA tag peptide, H-Tyr-Pro-Tyr-Asp-Val-Pro-Asp-Tyr-Ala-OH (YPYDVPDYA), used for tracking Cas13a; Cas13a: the catalytically inactive CRISPR Cas13a; MLS: mitochondria-localization signal peptide derived from COX8A, which helps the specific localization of the Cas13a-mBN in the mitochondria; gCT: a random gRNA control.
- B** Mitochondria-specific targeting of *EGR1* ntmRNA. In this system, Cas13a-gRNA provides the RNA targeting specificity. MLS provides the specific localization of the Cas13a-mBN in the mitochondria. The potent RNase activity of mBN efficiently degrades *EGR1* ntmRNA in the mitochondria. Working together, this system effectively reduces the levels of *EGR1* ntmRNA in the mitochondria, thereby allowing for the study of mitochondrial RNA function and its impact on cellular processes.
- C** The heatmap displays the top 10 differentially enriched RNAs in the mitochondria of HepG2 and HL7702 cells, based on RNA-seq analysis. Expression levels are represented by a color scale, with red indicating higher expression and white indicating lower expression. The color bar on the right shows the relative expression intensity, with yellow and blue corresponding to HepG2 and HL7702 cells, respectively. *EGR1* exhibits the most significant differential expression between the two cell lines, supporting its selection for further investigation.

Figure S2. Mitochondrial enrichment of *EGR1* ntmRNA in hepatoma cells.

- A** Quantification of *EGR1* ntmRNA in isolated HepG2 mitochondria by qPCR. The U6 RNA was used as quality control for isolated mitochondria. The Ct value of *EGR1* was normalized over that of the mitochondria-encoded COX2 and set as 1 for comparison.
- B** Quality check of isolated mitochondrial RNAs. The nuclear genome-encoded U6 RNA was used as the control. At the whole-cell level, COX2, *EGR1* and U6 RNA were detected (left panel). Both *EGR1* and mitochondrial control COX2 were detected in isolated HepG2 mitochondria. No nuclear U6 RNA was

detected in mitochondrial RNA samples (right panel).

- C** RNA-FISH detection of *EGR1* ntmRNA in Hepatoma SMMC7722 cells. The nuclei were stained with DAPI (blue). *EGR1* ntmRNA was probed by Dig-labeled single-stranded DNA probes (green). Mitochondria were labeled with MitoTracker (red). The nuclear-encoded *U6* RNA was used as a negative control, and the mitochondria-encoded *COX2* served as a positive control.
- D** Colocalization quantitation of *EGR1* ntmRNA and MitoTracker using Scatter plot. Pearson's correlation coefficient (PCC) was calculated for the entire image (R_{total}) and the pixels above thresholds (R_{coloc}). 1: perfect correlation; -1: completely excluded; 0: random relationship.
- E** Total *EGR1* RNA levels between normal hepatocytes and hepatocellular carcinoma (HCC) Cells. HepG2 and SMMC7721: hepatoma cells; THLE-2, THLE-3 and HHL-5: normal hepatic cells; 293T: normal human embryonic kidney cells. The Ct values were normalized over that of β -Actin and then standardized by setting 293T as 1 for comparison.

Data represents the mean $\pm$ SEM of three independent experiments. Significant differences were determined by an unpaired two-tailed *t*-test. **** $p < 0.0001$.

Figure S3. The mitochondria-enriched *EGR1* mRNA is not translated in the mitochondria of hepatoma cells.

- A** The nucleus-mitochondria-ribosome crosstalk model. LncRNAs can shuttle between nuclei and mitochondria and function as epigenetic messengers to coordinate cell metabolism. The nuclear-encoded lncRNAs that translocate to mitochondria are so-called anterograde signals. On the other hand, the mitochondria-encoded lncRNAs that shuttle to the nucleus, function as retrograde signals. It is not clear if *EGR1* mRNA molecules in the HCC mitochondria function as an anterograde signal or translate to *EGR1* peptides as they do in the ribosome. Dashed line: unproven crosstalk pathways.
- B** Western blot of *EGR1* protein levels in total cells and isolated mitochondria from HepG2 cells. β -ACTIN and TOM20 were used as the controls. No *EGR1* proteins were detected in isolated mitochondria, suggesting an anterograde messenger role of *EGR1* mRNA as a non-translating mRNA (ntmRNA) in

HCC cells.

C Immunofluorescence staining of EGR1 protein under hypoxia 0h and 24h. Nuclei were stained with DAPI (blue) and EGR1 protein was immunostained by the anti-EGR1 antibody (green). Mitochondria were labeled with MitoTracker (purple). No EGR1 protein was detected in mitochondria. Scale bar: 10µm.

Figure S4. *EGR1* knockdown affects mitochondrial functions in HepG2 cells.

A Schematic diagram of *EGR1* shRNA vectors.

B Knockdown of *EGR1* by shRNA lentiviruses in HepG2 cells. shEGR1-1, shEGR1-2: two *EGR1* shRNAs; shCtrl: random shRNA control. *EGR1* was quantitated by qPCR, and the Ct value was normalized over that of β -Actin and then standardized by setting untreated HepG2 cells as 1.

C ATP synthesis in shCtrl and shEGR1-treated HepG2 cells.

D Mitochondrial membrane potential in shCtrl and shEGR1-treated HepG2 cells following the CCCP treatment.

Data represents the mean $\pm$ SEM and are representative of three independent experiments. Significant differences were determined by an unpaired two-tailed *t*-test. ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$.

Figure S5. *EGR1* Knockdown interferes with mitochondrial function in SMMC7721 cells.

A Knockdown of *EGR1* by shRNA lentiviruses in SMMC7721 cells. shEGR1-1, shEGR1-2: two *EGR1* shRNAs; shCtrl: random shRNA control. *EGR1* was quantified by qPCR, and the Ct value was normalized over that of β -Actin and then standardized by setting untreated SMMC7721 cells as 1.

B ATP synthesis in shCtrl and shEGR1-treated SMMC7721 cells.

C Mitochondrial membrane potential in shCtrl and shEGR1-treated SMMC7721 cells with or without CCCP treatment.

D Rescue assay in SMMC7721 cells. siEGR1-treated cells were rescued by transfection of *EGR1* plasmid DNA. Rescue cells were cultured under hypoxic conditions for 12h and were used for ROS fluorescence staining using the ROS probe DCFDA/H2DCFDA (green). Mitochondria were tracked by MitoTracker

Deep Red (MTDR). The yellow color indicates accumulated ROS within the mitochondria. Quantitative changes in the ROS green fluorescence intensity were analyzed by Image J. Scale bar: 20µm.

E Cellular ROS in SMMC7721 cells. ROS was examined using DCFDA probe followed by flow cytometry in the siCtrl (yellow), siEGR1 (blue) and siEGR1-rescue (pink) Groups.

Data represents the mean $\pm$ SEM and are representative of three independent experiments. Significant differences were determined by an unpaired two-tailed *t*-test. ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$.

Figure S6. Cas13a-mBN-MLS targeting of *EGR1* ntmRNA affects mitochondria mass in HepG2 cells.

A Immunofluorescent quantification of TOM20. HepG2 cells were transfected with lentiviruses carrying the Cas13a-mBN-MLS system and were incubated under normoxic and hypoxic conditions. Cas13a-gCT: random Cas13a gRNA; Cas13a-gEGR1: *EGR1* Cas13a gRNA1. Mitochondria were tracked by immunostaining of TOM20 (red). Nuclei were stained with DAPI (blue). In response to hypoxia stress, cells eliminated mitochondria using the mitophagy pathway. Mitochondria-specific knockdown of *EGR1* inhibited mitophagy.

B Western blot of COX4 in Cas13a-mBN-MLS-treated cells. Cells were collected for Western blotting after exposure to hypoxia for 0h, 12h, and 24h.

C Quantification for TOM20 level after hypoxia treatment in Figure A. (40 cells were counted per group).

D Quantification of COX4 Western blot in Figure B.

Data represents the mean $\pm$ SEM of three independent experiments. Significant differences were determined by an unpaired two-tailed *t*-test (C) or two-way ANOVA with Tukey's multiple comparison test (D). * $p < 0.05$, ** $p < 0.01$, **** $p < 0.0001$.

Figure S7. Mitochondria mass in shEGR1 knockdown HepG2 cells.

A Immunofluorescent staining of TOM20 in shEGR1-treated cells under normoxic and hypoxic conditions.

Nuclei were stained with DAPI (blue), and TOM20 was immunostained in red.

B Quantification for TOM20 level after hypoxia treatment in Figure A. (40 cells were counted per group).

C Western blot of COX4 in shEGR1-rescue cells under normoxic and hypoxic conditions. β -Actin was used as the control.

D Quantification of COX4 in Figure C.

Data represents the mean $\pm$ SEM of three independent experiments. Significant differences were determined by an unpaired two-tailed t-test (C) and two-way ANOVA with Tukey's multiple comparison test (D). * $p < 0.05$, ** $p < 0.01$.

Figure S8. *EGR1* ntmRNA is required for hypoxia-induced mitochondrial fission and mitochondrial fusion.

A Western blot measurement of mitochondria fission and fusion proteins. After hypoxia treatment for 0h, 12h and 24h, HepG2 cells were collected for Western blotting. β -ACTIN was used as the control.

B Quantification of Western blot for mitochondria fission and fusion proteins. The 0h group was set as 1 for comparison.

Data represents the mean $\pm$ SEM of three independent experiments. Significant differences were determined by two-way ANOVA with Tukey's multiple comparison test. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$.

Figure S9. *EGR1* ntmRNA interacts with the mitophagy receptor NIX in mitochondria.

A *EGR1* ntmRNA-NIX interaction by the RIP assay. HepG2 and SMMC7721 cells were collected after exposure to hypoxia for 0h and 24h, and the RIP assay was used to detect the interaction of *EGR1* ntmRNA with the mitophagy receptor NIX. Ct value was normalized over that of β -ACTIN and then standardized by setting IgG as 1.

B Colocalization of *EGR1* ntmRNA with mitochondrial NIX in HepG2 cells by RNA-FISH and immunofluorescent staining. The nuclei were stained with DAPI (blue), and mitochondria were labeled with Mito-Tracker (yellow). *EGR1* ntmRNA was probed with Dig-labeled single-stranded DNA probes and detected with FITC-coupled anti-dig antibody (green). Anti-NIX antibody was used to label NIX protein (Red). The overlapping part of *EGR1* mRNA with NIX proteins appeared in yellow. Scale bar: 10µm.

C Colocalization of *EGR1* ntmRNA with mitochondrial NIX in SMMC7721 cells. Scale bar: 10µm.

D Quantitation of *EGR1* ntmRNA-NIX interaction yellow puncta numbers in HepG2 cells (fluorescent scanning of Figure B).

E Quantitation of *EGR1* ntmRNA-NIX interaction yellow puncta numbers in SMMC7721 cells (fluorescent scanning of Figure C).

Data represents the mean $\pm$ SEM of four independent experiments. Significant differences were determined by an unpaired two-tailed t-test. ** $p < 0.01$, *** $p < 0.001$.

Figure S10. *EGR1* ntmRNA interacts with mitochondrial BNIP3 in SMMC7721 cells.

A Colocalization of *EGR1* ntmRNA with mitochondrial BNIP3 in SMMC7721 cells by RNA-FISH and immunofluorescent staining. The nuclei were stained with DAPI (blue) and mitochondria were labeled with Mito-Tracker (yellow). *EGR1* ntmRNA was probed with Dig-labeled single-stranded DNA probes and detected with FITC-coupled anti-dig antibody (green). Anti-BNIP3 antibodies were used to label BNIP3 proteins (Red). The overlapping portion of *EGR1* ntmRNA with BNIP3 proteins appeared in yellow. Scale bar: 10µm.

B Quantitation of *EGR1* ntmRNA-BNIP3 interaction yellow puncta numbers in SMMC7721 cells (fluorescent scanning of Figure A) ($n = 4$). Data represents the mean $\pm$ SEM of three independent experiments. Significant differences were determined by an unpaired two-tailed *t*-test. *** $p < 0.001$.

Figure S11. Interaction model construction between *EGR1* ntmRNA MRE and BNIP3 monomer.

A *EGR1* MRE and BNIP3 monomer binding nucleotides. Specific MRE nucleotides (A69, C71, and G150) that interact with BNIP3 monomer are marked in red.

B Model construction using PYMOL. After docking, the top 10 binding models were extracted.

The scores of the top 10 binding models.

C Molecular model of the interaction between *EGR1* ntmRNA MRE and BNIP3 monomer. The size and location of the interaction is visualized with PyMOL. The insert shows the specific interaction sites and hydrogen bonds ranging from 2.2 to 3.3 Å between *EGR1* MRE nucleotides (A69, C71, G150) and BNIP3 amino acid residues (Ser173, Lys177, Lys176, Gln139).

Figure S12. Interaction analysis between *EGR1* ntmRNA MRE and BNIP3 dimer.

A *EGR1* MRE and BNIP3 dimer binding nucleotides. The *EGR1* MRE nucleotides that interact with BNIP3.

B dimer chains A and B are shown in blue and purple, respectively.

Model construction using PYMOL. After docking, the top 10 binding models were extracted.

C The scores of the top 10 binding models between *EGR1* ntmRNA MRE and BNIP3 dimer.

Figure S13. *EGR1* ntmRNA induces BNIP3 dimerization.

A The intera3 dimeric protein chain A amino acids (Lys130, Lys135, Arg139), as well as the hydrogen bonds between *EGR1* MRE nucleotides (C115, T60, DA56) and BNIP3 dimer chain B residues (Lys130, Lys135, Thr140).

B *EGR1* ntmRNA MRE induces BNIP3 dimerization on isolated mitochondria. Top panel: Schematic diagram of the BNIP3 dimerization assay. Mitochondria from hypoxic HepG2 cells were incubated with BNIP3 protein in the binding buffer containing *EGR1* ntmRNA. BNIP3 dimerization was detected by the Western Blot. Bottom panel: BNIP3 dimerization. After in vitro incubation, BNIP3 dimerization was determined by the Western Blot. A random RNA (CtRNA) was used as the RNA control in the assay.

Figure S14. *EGR1* affects malignant phenotypes of hepatocellular carcinoma cells in mitophagy dependent manner.

A Cell invasion. Transwell assay was used to assess cell invasion in shEGR1-treated HepG2 cells and SMMC7721 cells.

B Quantitation of the Transwell assay. Five randomly selected fields were photographed and counted per well.

C Colony formation assays of shEGR1-treated HepG2 cells and SMMC7721 cells in 6-well plates.

D Quantitation of the colony formation assays by ImageJ.

E Cell Migration by the wound healing assay in shEGR1-treated HepG2 cells and SMMC7721 cells.

F The wound closed area (%) was measured by ImageJ.

G Cell proliferation assay. Cell proliferation was measured by the CCK-8 kit in shEGR1-treated HepG2 cells and SMMC7721 cells and was calculated as the slope ratio of the growth OD curves.

H Expression of apoptotic proteins by Western blot. β -ACTIN was used as the control.

I Quantitation of apoptotic proteins.

Data represents the mean $\pm$ SEM of three independent experiments. Significant differences were determined by an unpaired two-tailed *t*-test or two-way ANOVA with Tukey's multiple comparison test. **p* < 0.05, ***p* < 0.01, ****p* < 0.001, *****p* < 0.0001.

Figure S15. Mitochondria-targeted knockdown of *EGR1* affects HCC phenotypes.

A Transwell invasion assays were performed to assess cell invasion capacity in the following groups: control group, mitochondria-targeted *EGR1* knockdown group, and mitochondria-targeted *EGR1* knockdown combined with MRE fragment rescue group in HepG2 cells and SMMC7721 cells.

B Quantitation of the Transwell assay. Five randomly selected fields were photographed and counted per well.

C Colony formation assays were performed to assess cell invasion capacity in the following groups: control group, mitochondria-targeted *EGR1* knockdown group, and mitochondria-targeted *EGR1* knockdown combined with MRE fragment rescue group in HepG2 cells and SMMC7721 cells.

D Quantitation of the colony formation assays by ImageJ.

E The wound healing assay was performed to assess cell migration capacity in the following groups: control group, mitochondria-targeted *EGR1* knockdown group, and mitochondria-targeted *EGR1* knockdown combined with MRE fragment rescue group in HepG2 cells and SMMC7721 cells.

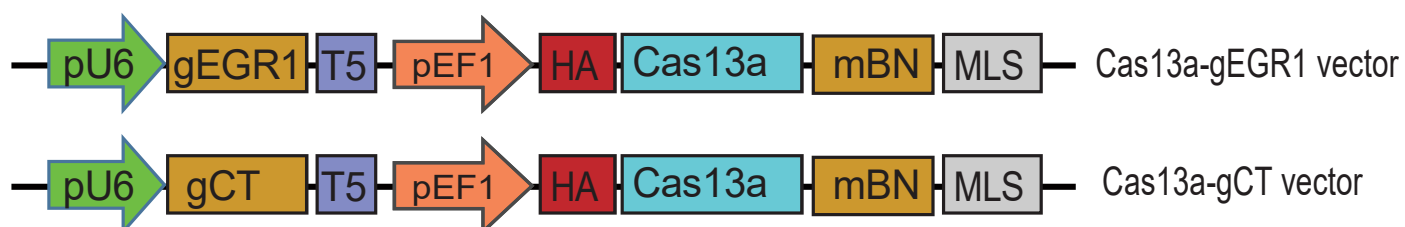
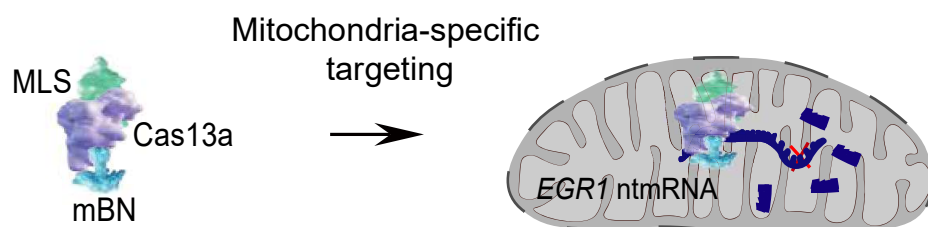
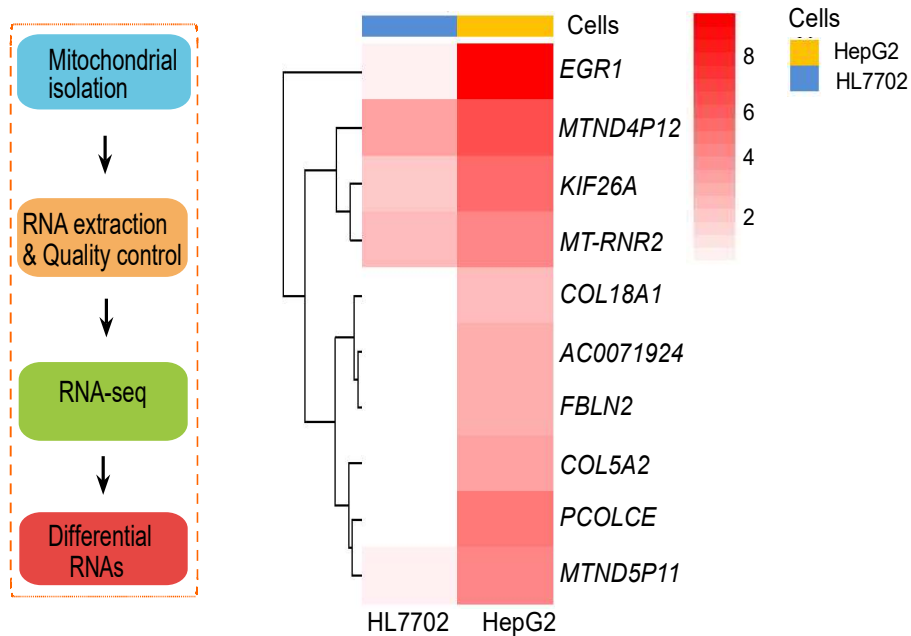
F The wound closed area (%) was measured by ImageJ.

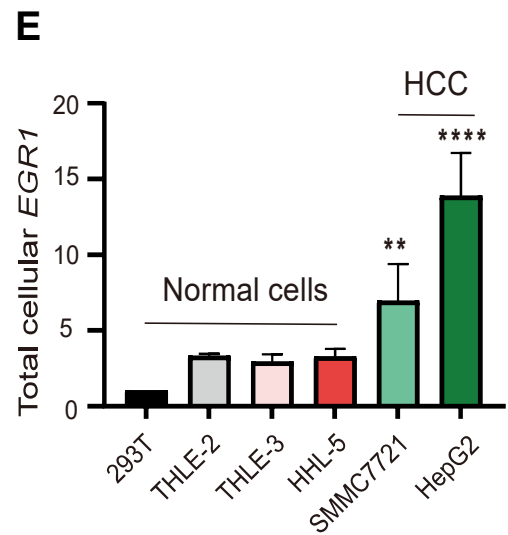
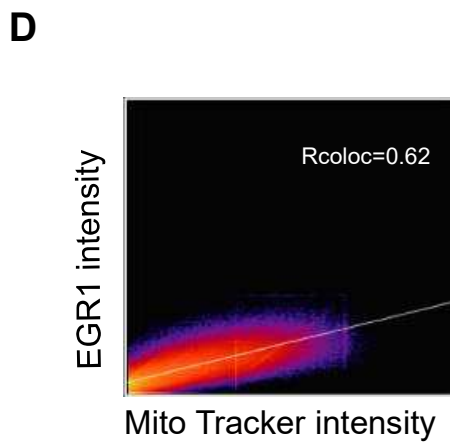
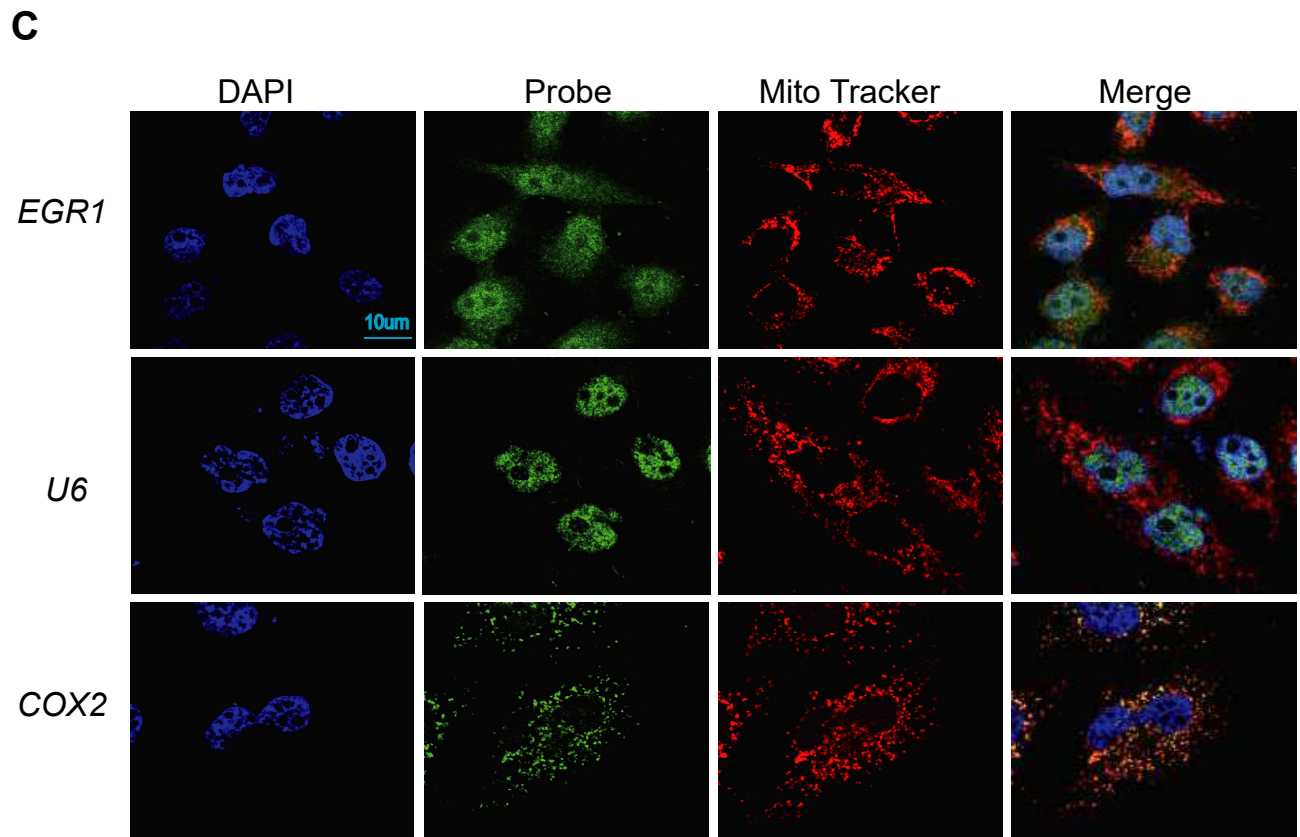
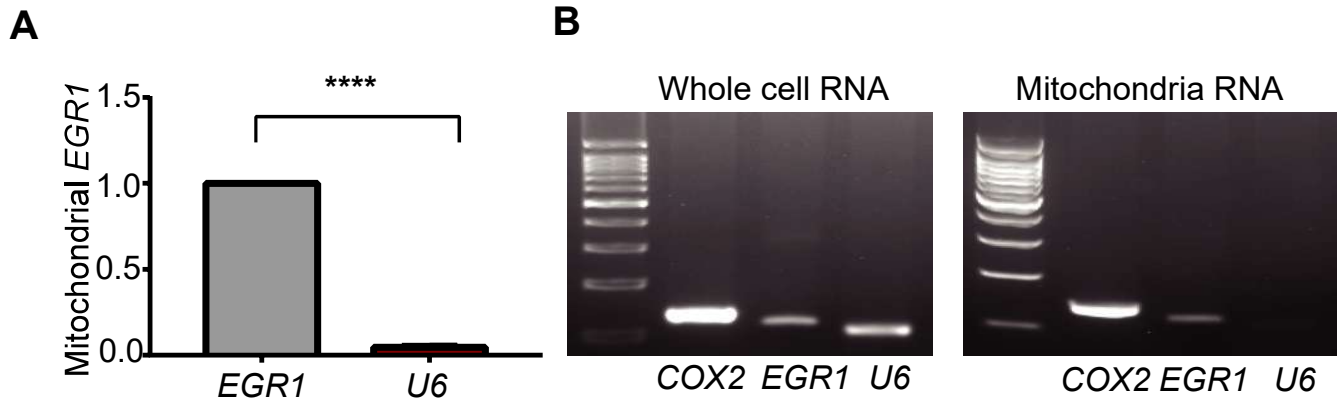
G Cell proliferation was measured by the CCK-8 OD slopes in control group, mitochondria-targeted *EGR1* knockdown group, and mitochondria-targeted *EGR1* knockdown combined with MRE fragment rescue group in HepG2 cells and SMMC7721 cells.

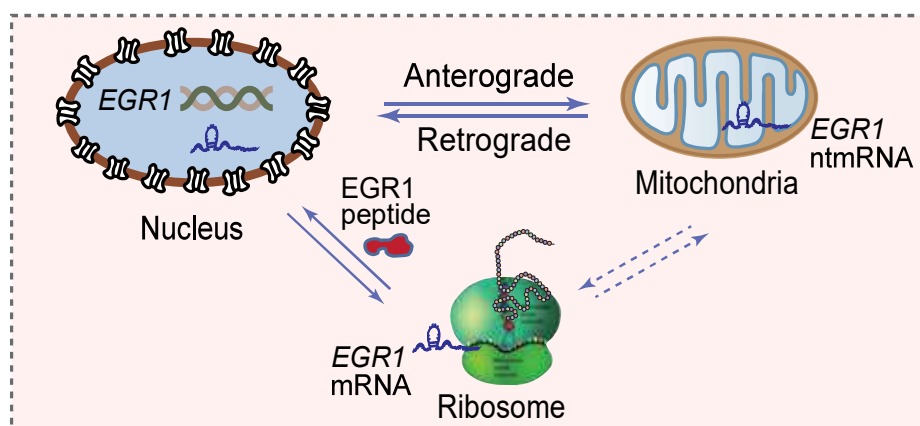
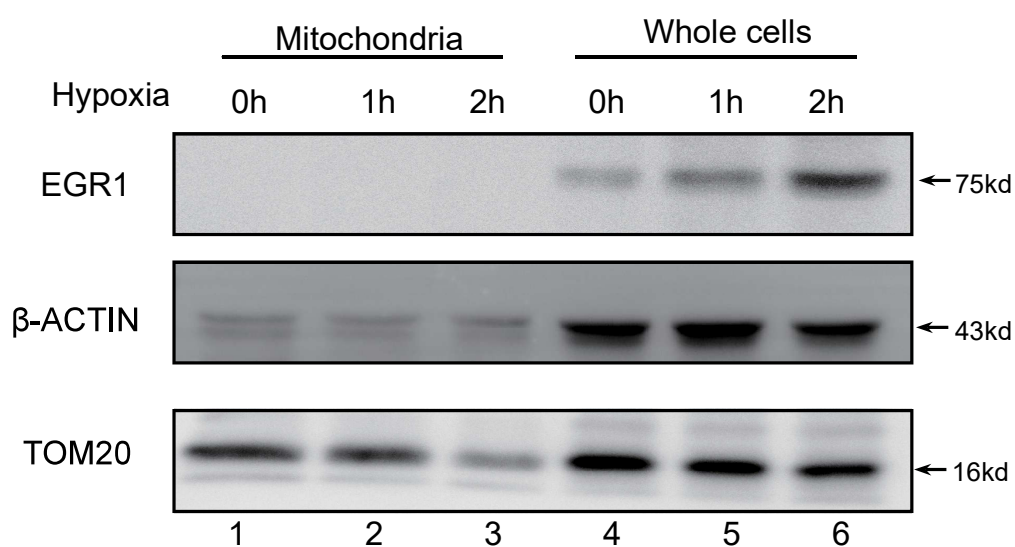
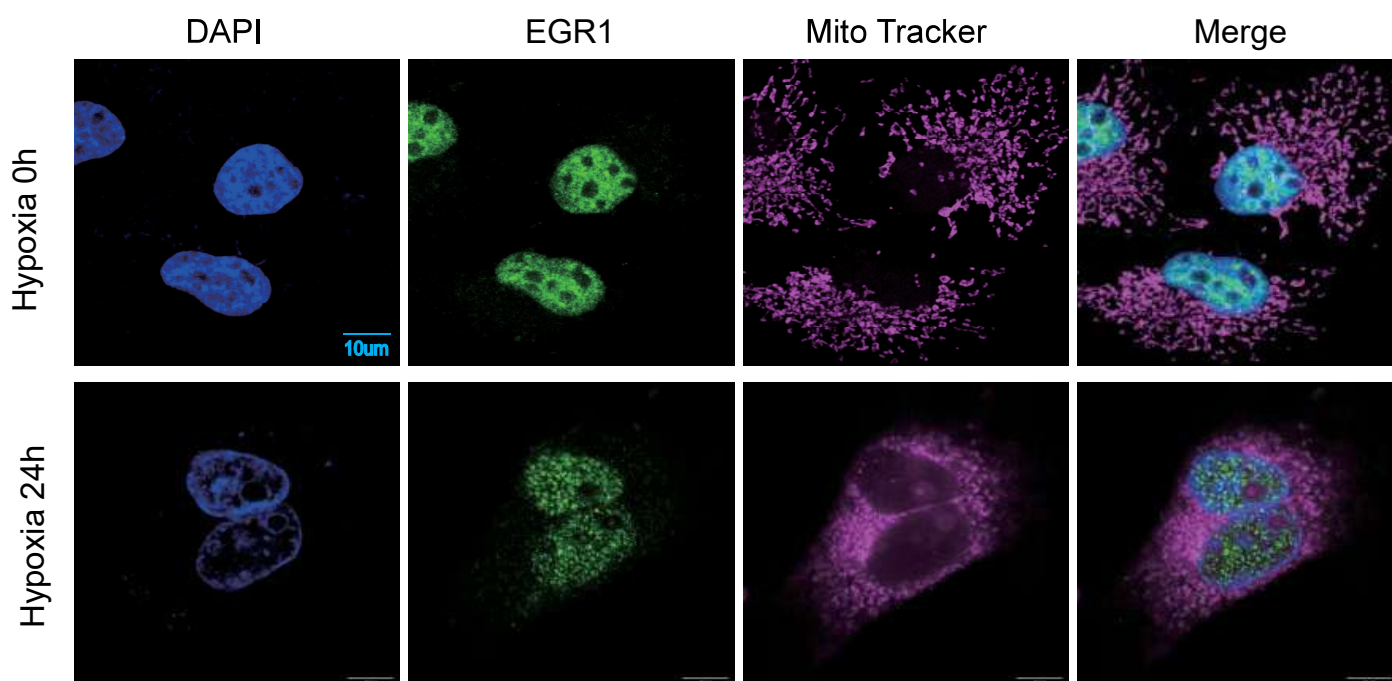
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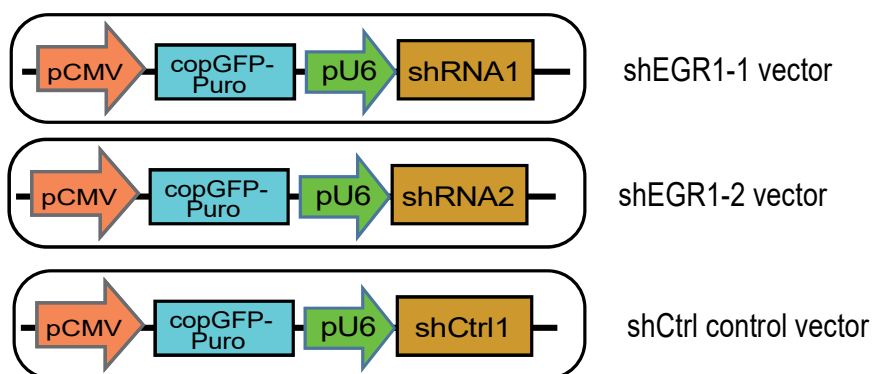
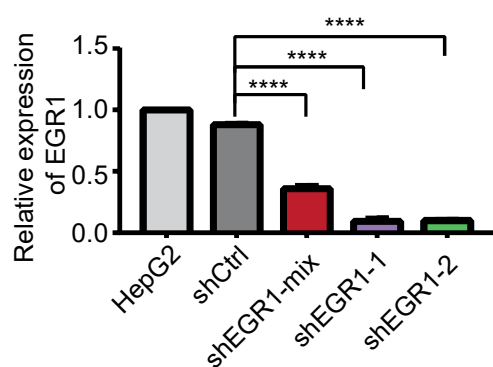
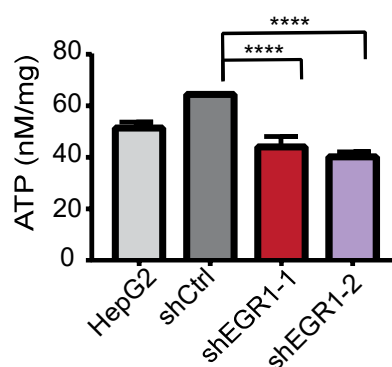
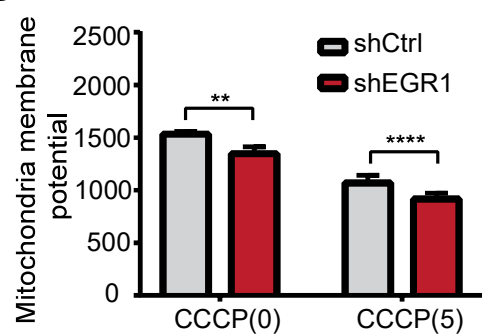
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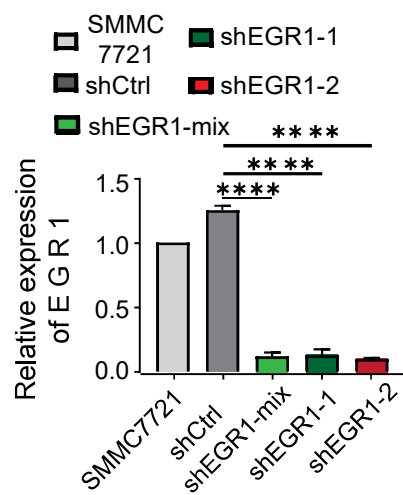
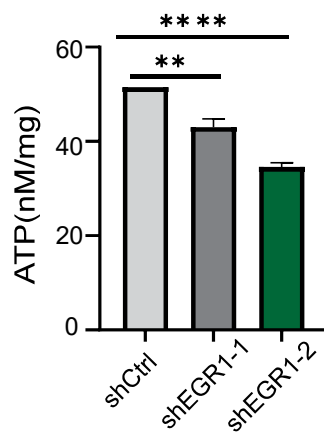
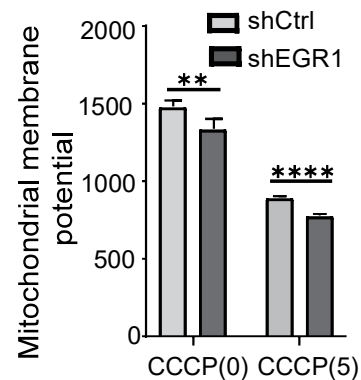
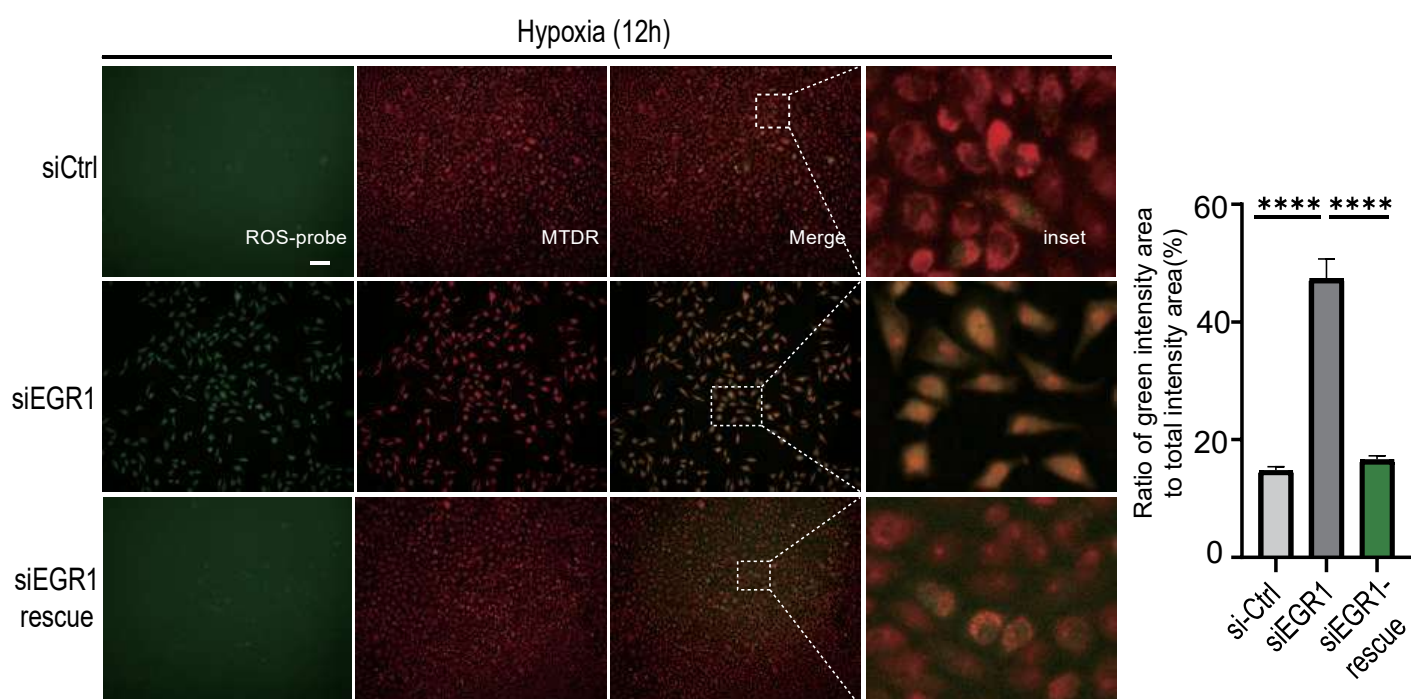
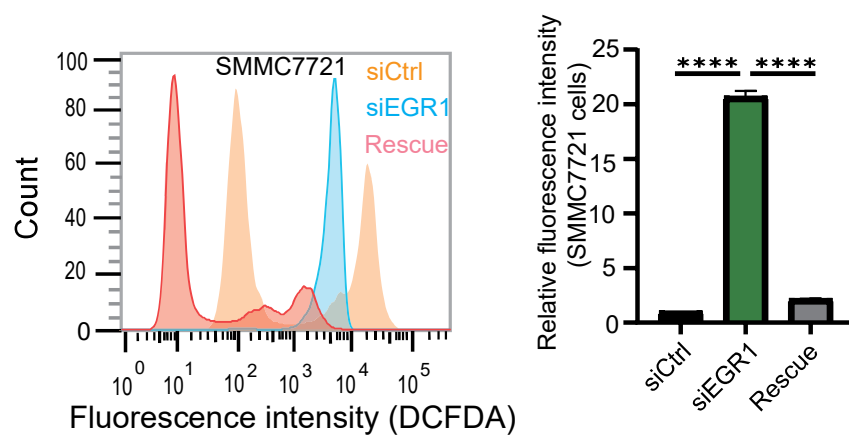
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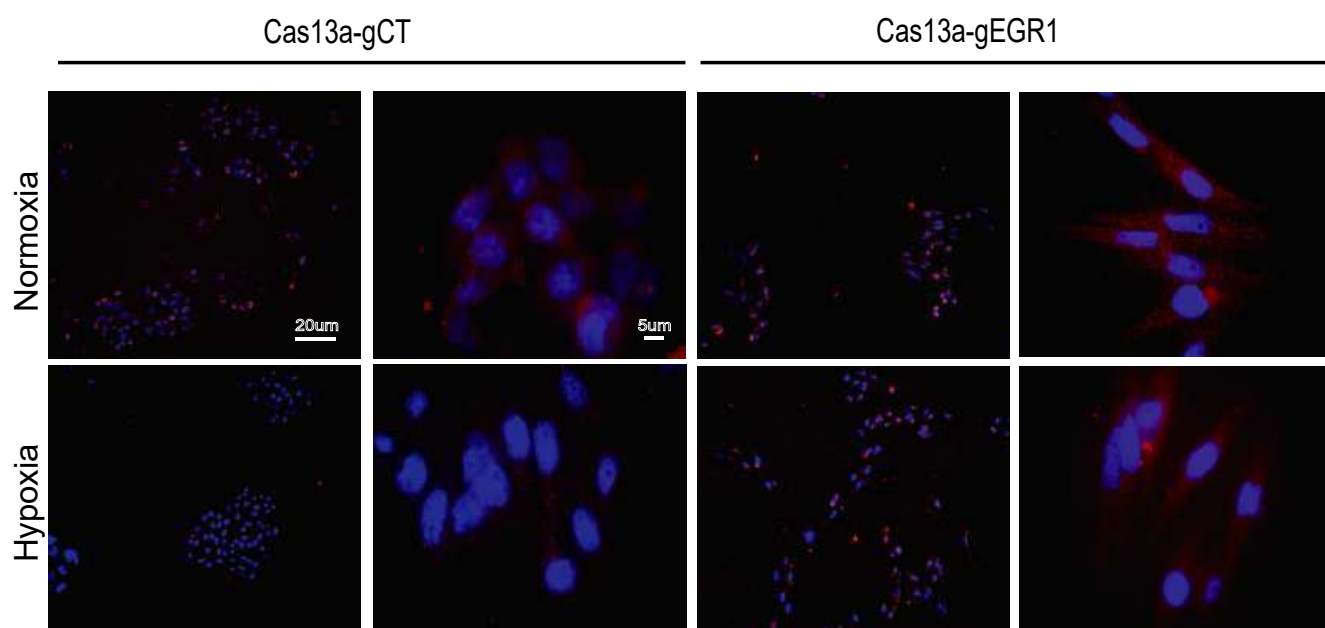
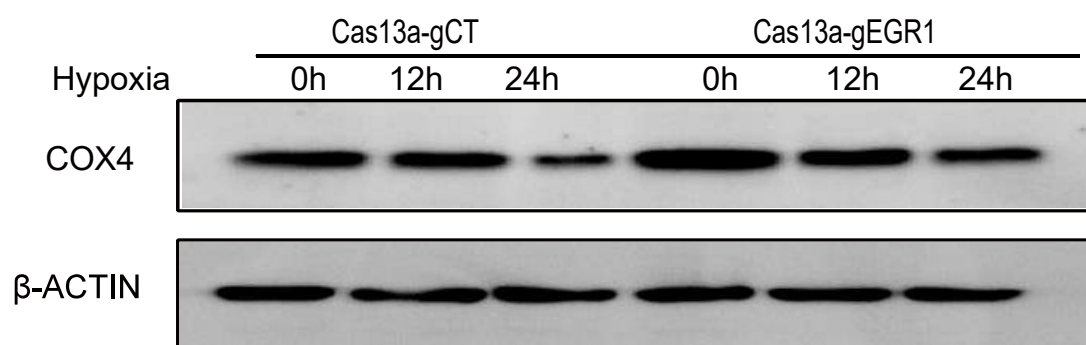
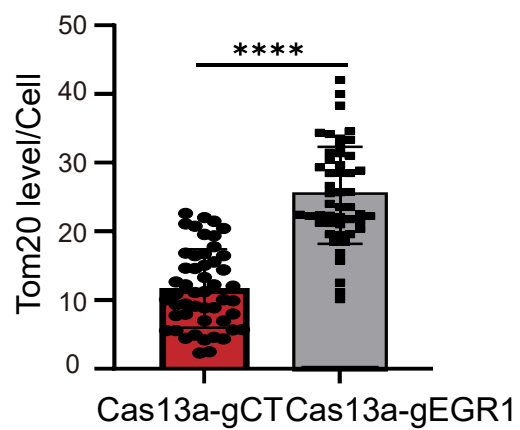
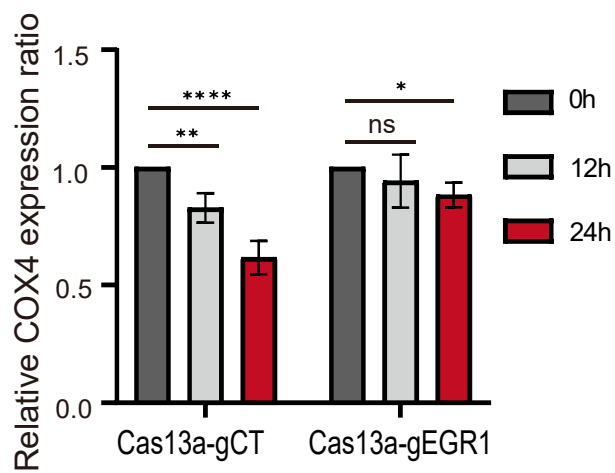
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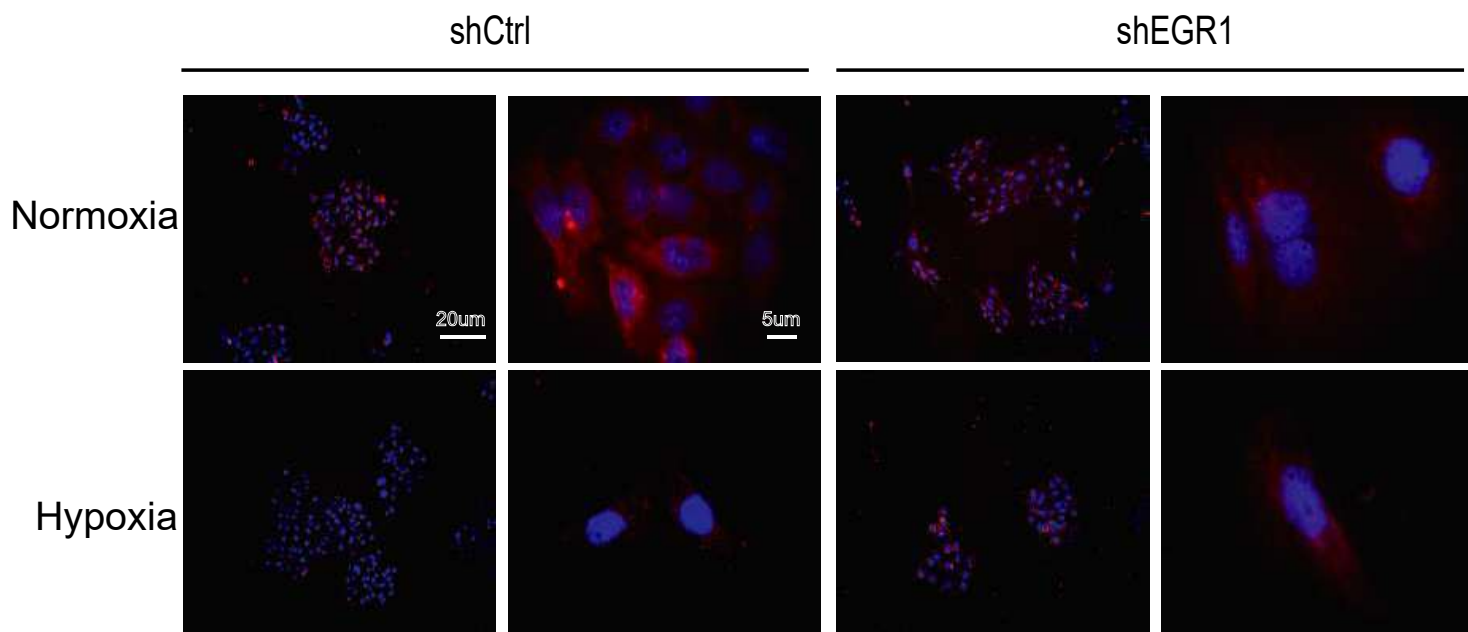
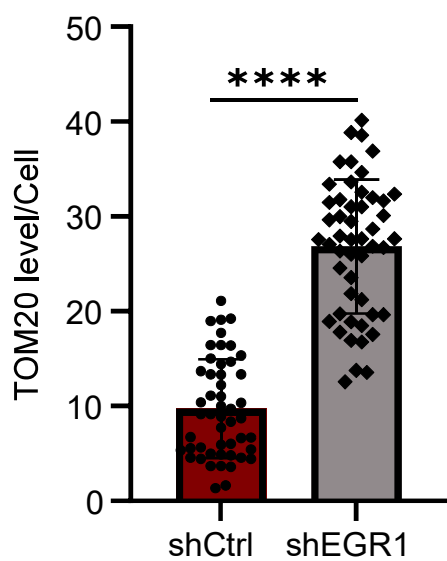
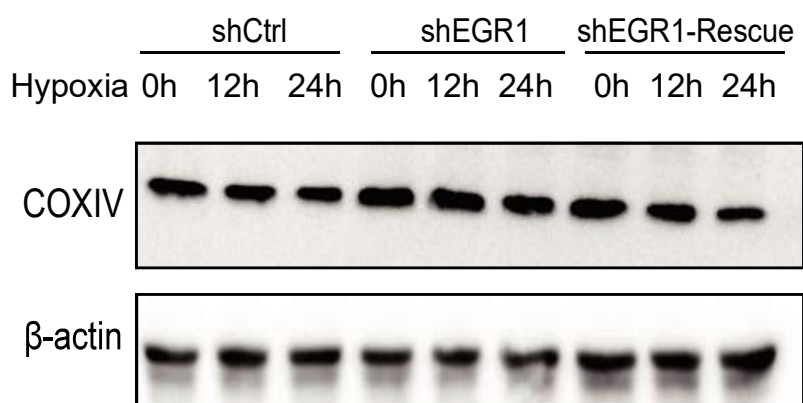
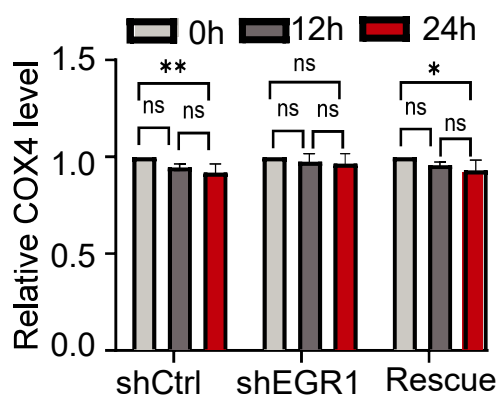


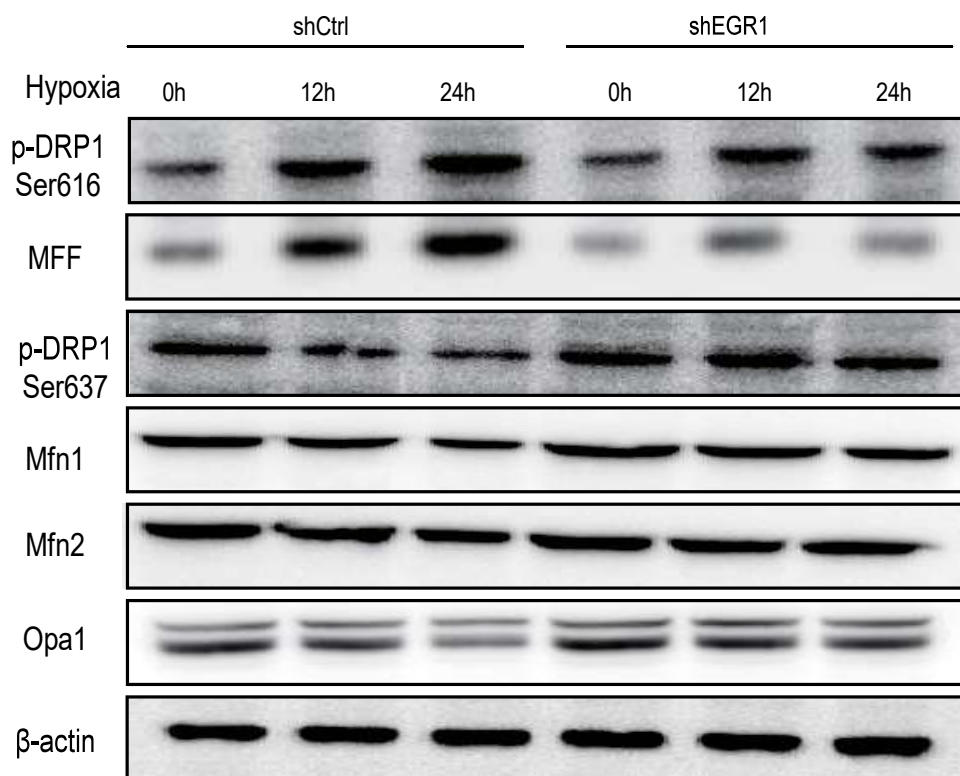
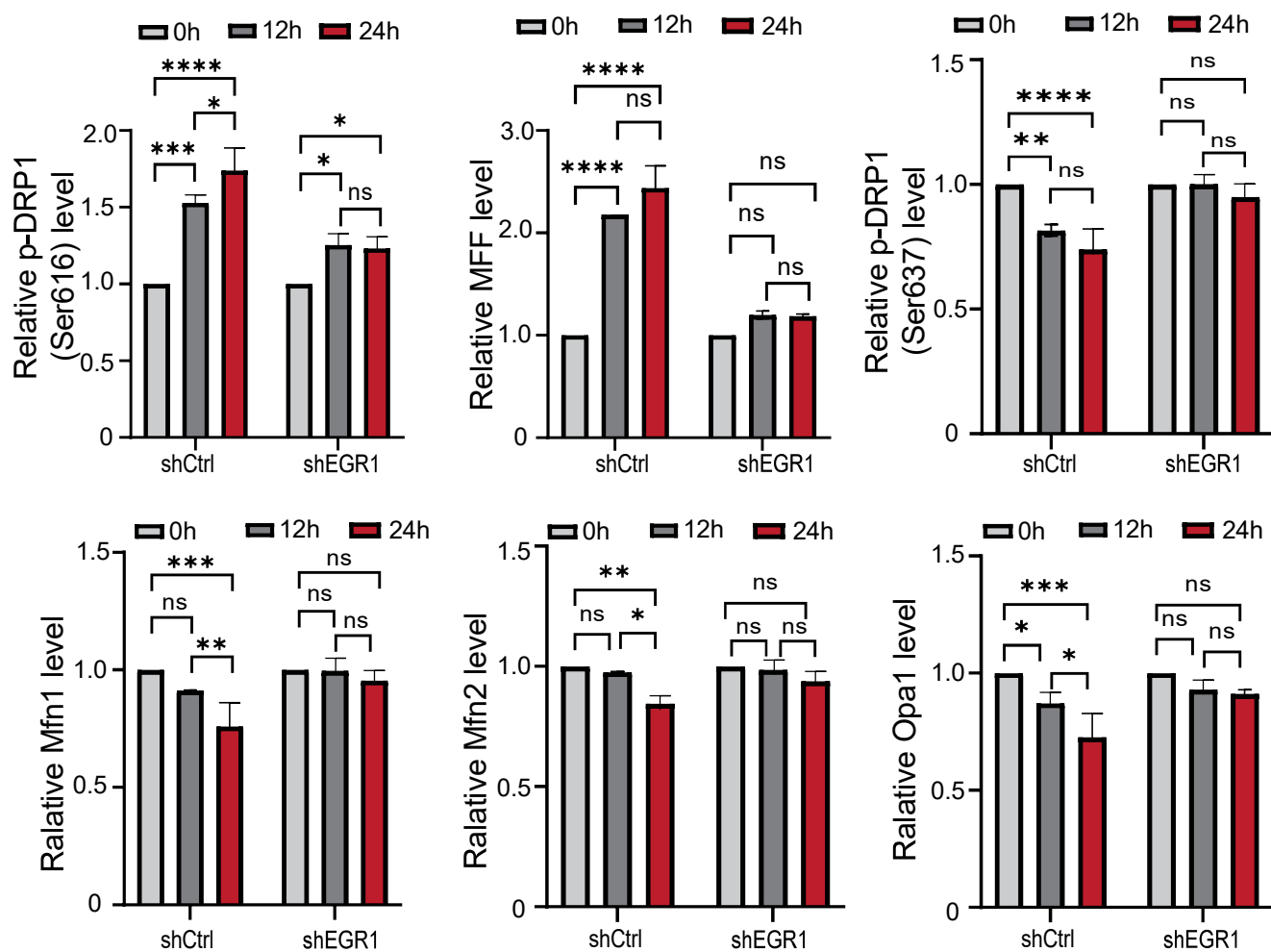
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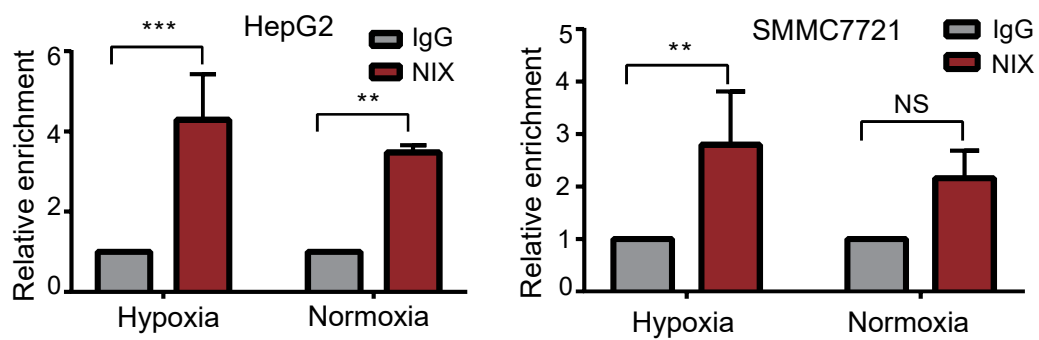
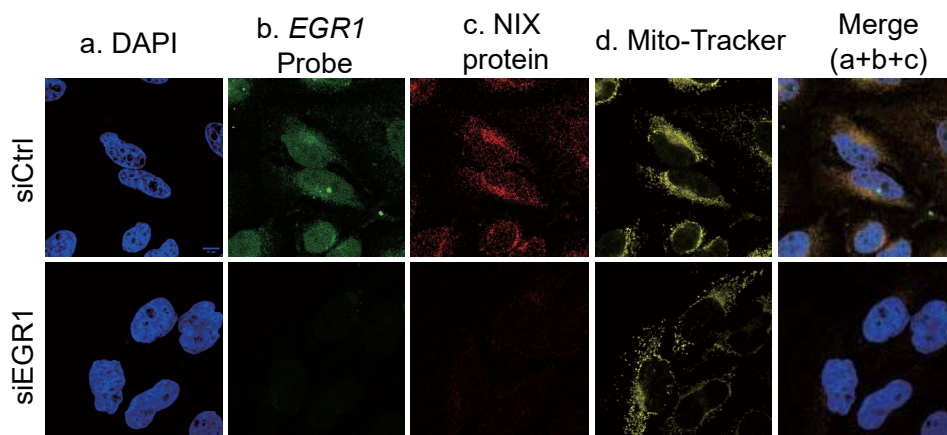
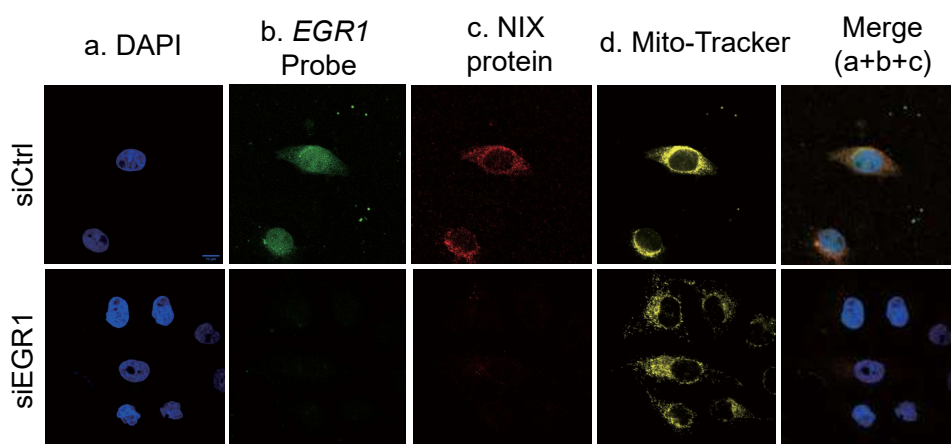
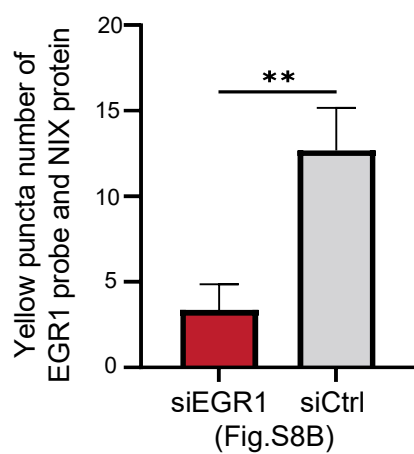
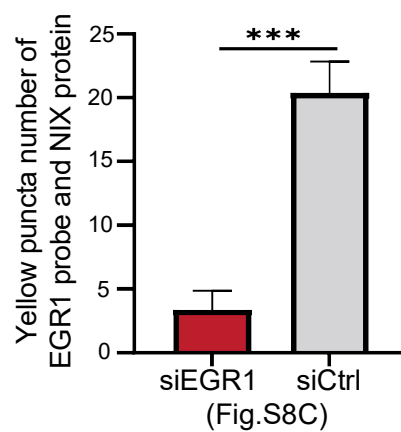
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A**B****C****D****E**

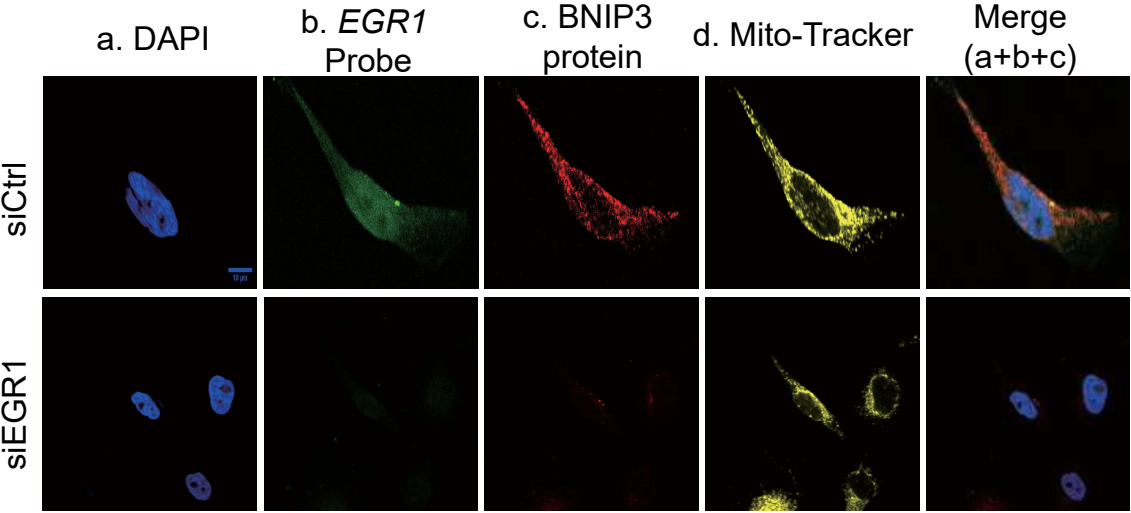
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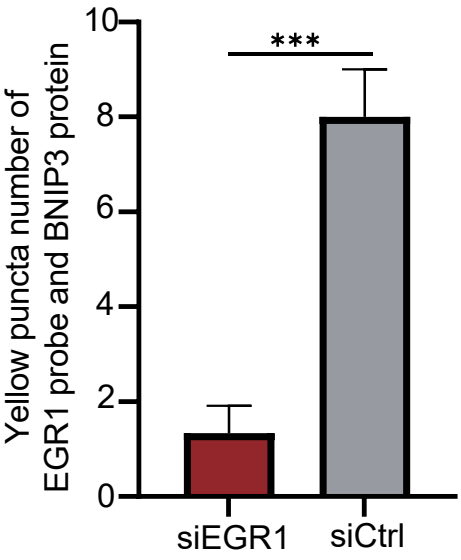
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A**B****C****D****E**

A



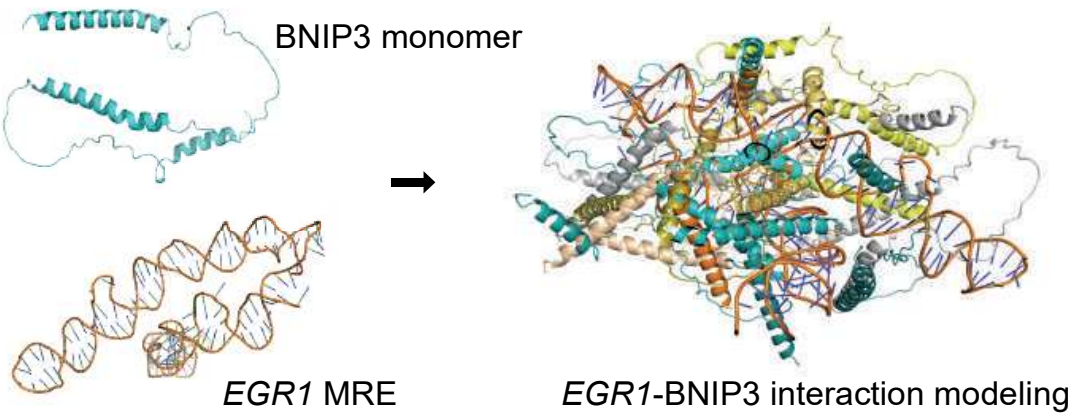
B



A

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70 80 90 100 110 120
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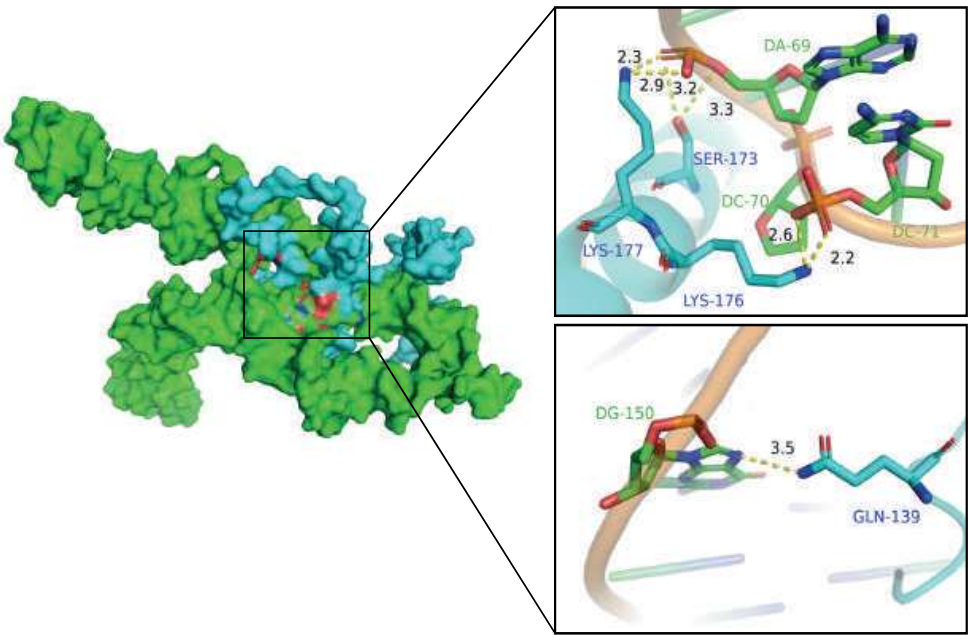
B



C

Models	Model-1	Model-2	Model-3	Model-4	Model-5	Model-6	Model-7	Model-8	Model-9	Model-10
Score	-372.36	-369.97	-362.06	-354.06	-351.48	-349.66	-332.1	-325.39	-323.06	-322.64
RMSD	159.6	178.48	176.43	169.82	155.53	158.78	168.11	164.72	135.64	159.13

D



A

102030405060

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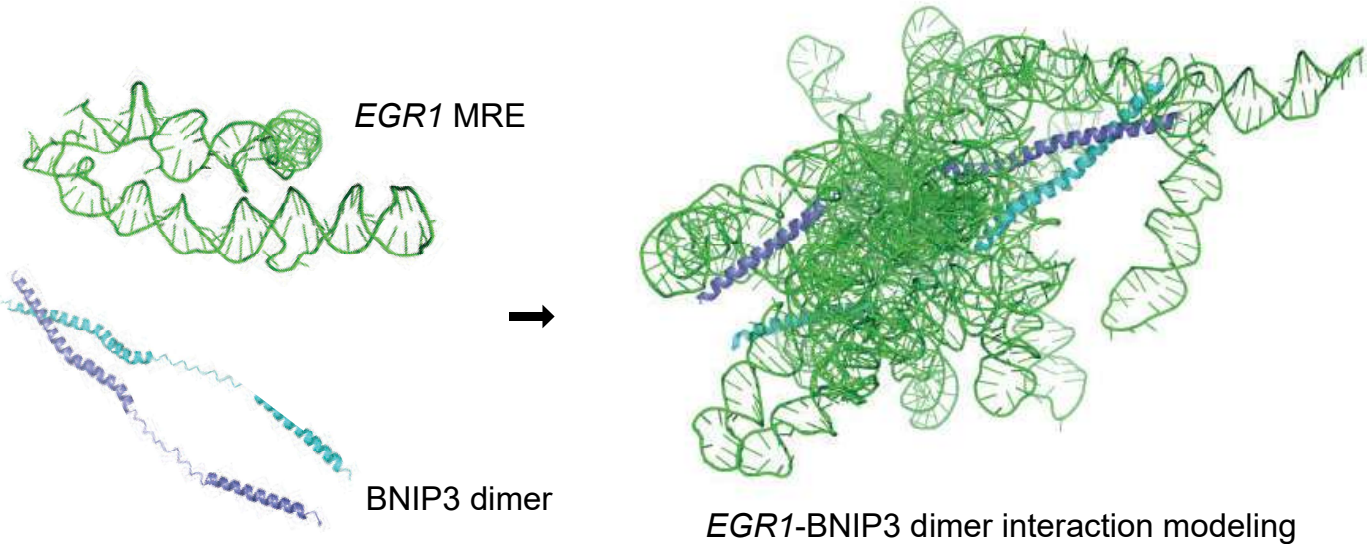
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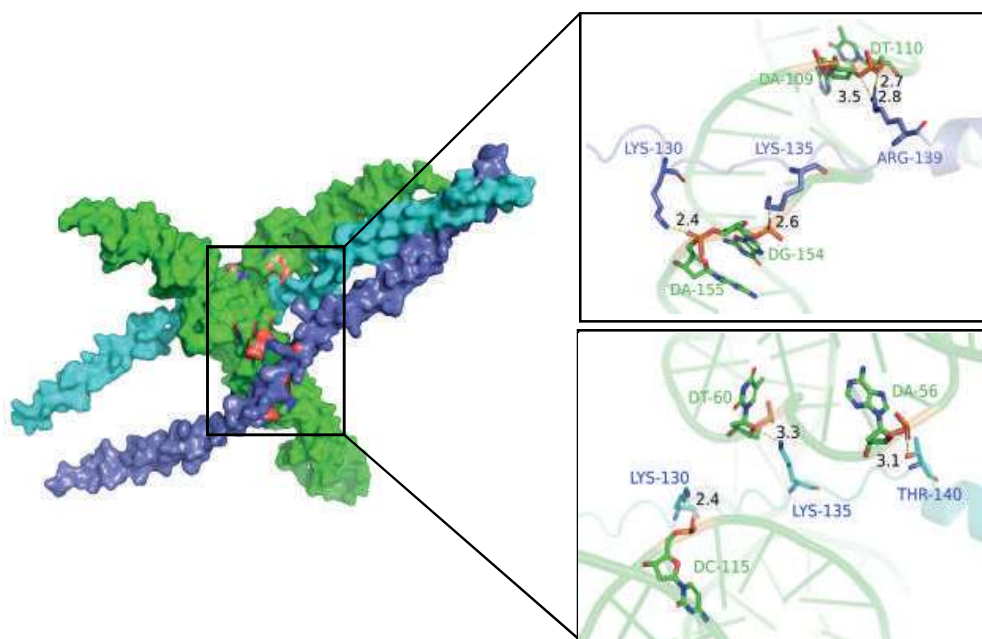
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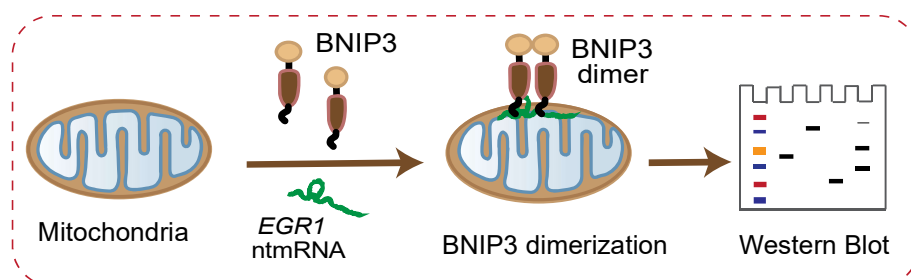
C

Models	Model-1	Model-2	Model-3	Model-4	Model-5	Model-6	Model-7	Model-8	Model-9	Model-10
Score	-423.95	-403.4	-402.16	-390.79	-385.84	-380.6	-376.24	-370.66	-367.68	-364.99
RMSD	180.08	196.26	165.55	169.26	171.77	186.5	167.92	165.82	184.55	163.48

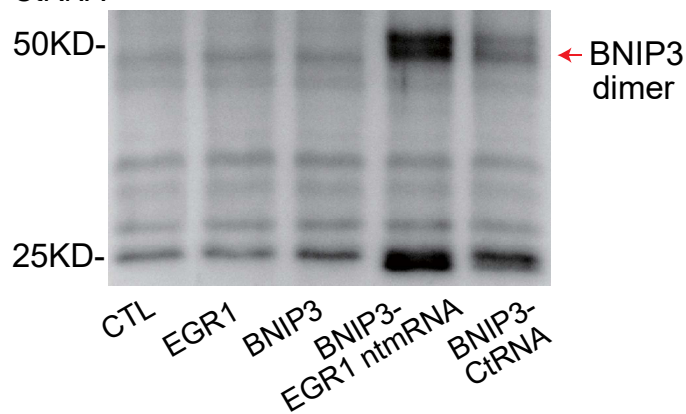
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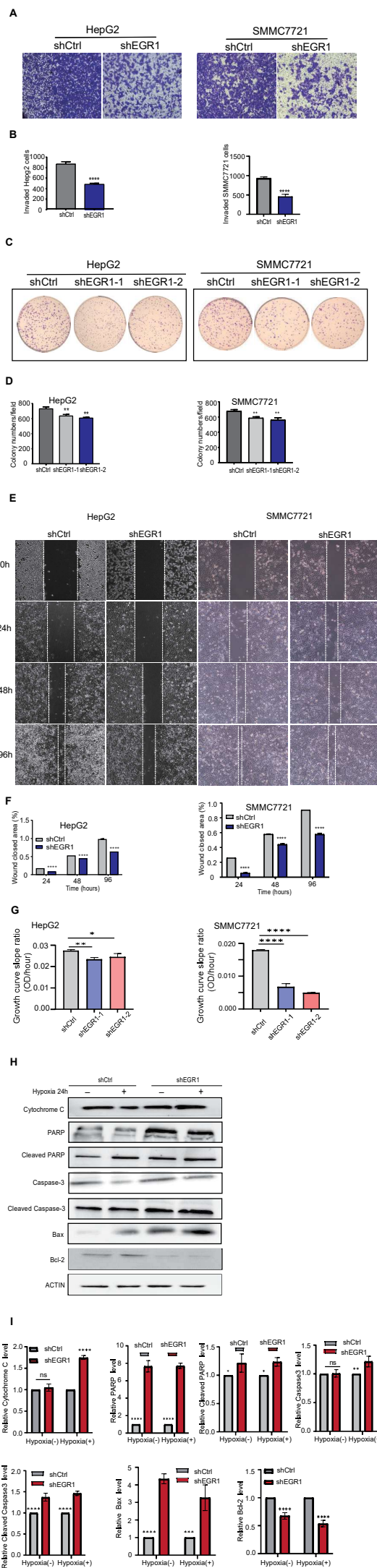


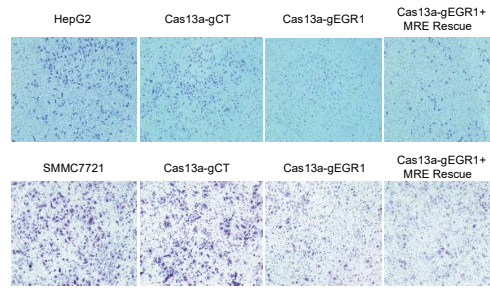
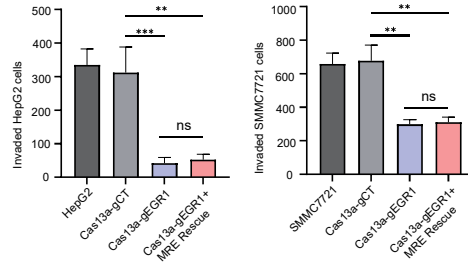
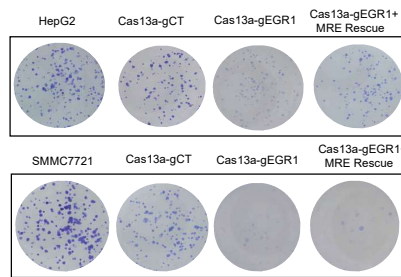
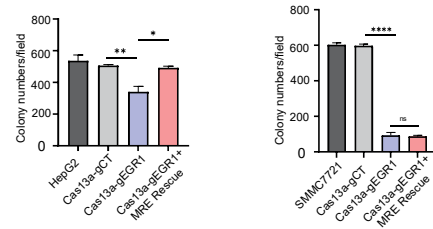
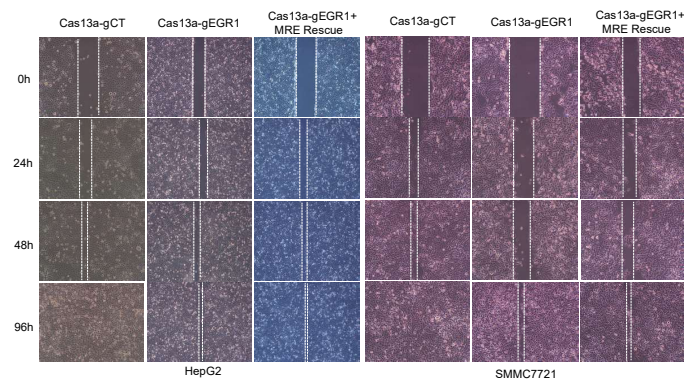
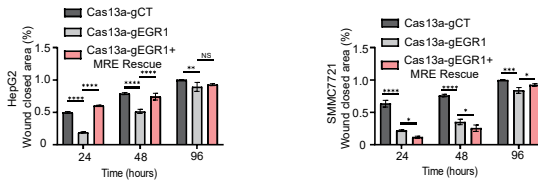
B



Mitochondria	+	+	+	+	+
BNIP3	-	-	+	+	+
<i>EGR1</i> ntmRNA	-	+	-	+	-
CtRNA	-	-	-	-	+





A**B****C****D****E****F****G**