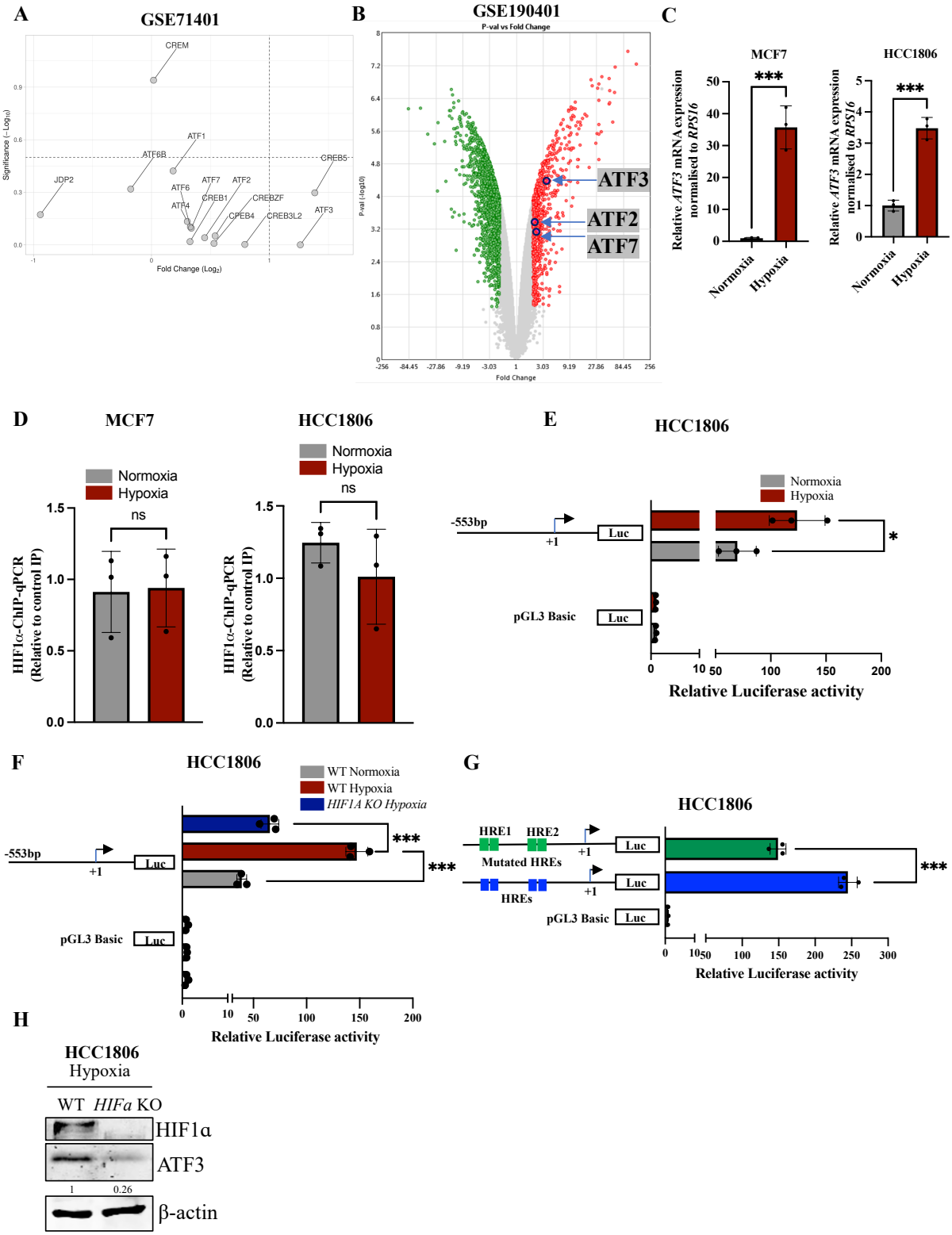
Supplementary Figures



I

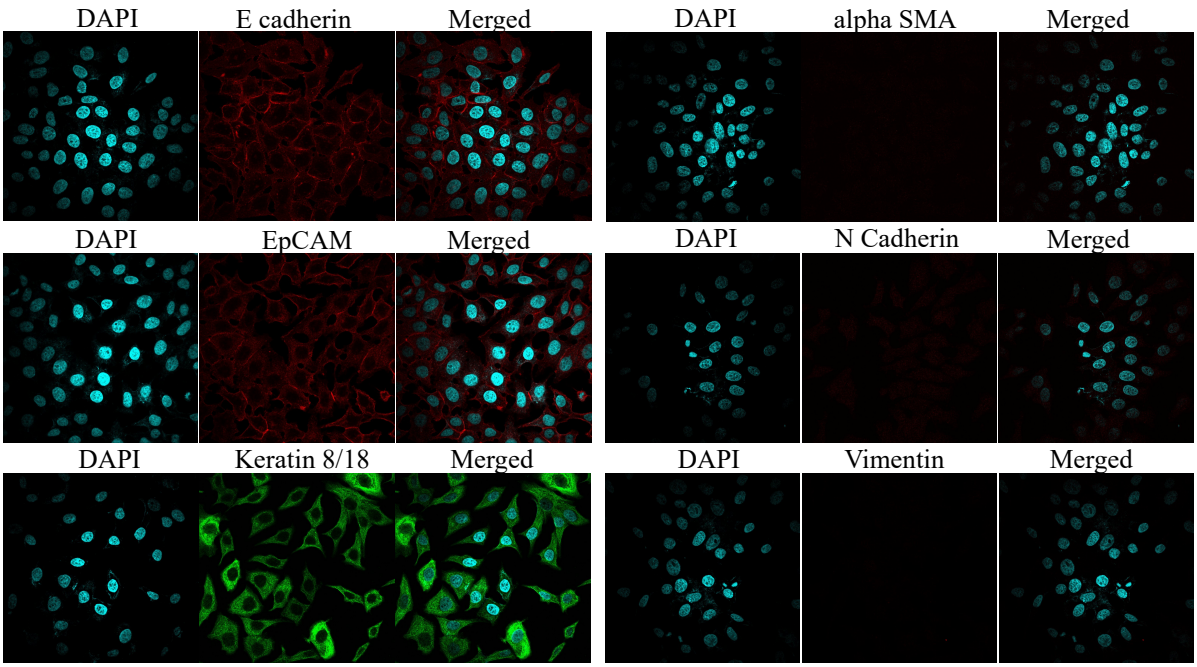
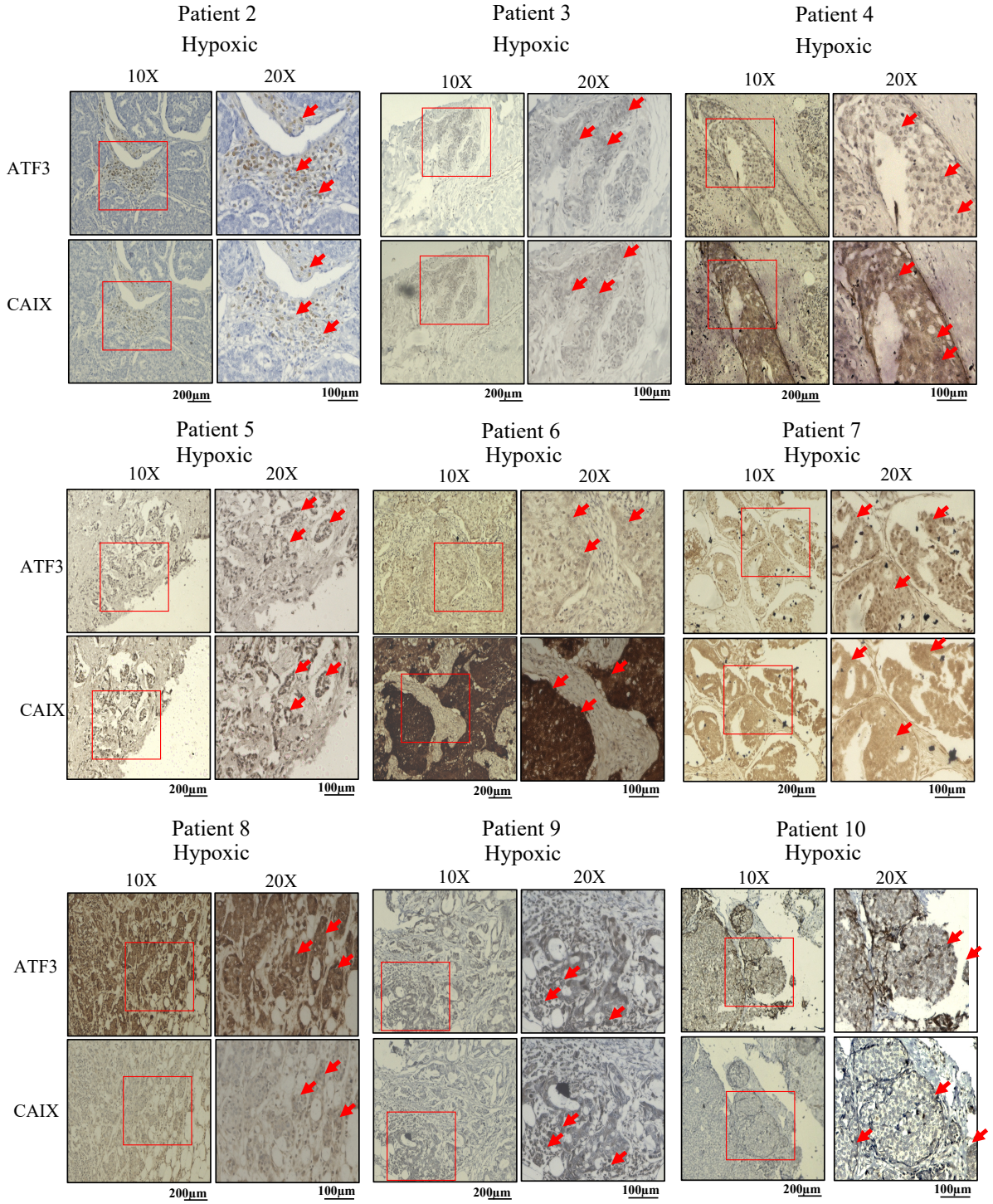


Figure S1. Regulation of ATF3 induction in hypoxic breast cancer cells via HIF1α. A) Heat map representation of ATF/CREB family members from a Normoxia Vs Hypoxia RNA seq data analysis (GSE71401) **B)** Volcano Plot from HTA 2.0 microarray data analysis (GSE190401) showing expression of ATFs, ATF3 is seen to be most significantly induced under hypoxia **C)** qPCR analysis for ATF3 showing induction in hypoxia in MCF7 and HCC1806 cells **D)** HIF1α-ChIP-qPCR showing no significant difference in the occupancy of HIF1α at a region 10kb upstream of TSS in VEGFA promoter in MCF7 and HCC1806 cells **E)** Luciferase promoter assay for *ATF3* promoter in HCC1806 cells **F)** Luciferase promoter assay for *ATF3* promoter showing decreased activity in *HIF1A* knockout HCC1806 cells (one-way ANOVA) **G)** Luciferase promoter assay comparing wild type pGL3_*ATF3*pro to mutant pGL3_*ATF3*pro luciferase activity in HCC1806 cells (one-way ANOVA) **H)** Immunoblot depicting decreased expression of ATF3 in *HIF1A* knockout HCC1806 cells **I)** Characterization of BC8322E patient derived cell line by immunostaining for E cadherin,

EpCAM, Keratin 8/18 (epithelial markers); N cadherin, Vimentin (mesenchymal markers) and alpha SMA (fibroblast marker). Error bars show mean values ± SD (n=3, unless otherwise specified) as calculated using two-tailed Student's t-test, unless otherwise specified, *$P \leq 0.05$, **$P \leq 0.01$, ***$P \leq 0.001$, ns = not significant.



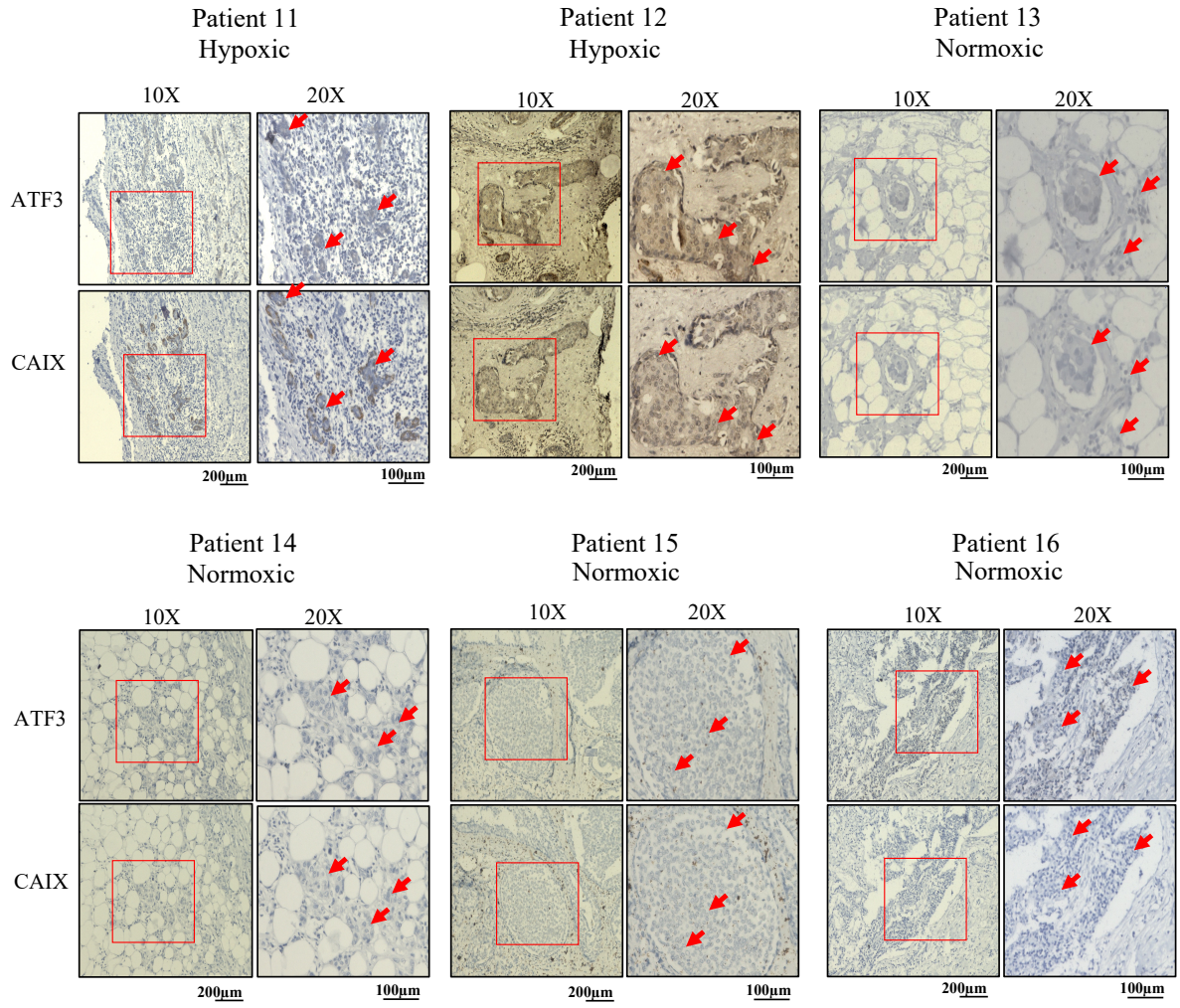


Figure S2. Immunohistochemistry for ATF3 and CAIX in breast cancer patient tissue samples (scale bars, 10×, 200 μm; 20×, 100 μm)

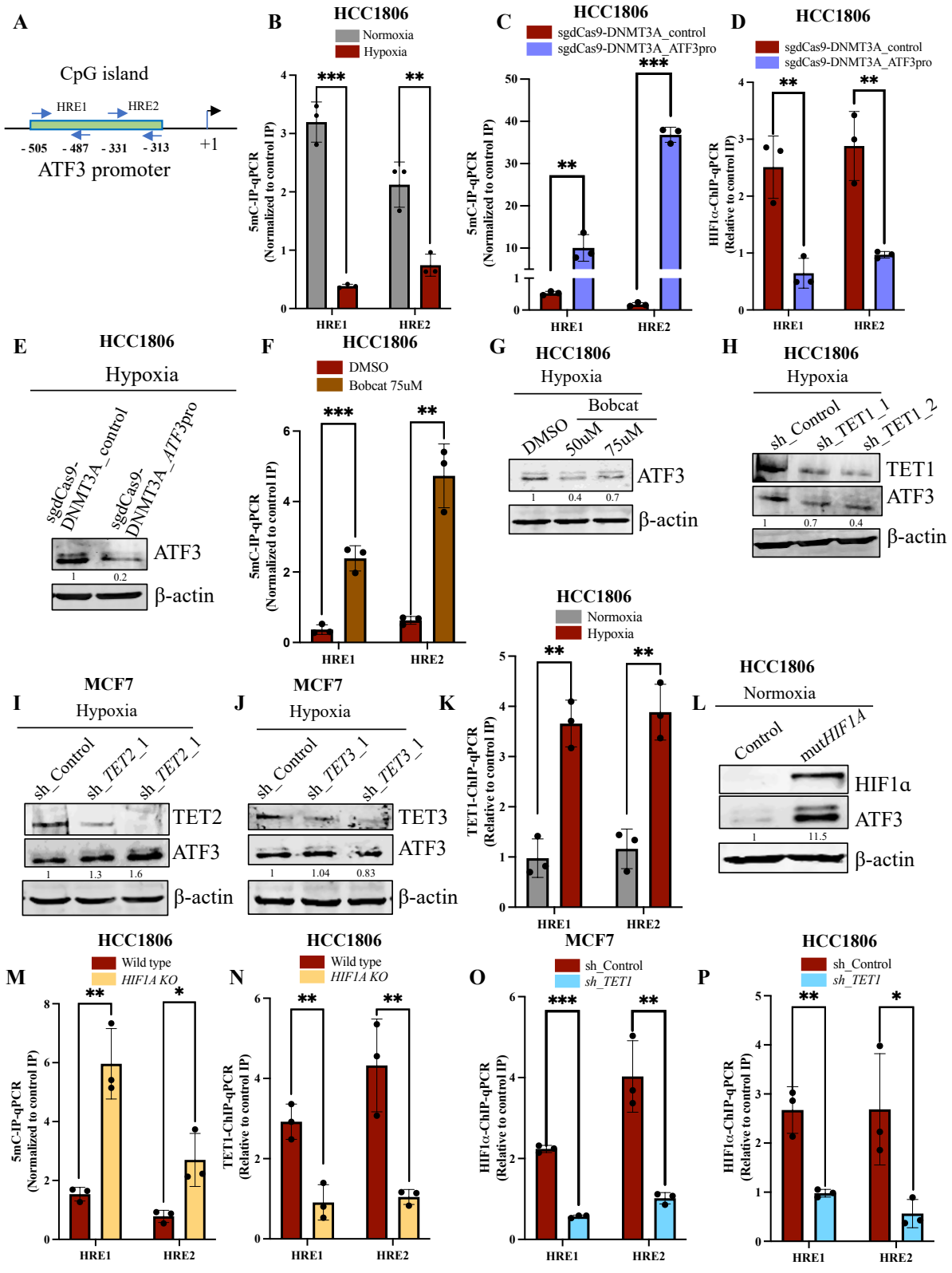
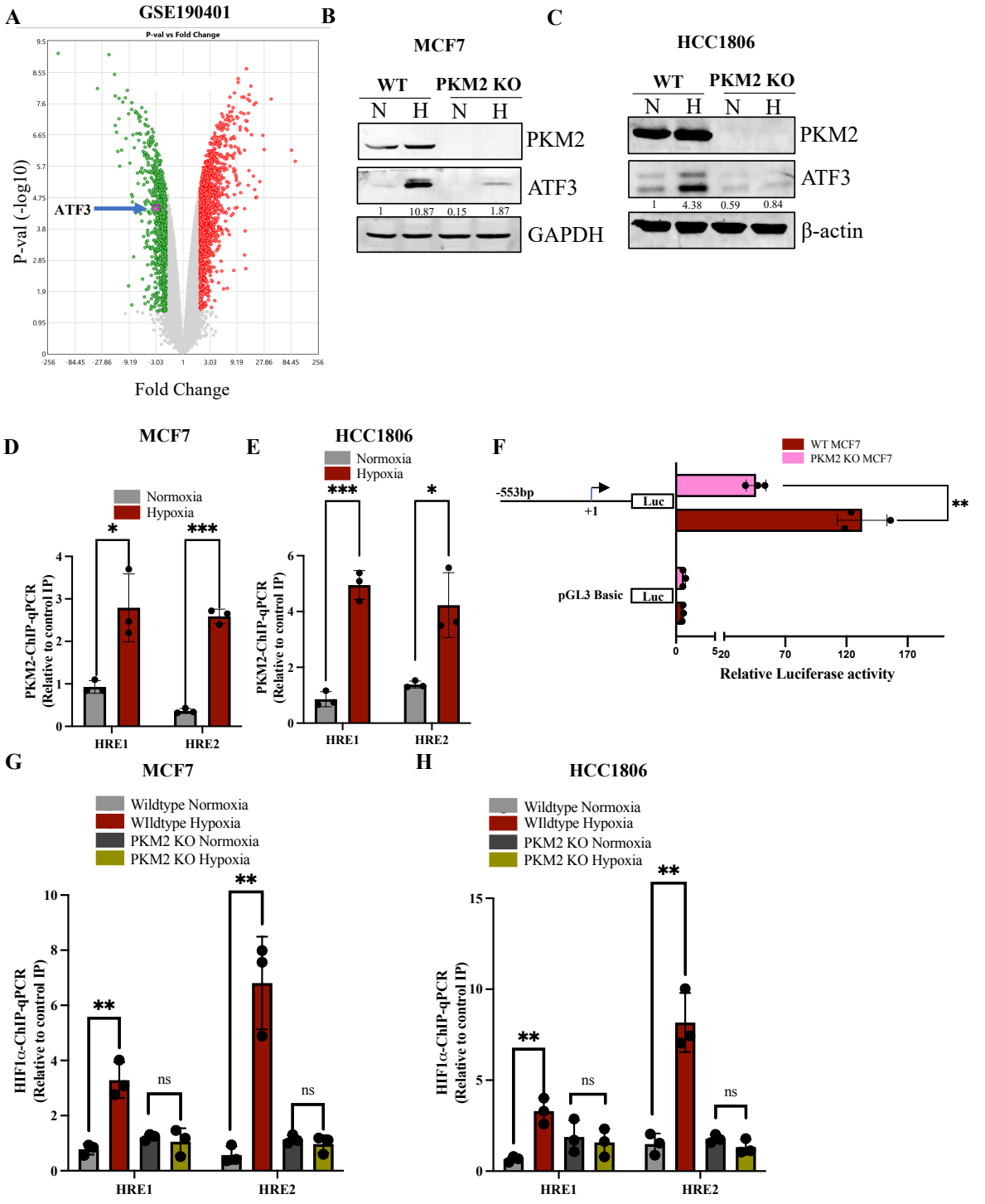


Figure S3. Epigenetic basis of regulation of *ATF3* transcription under hypoxia. A) Schematic representing the dense CpG island at the ATF3 promoter along with the positions of the primers used to study the two HREs **B)** MeDIP-qPCR showing decreased methylation

at the *ATF3* promoter under hypoxia in HCC1806 cells **C)** MeDIP-qPCR showing increased methylation at *ATF3* promoter in sgdCas9-DNMT3A_ATFpro transfected HCC1806 cells under hypoxia **D)** HIF1α-ChIP-qPCR depicting decreased occupancy of HIF1α at the *ATF3* promoter in sgdCas9-DNMT3A_ATFpro transfected HCC1806 cells compared to the sgdCas9-DNMT3A_control transfected control HCC1806 cells under hypoxia **E)** Immunoblot comparing ATF3 expression in sgdCas9-DNMT3A_ATFpro transfected HCC1806 cells and sgdCas9-DNMT3A_control transfected HCC1806 cells under hypoxia **F)** MeDIP-qPCR showing increased methylation at *ATF3* promoter after Bobcat treatment in HCC1806 cells under hypoxic condition **G)** Immunoblot for ATF3 expression after Bobcat treatment revealing decreased expression of ATF3 after treatment in HCC1806 cells **H)** Immunoblot showing decreased expression of ATF3 in *TET1* knockdown HCC1806 cells under hypoxic condition **I)** Immunoblot showing expression of ATF3 in TET2 knock down cells and **J)** TET3 knock down cells **K)** TET1-ChIP-qPCR showing increased occupancy of TET1 at *ATF3* promoter in HCC1806 cells under hypoxia **L)** Immunoblot for comparing ATF3 expression in control and mut *HIF1A* transfected HCC1806 cells under normoxic condition **M)** MeDIP-qPCR showing increased methylation at *ATF3* promoter in *HIF1A* knockout HCC1806 cells under hypoxic condition **N)** TET1-ChIP-qPCR showing decreased occupancy of TET1 at *ATF3* promoter in *HIF1A* knockout HCC1806 cells under hypoxic condition **O)** HIF1α-ChIP-qPCR showing decreased occupancy of HIF1α at *ATF3* promoter in *TET1* knockdown MCF7 cells and **P)** HCC1806 cells. Error bars show mean values $\pm$ SD (n=3, unless otherwise specified) as calculated using two-tailed Student's t-test, unless otherwise specified, *$P \leq 0.05$, **$P \leq 0.01$, ***$P \leq 0.001$, ns = not significant.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GSE190401
P-val vs Fold Change
ATF3
P-val (-log10)
Fold Change
B
MCF7
WT
PKM2 KO
N
H
N
H
PKM2
ATF3
1
10.87
0.15
1.87
GAPDH
C
HCC1806
WT
PKM2 KO
N
H
N
H
PKM2
ATF3
1
4.38
0.59
0.84
β-actin
D
MCF7
Normoxia
Hypoxia
PKM2-ChIP-qPCR (Relative to control IP)
HRE1
HRE2
E
HCC1806
Normoxia
Hypoxia
PKM2-ChIP-qPCR (Relative to control IP)
HRE1
HRE2
F
WT MCF7
PKM2 KO MCF7
-553bp
+1
Luc
pGL3 Basic
Luc
Relative Luciferase activity
G
MCF7
Wildtype Normoxia
WIldtype Hypoxia
PKM2 KO Normoxia
PKM2 KO Hypoxia
HIF1α-ChIP-qPCR (Relative to control IP)
ns
HRE1
HRE2
H
HCC1806
Wildtype Normoxia
WIldtype Hypoxia
PKM2 KO Normoxia
PKM2 KO Hypoxia
HIF1α-ChIP-qPCR (Relative to control IP)
ns
HRE1
HRE2

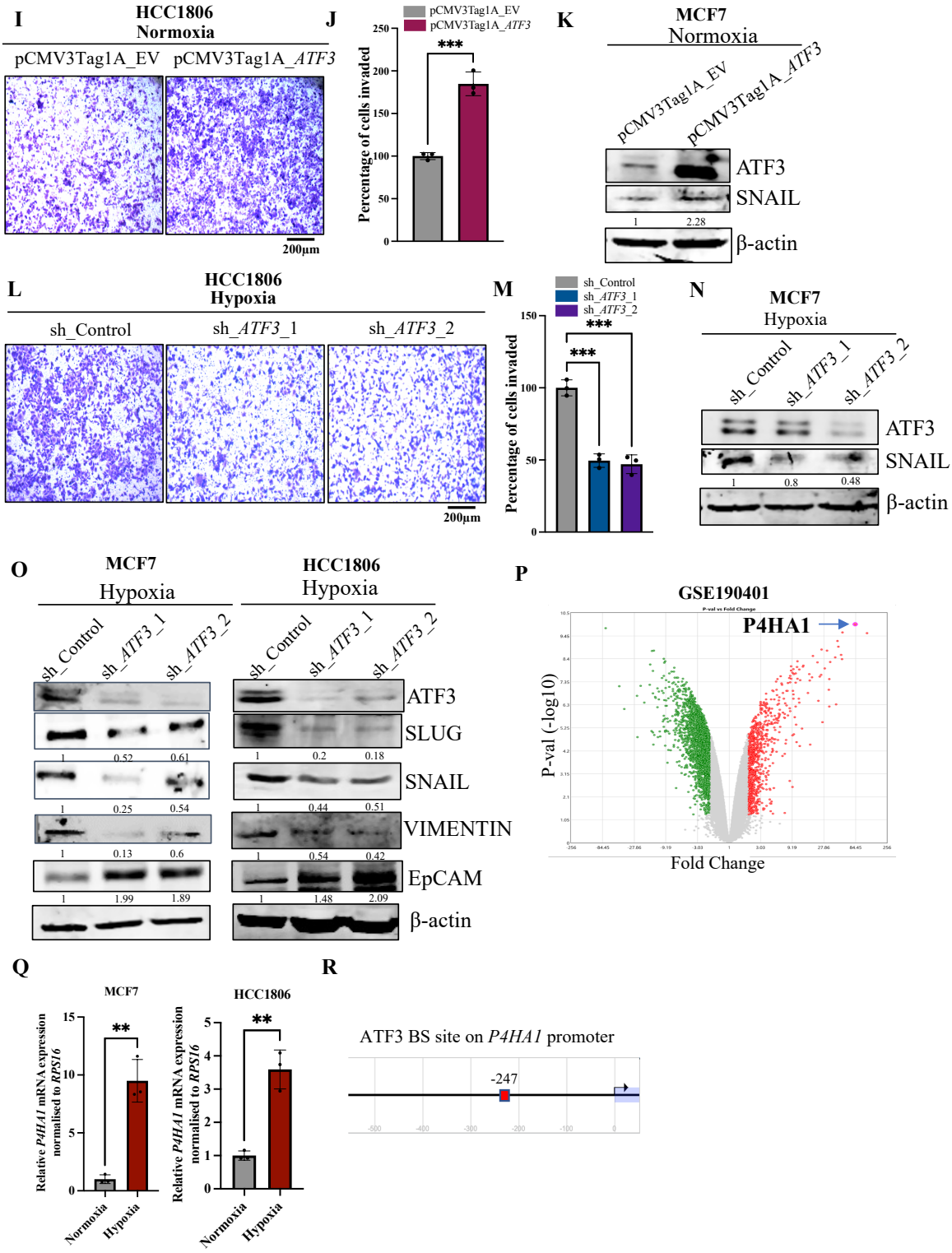
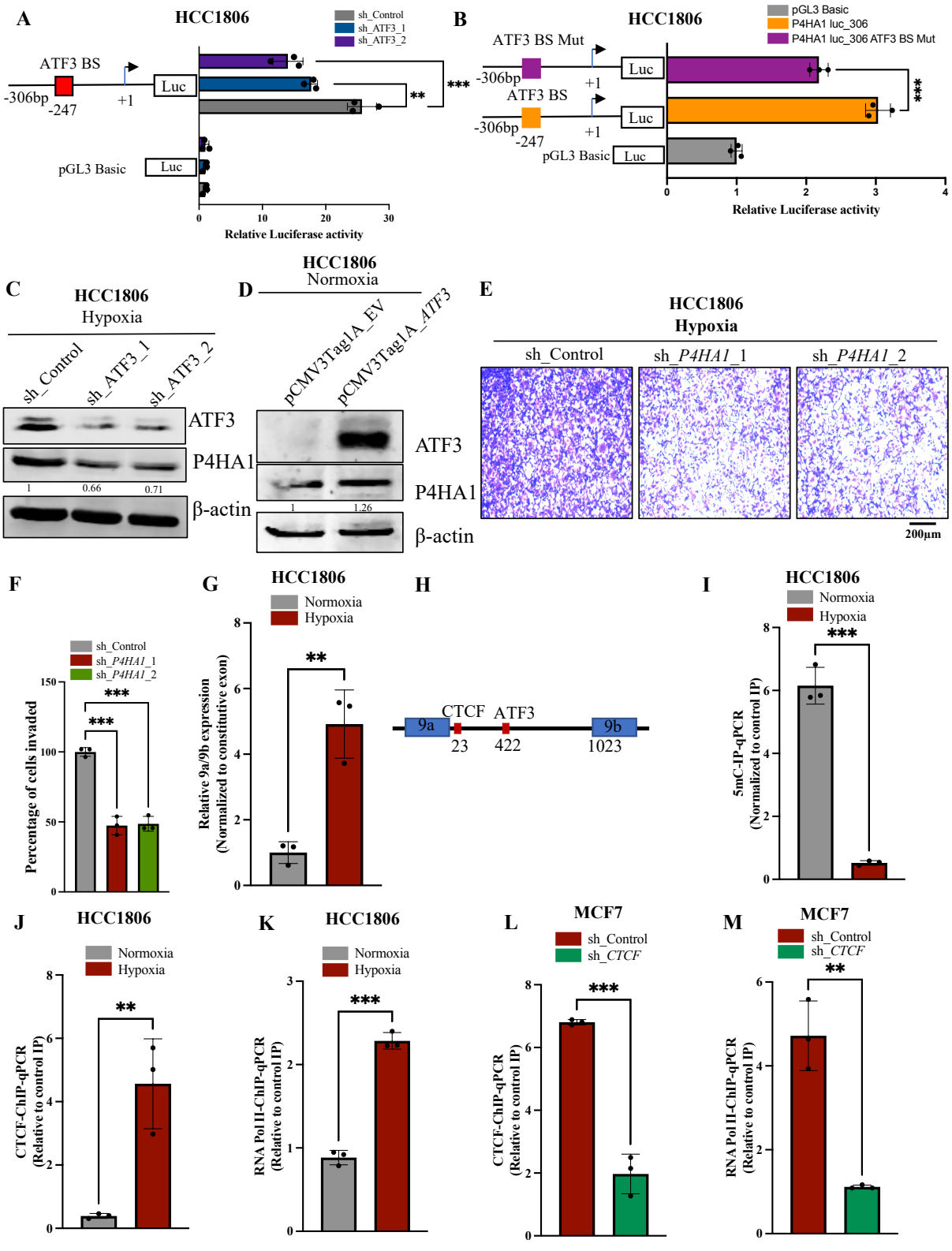


Figure S4. Role of PKM2 in regulation of *ATF3* transcription under hypoxia and enhancement of invasive potential of hypoxic breast cancer cells by ATF3 via induction of P4HA1. A) Volcano Plot from HTA 2.0 microarray data analysis (GSE190401) showing

decreased expression of ATF3 in *PKM2* knockout MCF7 cells under hypoxia **B)** Immunoblot showing expression of ATF3 in wild type and *PKM2* knockout MCF7 cells and **C)** HCC1806 cells **D)** PKM2-ChIP-qPCR showing increased occupancy of PKM2 at *ATF3* promoter in MCF7 cells and **E)** HCC1806 cells **F)** Luciferase promoter assay for *ATF3* promoter showing decreased activity in *PKM2* knockout MCF7 cells **G)** HIF1α-ChIP-qPCR showing increased occupancy of HIF1α at *ATF3* promoter in wildtype MCF7 cells and no significant difference in HIF1α occupancy in *PKM2* knockout MCF7 cells **H)** HIF1α-ChIP-qPCR showing increased occupancy of HIF1α at *ATF3* promoter in wildtype HCC1806 cells and no significant difference in HIF1α occupancy in *PKM2* knockout HCC1806 cells **I)** Invasion assay and **J)** its quantification in control and *ATF3* overexpressing HCC1806 cells **K)** Immunoblot showing increased expression of SNAIL in *ATF3* overexpressing MCF7 cells under normoxia **L)** Invasion assay and **M)** its quantification in control and *ATF3* knockdown (two hairpins used) HCC1806 cells (one-way ANOVA) **N)** Immunoblot showing decreased expression of SNAIL in *ATF3* knockdown MCF7 cells **O)** Immunoblot showing decreased expression of SLUG, SNAIL, Vimentin and increased expression EpCAM in *ATF3* knockdown MCF7 and HCC1806 cells **P)** Volcano Plot from HTA 2.0 microarray data analysis showing expression of P4HA1 to be most significantly induced under hypoxia (GSE190401) **Q)** qPCR analysis for P4HA1 expression in normoxic and hypoxic MCF7 and HCC1806 cells **R)** Schematic representation of ATF3 binding site on *P4HA1*promoter from Eukaryotic Promoter Database. Error bars show mean values $\pm$ SD (n=3, unless otherwise specified) as calculated using two-tailed Student's t-test, unless otherwise specified, *$P \leq 0.05$, **$P \leq 0.01$, ***$P \leq 0.001$, ns = not significant.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HCC1806
sh_Control
sh_ATF3_1
sh_ATF3_2
ATF3 BS
-306bp
-247
+1
Luc
pGL3 Basic
Relative Luciferase activity
B
HCC1806
pGL3 Basic
P4HA1 luc_306
P4HA1 luc_306 ATF3 BS Mut
ATF3 BS Mut
Relative Luciferase activity
C
HCC1806
Hypoxia
sh_Control
sh_ATF3_1
sh_ATF3_2
ATF3
P4HA1
β-actin
D
HCC1806
Normoxia
pCMV3Tag1A_EV
pCMV3Tag1A_ATF3
E
HCC1806
Hypoxia
sh_Control
sh_P4HA1_1
sh_P4HA1_2
200μm
F
Percentage of cells invaded
G
HCC1806
Normoxia
Hypoxia
Relative 9a/9b expression (Normalized to constitutive exon)
H
CTCF
ATF3
9a
9b
23
422
1023
I
HCC1806
5mC-IP-qPCR (Normalized to control IP)
J
HCC1806
CTCF-ChIP-qPCR (Relative to control IP)
K
HCC1806
RNA Pol II-ChIP-qPCR (Relative to control IP)
L
MCF7
sh_Control
sh_CTCF
CTCF-ChIP-qPCR (Relative to control IP)
M
MCF7
RNA Pol II-ChIP-qPCR (Relative to control IP)

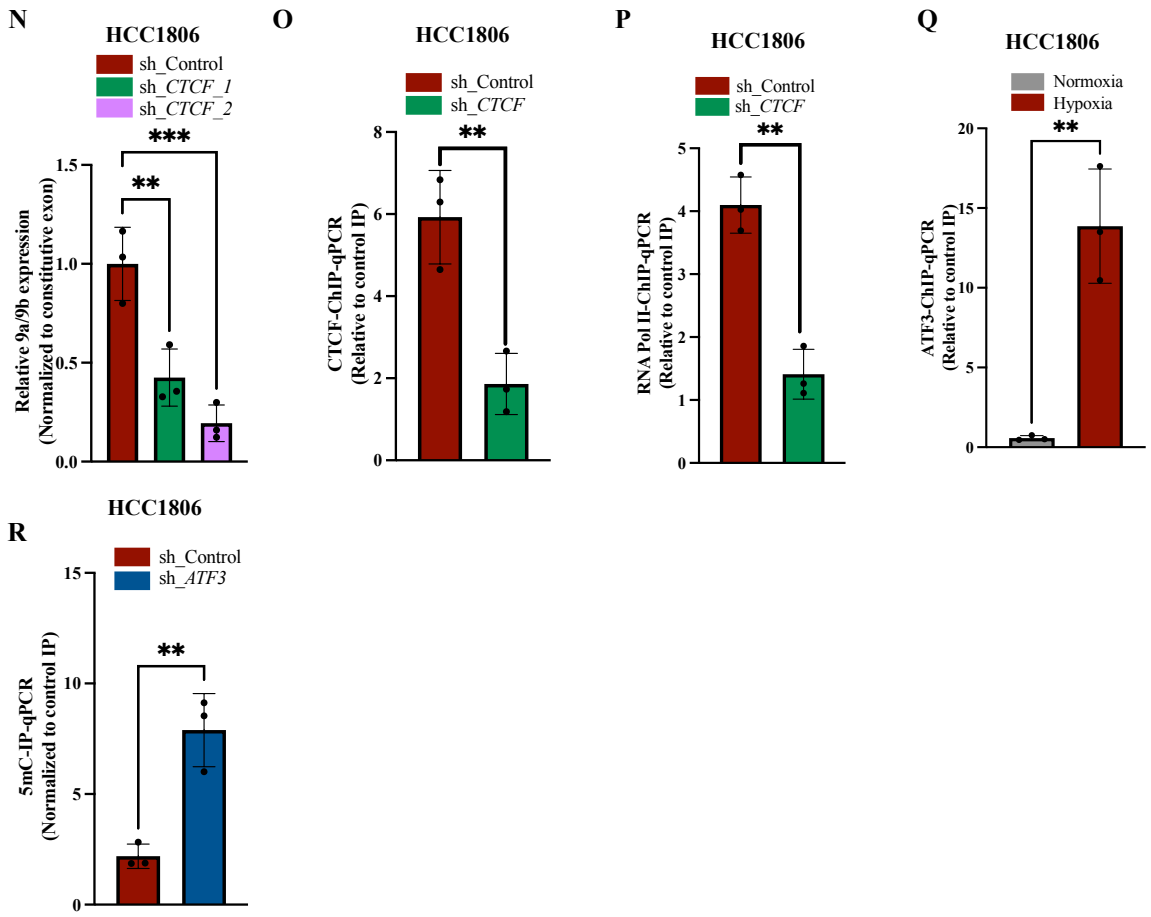
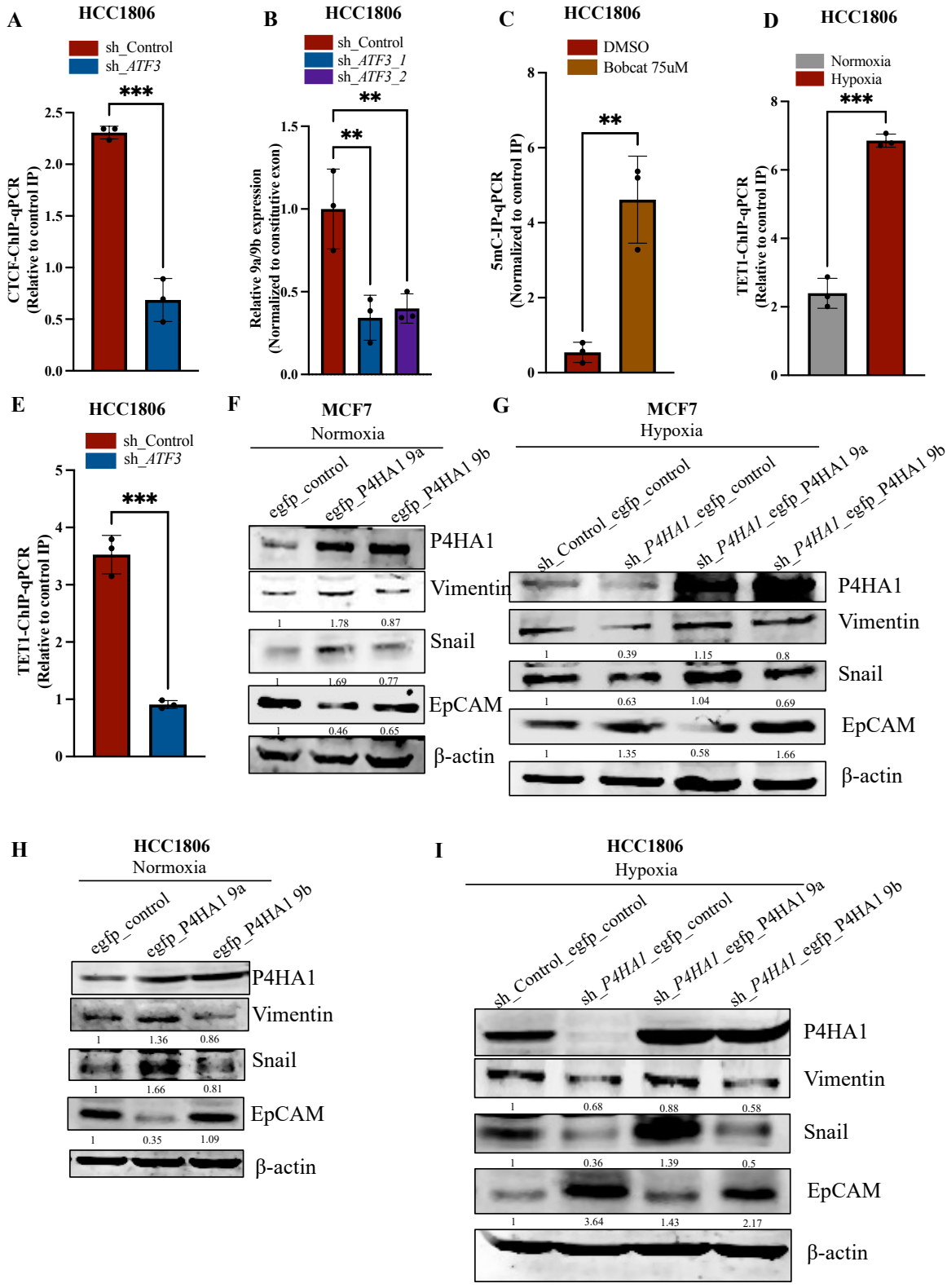


Figure S5. Role of ATF3 in P4HA1 induction under hypoxia and mechanism of *P4HA1* splicing under hypoxic condition. A) Luciferase promoter assay for *P4HA1* promoter showing decreased activity in *ATF3* knockdown HCC1806 cells (one-way ANOVA) **B)** Luciferase promoter assay comparing wild type pGL3_*P4HA1*pro to mutant pGL3_*P4HA1*pro luciferase activity in HCC1806 cells (one-way ANOVA) **C)** Immunoblot showing decreased expression of P4HA1 in *ATF3* knockdown HCC1806 cells **D)** Immunoblot showing increased expression of P4HA1 in *ATF3* overexpressing HCC1806 cells **E)** Invasion assay and **F)** its quantification in control and *P4HA1* knockdown (two hairpins used) HCC1806 cells (one-way ANOVA) **G)** qPCR analysis showing increased 9a/9b ratio in hypoxic conditions in HCC1806 cells **H)** Schematic showing positions of CTCF and ATF3 binding sites at intron9a as obtained from JASPAR **I)** MeDIP-qPCR depicting decreased methylation at the intron9a under hypoxia in HCC1806 cells **J)** CTCF-ChIP-qPCR showing increased occupancy of CTCF at intron9a in

hypoxic HCC1806 cells **K)** RNA PolII-ChIP-qPCR showing increased occupancy of RNA PolII at intron9a in hypoxic HCC1806 cells **L)** CTCF-ChIP-qPCR showing decreased occupancy of CTCF at intron9a in hypoxic *CTCF* knockdown MCF7 cells **M)** RNA PolII-ChIP-qPCR showing decreased occupancy of RNA PolII at intron9a in hypoxic *CTCF* knockdown MCF7 cells **N)** qPCR analysis showing decreased 9a/9b ratio in hypoxic *CTCF* knockdown HCC1806 cells **O)** CTCF-ChIP-qPCR showing decreased occupancy of CTCF at intron9a in hypoxic *CTCF* knockdown HCC1806 cells **P)** RNA PolII-ChIP-qPCR showing decreased occupancy of RNA PolII at intron9a in hypoxic *CTCF* knockdown HCC1806 cells **Q)** ATF3-ChIP-qPCR showing increased occupancy of ATF3 at intron9a in hypoxic HCC1806 cells **R)** MeDIP-qPCR depicting increased methylation at the intron9a under hypoxia in *ATF3* knockdown HCC1806 cells. Error bars show mean values $\pm$ SD (n=3, unless otherwise specified) as calculated using two-tailed Student's t-test, unless otherwise specified, *$P \leq 0.05$, **$P \leq 0.01$, ***$P \leq 0.001$, ns = not significant.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sh_ATF3
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CTCF-ChIP-qPCR (Relative to control IP)
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sh_ATF3_1
sh_ATF3_2
**
**
Relative 9a/9b expression (Normalized to constitutive exon)
C
HCC1806
DMSO
Bobcat 75uM
**
5mC-IP-qPCR (Normalized to control IP)
D
HCC1806
Normoxia
Hypoxia
***
TET1-ChIP-qPCR (Relative to control IP)
E
HCC1806
sh_Control
sh_ATF3
***
TET1-ChIP-qPCR (Relative to control IP)
F
MCF7
Normoxia
egfp_control
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egfp_P4HA1 9b
P4HA1
Vimentin
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Snail
1 1.69 0.77
EpCAM
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β-actin
G
MCF7
Hypoxia
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sh_P4HA1_egfp_control
sh_P4HA1_egfp_P4HA1 9a
sh_P4HA1_egfp_P4HA1 9b
P4HA1
Vimentin
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Snail
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EpCAM
1 1.35 0.58 1.66
β-actin
H
HCC1806
Normoxia
egfp_control
egfp_P4HA1 9a
egfp_P4HA1 9b
P4HA1
Vimentin
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Snail
1 1.66 0.81
EpCAM
1 0.35 1.09
β-actin
I
HCC1806
Hypoxia
sh_Control_egfp_control
sh_P4HA1_egfp_control
sh_P4HA1_egfp_P4HA1 9a
sh_P4HA1_egfp_P4HA1 9b
P4HA1
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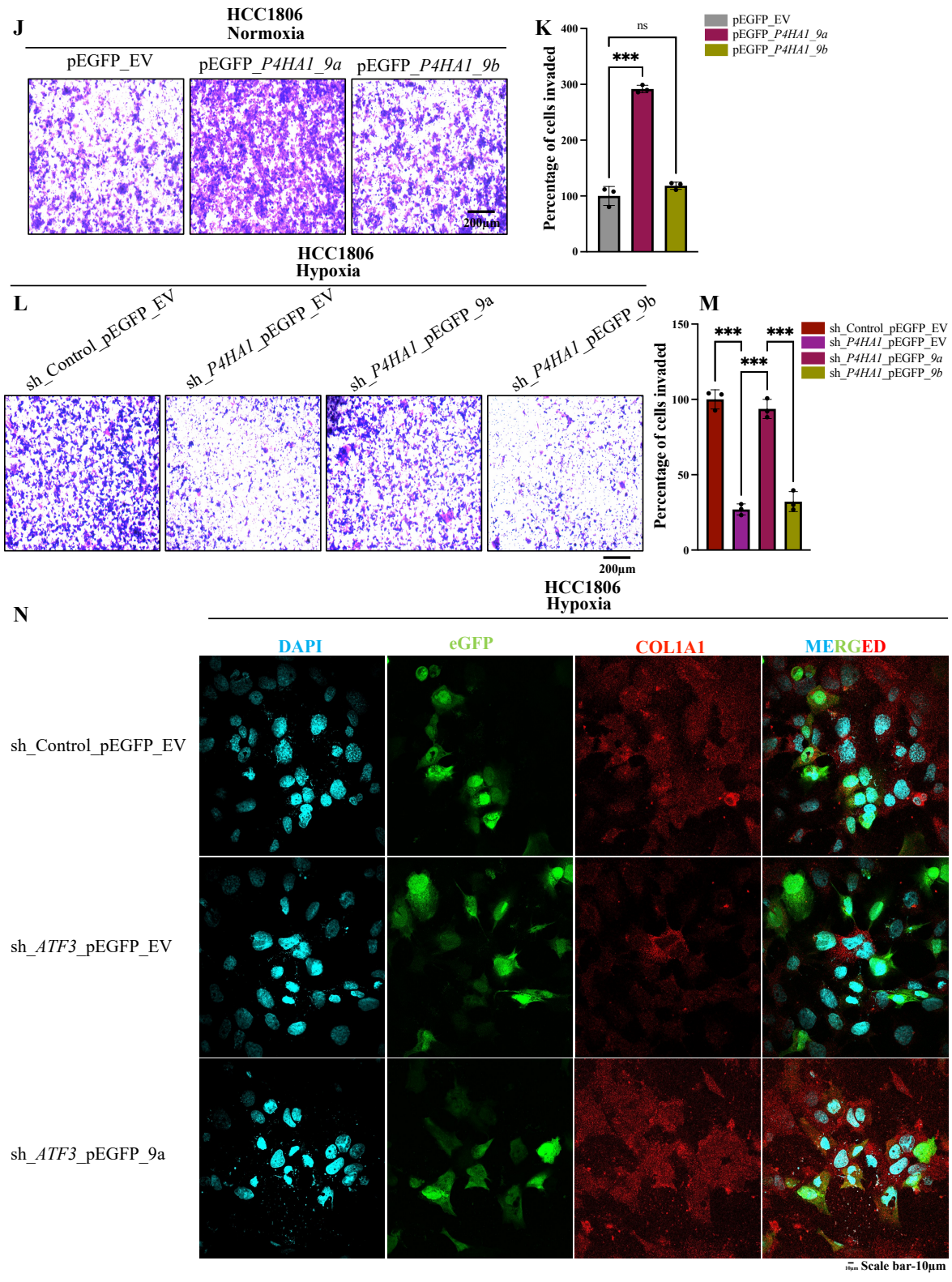
β-actin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Normoxia
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pEGFP_P4HA1_9a
pEGFP_P4HA1_9b
200μm
K
Percentage of cells invaded
ns
***
pEGFP_EV
pEGFP_P4HA1_9a
pEGFP_P4HA1_9b
HCC1806
Hypoxia
L
sh_Control_pEGFP_EV
sh_P4HA1_pEGFP_EV
sh_P4HA1_pEGFP_9a
sh_P4HA1_pEGFP_9b
200μm
M
Percentage of cells invaded
***
***
***
sh_Control_pEGFP_EV
sh_P4HA1_pEGFP_EV
sh_P4HA1_pEGFP_9a
sh_P4HA1_pEGFP_9b
HCC1806
Hypoxia
N
DAPI
eGFP
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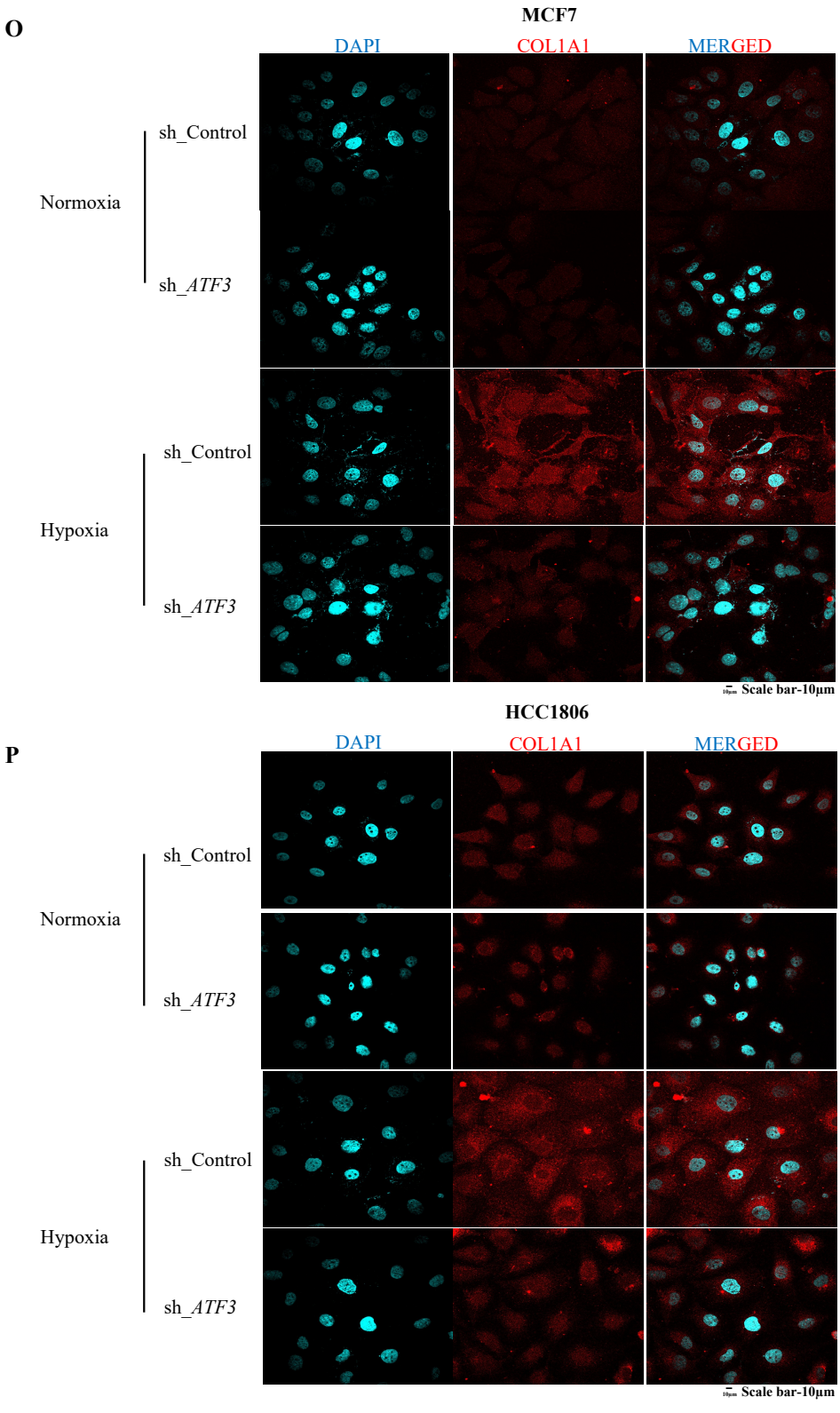
sh_ATF3_pEGFP_EV
sh_ATF3_pEGFP_9a
Scale bar-10μm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MCF7
DAPI
COL1A1
MERGED
Normoxia
sh_Control
sh_ATF3
Hypoxia
sh_Control
sh_ATF3
Scale bar-10μm
P
HCC1806
DAPI
COL1A1
MERGED
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sh_ATF3
Hypoxia
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Scale bar-10μm

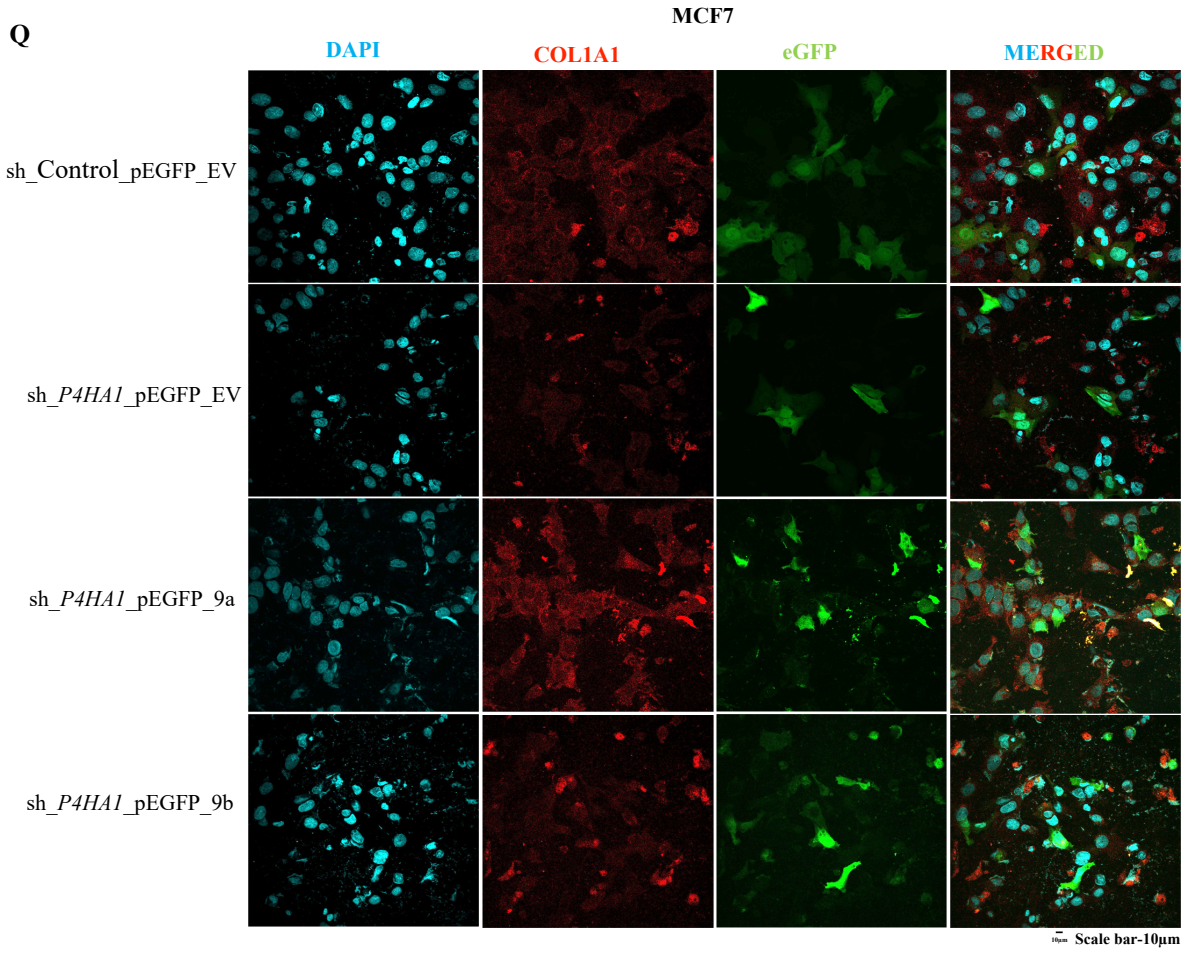
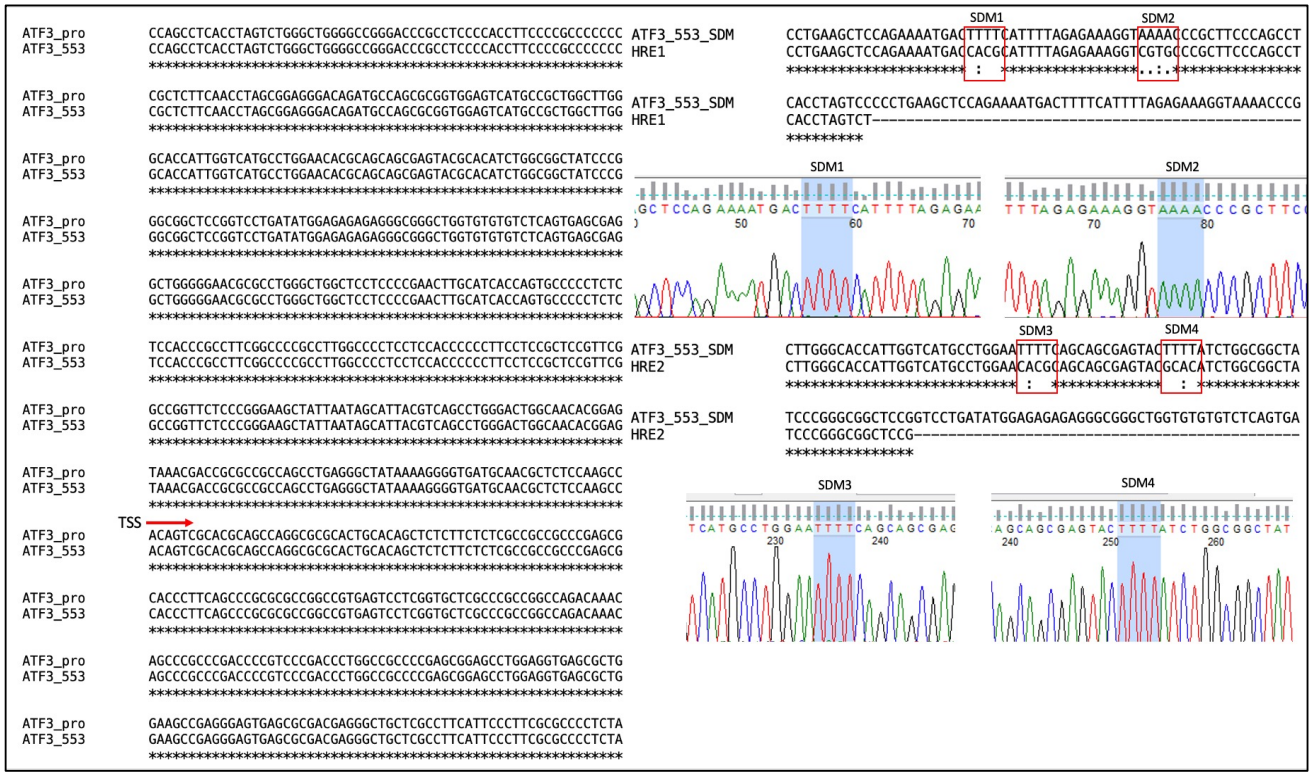


Figure S6. Mechanism of *P4HA1* splicing under hypoxic condition and functional roles of *P4HA1* isoforms in Collagen deposition. A) CTCF-ChIP-qPCR showing decreased occupancy of CTCF at intron9a in hypoxic *ATF3* knockdown HCC1806 cells **B)** qPCR analysis showing decreased 9a/9b ratio in hypoxic *ATF3* knockdown HCC1806 cells **C)** MeDIP-qPCR showing increased methylation at the intron9a upon Bobcat treatment in hypoxic HCC1806 cells **D)** TET1-ChIP-qPCR showing increased occupancy of TET1 at intron9a in hypoxic HCC1806 cells **E)** TET1-ChIP-qPCR showing decreased occupancy of TET1 at intron9a in hypoxic *ATF3* knockdown HCC1806 cells **F)** Immunoblot showing expression of Vimentin, SNAIL and EpCAM in MCF7 cells overexpressing *P4HA1* 9a or 9b isoform as compared to the control cells in normoxic conditions **G)** Immunoblot showing expression of Vimentin, SNAIL and EpCAM in *P4HA1* knockdown MCF7 cells overexpressing *P4HA1* 9a or 9b isoform as compared to the control *P4HA1* knockdown cells as well as the control cells

transfected with a non-targeting shRNA in hypoxic conditions **H)** Immunoblot showing expression of Vimentin, SNAIL and EpCAM in HCC1806 cells overexpressing *P4HA1* 9a or 9b isoform as compared to the control cells in normoxic conditions **I)** Immunoblot showing expression of Vimentin, SNAIL and EpCAM in *P4HA1* knockdown HCC1806 cells overexpressing *P4HA1* 9a or 9b isoform as compared to the control *P4HA1* knockdown cells as well as the control cells transfected with a non-targeting shRNA in hypoxic conditions **J)** Invasion assay and **K)** its quantification in control and *P4HA1 9a* or *9b* isoform overexpressing HCC1806 cells under normoxic condition **L)** Invasion assay and **M)** its quantification in *P4HA1* knockdown HCC1806 cells rescued by overexpressing *P4HA1* 9a or 9b isoform as compared to the control *P4HA1* knockdown cells as well as the control cells transfected with a non-targeting shRNA in hypoxic conditions **N)** Immunostaining of COL1A1 in *ATF3* knockdown HCC1806 cells which is then rescued by *P4HA1 9a* overexpression (DAPI staining is done to show the nucleus and overexpression of the *P4HA1* isoforms is confirmed by GFP, scale bars, 10 μm) **O)** Immunostaining of COL1A1 in *ATF3* knockdown MCF7 and **P)** HCC1806 cells in normoxic and hypoxic conditions (DAPI staining is done to show the nucleus, scale bars, 10 μm) **Q)** Immunostaining of COL1A1 in *P4HA1* knockdown MCF7 cells rescued by overexpressing *P4HA1* 9a or 9b isoform as compared to the control *P4HA1* knockdown cells as well as the control cells transfected with a non-targeting shRNA in hypoxic conditions (DAPI staining is done to show the nucleus and overexpression of the *P4HA1* isoforms is confirmed by GFP, scale bars, 10 μm). Error bars show mean values $\pm$ SD (n=3, unless otherwise specified) as calculated using two-tailed Student's t-test, unless otherwise specified, *$P \leq 0.05$, **$P \leq 0.01$, ***$P \leq 0.001$, ns = not significant.

A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ATF3_553_SDM HRE2
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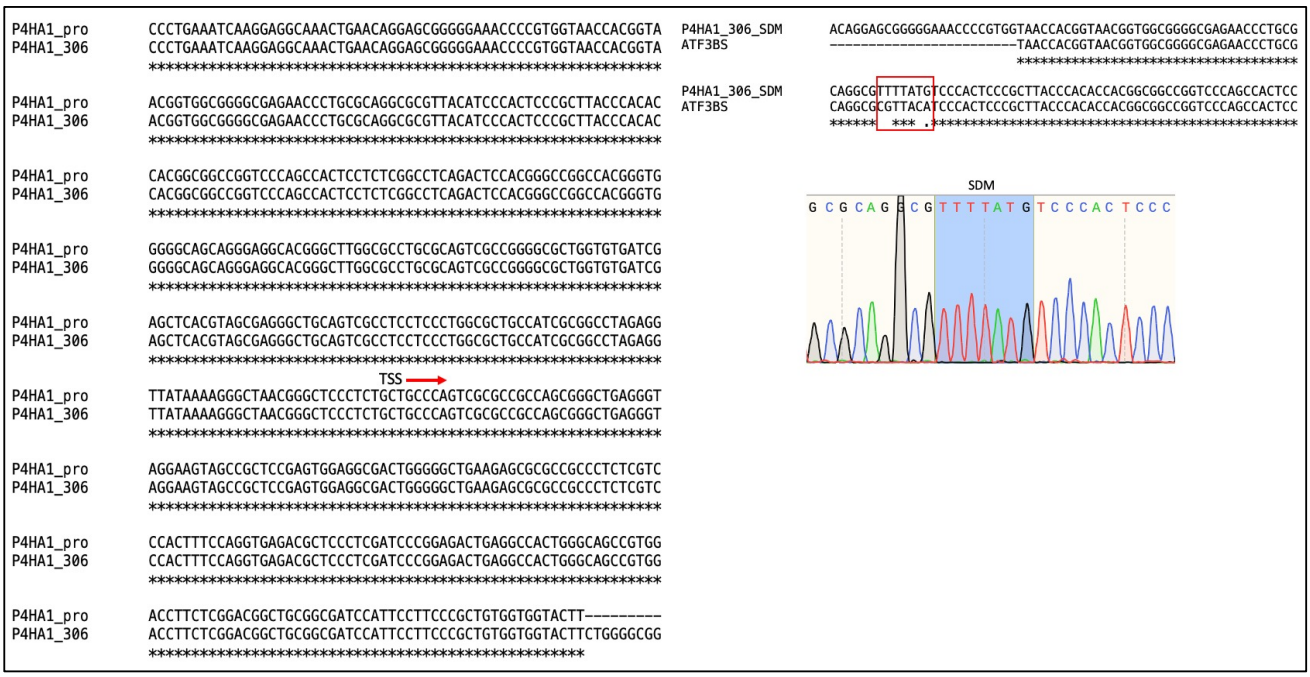
SDM2
SDM3
SDM4
TSS

B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SDM
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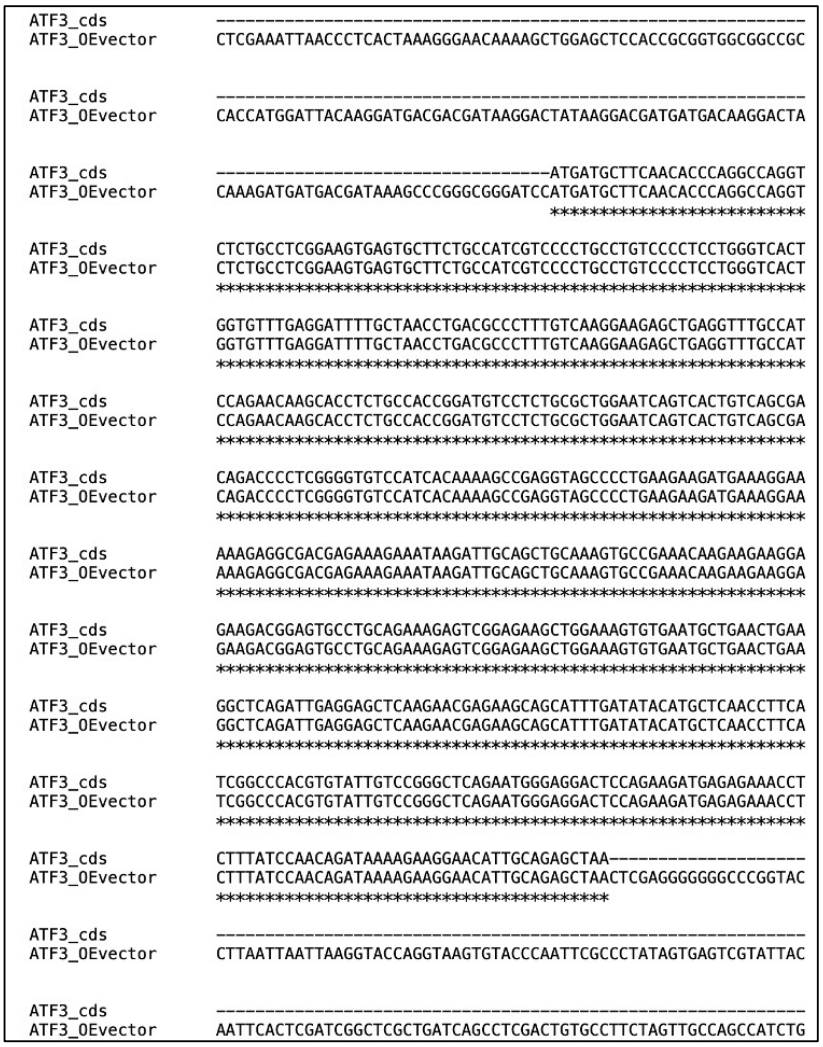
C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ATF3_cds ----------ATGATGCTTCAACACCCAGGCCAGGT
ATF3_0Evector CAAAGATGATGACGATAAAGCCCGGGCGGGATCCATGATGCTTCAACACCCAGGCCAGGT
****
ATF3_cds CTCTGCCTCGGAAGTGAGTGCTTCTGCCATCGTCCCCTGCCTGTCCCCTCCTGGGTCACT
ATF3_0Evector CTCTGCCTCGGAAGTGAGTGCTTCTGCCATCGTCCCCTGCCTGTCCCCTCCTGGGTCACT
****
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****
ATF3_cds CCAGAACAAGCACCTCTGCCACCGGATGTCCTCTGCGCTGGAATCAGTCACTGTCAGCGA
ATF3_0Evector CCAGAACAAGCACCTCTGCCACCGGATGTCCTCTGCGCTGGAATCAGTCACTGTCAGCGA
****
ATF3_cds CAGACCCCTCGGGGTGTCCATCACAAAAGCCGAGGTAGCCCCTGAAGAAGATGAAAGGAA
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ATF3_cds AAAGAGGCGACGAGAAAGAAATAAGATTGCAGCTGCAAAGTGCCGAAACAAGAAGAAGGA
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****
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****
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****
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ATF3_0Evector CTTAATTAATTAAGGTACCAGGTAAGTGTACCCAATTCGCCCTATAGTGAGTCGTATTAC
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P4HA1_204_9a__cds   ------------------------------------------------------------
P4HA1_9a_OEvector   CACCATGGATTACAAGGATGACGACGATAAGGACTATAAGGACGATGATGACAAGGACTA
                                                                               

P4HA1_204_9a__cds   ------------------------------------ATGATCTGGTATATATTAATTATAGG
P4HA1_9a_OEvector   CAAAGATGATGACGATAAAGCCCGGGCGGGATCCATGATCTGGTATATATTAATTATAGG
                                                         ***************************

P4HA1_204_9a__cds   AATTCTGCTTCCCCAGTCTTTGGCTCATCCAGGCTTTTTTACTTCAATTGGTCAGATGAC
P4HA1_9a_OEvector   AATTCTGCTTCCCCAGTCTTTGGCTCATCCAGGCTTTTTTACTTCAATTGGTCAGATGAC
                    ************************************************************

P4HA1_204_9a__cds   TGATTTGATCCATACTGAGAAAGATCTGGTGACTTCTCTGAAAGATTATATTAAGGCAGA
P4HA1_9a_OEvector   TGATTTGATCCATACTGAGAAAGATCTGGTGACTTCTCTGAAAGATTATATTAAGGCAGA
                    ************************************************************

P4HA1_204_9a__cds   AGAGGACAAGTTAGAACAAATAAAAAAATGGGCAGAGAAGTTAGATCGGCTAACTAGTAC
P4HA1_9a_OEvector   AGAGGACAAGTTAGAACAAATAAAAAAATGGGCAGAGAAGTTAGATCGGCTAACTAGTAC
                    ************************************************************

P4HA1_204_9a__cds   AGCGACAAAAGATCCAGAAGGATTTGTTGGGCATCCAGTAAATGCATTCAAATTAATGAA
P4HA1_9a_OEvector   AGCGACAAAAGATCCAGAAGGATTTGTTGGGCATCCAGTAAATGCATTCAAATTAATGAA
                    ************************************************************

P4HA1_204_9a__cds   ACGTCTGAATACTGAGTGGAGTGAGTTGGAGAATCTGGTCCTTAAGGATATGTCAGATGG
P4HA1_9a_OEvector   ACGTCTGAATACTGAGTGGAGTGAGTTGGAGAATCTGGTCCTTAAGGATATGTCAGATGG
                    ************************************************************

P4HA1_204_9a__cds   CTTTATCTCTAACCTAACCATTCAGAGACAGTACTTTCCTAATGATGAAGATCAGGTTGG
P4HA1_9a_OEvector   CTTTATCTCTAACCTAACCATTCAGAGACAGTACTTTCCTAATGATGAAGATCAGGTTGG
                    ************************************************************

P4HA1_204_9a__cds   GGCAGCCAAAGCTCTGTTACGTCTCCAGGATACCTACAATTTGGATACAGATACCATCTC
P4HA1_9a_OEvector   GGCAGCCAAAGCTCTGTTACGTCTCCAGGATACCTACAATTTGGATACAGATACCATCTC
                    ************************************************************

P4HA1_204_9a__cds   AAAGGGTAATCTTCCAGGAGTGAAACACAAATCTTTTCTAACGGCTGAGGACTGCTTTGA
P4HA1_9a_OEvector   AAAGGGTAATCTTCCAGGAGTGAAACACAAATCTTTTCTAACGGCTGAGGACTGCTTTGA
                    ************************************************************

P4HA1_204_9a__cds   GTTGGGCAAAGTGGCCTATACAGAAGCAGATTATTACCATACGGAACTGTGGATGGAACA
P4HA1_9a_OEvector   GTTGGGCAAAGTGGCCTATACAGAAGCAGATTATTACCATACGGAACTGTGGATGGAACA
                    ************************************************************

P4HA1_204_9a__cds   AGCCCTAAGGCAACTGGATGAAGGCGAGATTTCTACCATAGATAAAGTCTCTGTTCTAGA
P4HA1_9a_OEvector   AGCCCTAAGGCAACTGGATGAAGGCGAGATTTCTACCATAGATAAAGTCTCTGTTCTAGA
                    ************************************************************

P4HA1_204_9a__cds   TTATTTGAGCTATGCGGTATATCAGCAGGGAGACCTGGATAAGGCACTTTTGCTCACAAA
P4HA1_9a_OEvector   TTATTTGAGCTATGCGGTATATCAGCAGGGAGACCTGGATAAGGCACTTTTGCTCACAAA
                    ************************************************************

P4HA1_204_9a__cds   GAAGCTTCTTGAACTAGATCCTGAACATCAGAGAGCTAATGGTAACTTAAAATATTTTGA
P4HA1_9a_OEvector   GAAGCTTCTTGAACTAGATCCTGAACATCAGAGAGCTAATGGTAACTTAAAATATTTTGA
                    ************************************************************

P4HA1_204_9a__cds   GTATATAATGGCTAAAGAAAAAGATGTCAATAAGTCTGCTTCAGATGACCAATCTGATCA
P4HA1_9a_OEvector   GTATATAATGGCTAAAGAAAAAGATGTCAATAAGTCTGCTTCAGATGACCAATCTGATCA
                    ************************************************************

P4HA1_204_9a__cds   GAAAACTACACCAAAGAAAAAAGGGGTTGCTGTGGATTACCTGCCAGAGAGACAGAAGTA
P4HA1_9a_OEvector   GAAAACTACACCAAAGAAAAAAGGGGTTGCTGTGGATTACCTGCCAGAGAGACAGAAGTA
                    ************************************************************

P4HA1_204_9a__cds   CGAAATGCTGTGCCGTGGGGAGGGTATCAAAATGACCCCTCGGAGACAGAAAAAACTCTT
P4HA1_9a_OEvector   CGAAATGCTGTGCCGTGGGGAGGGTATCAAAATGACCCCTCGGAGACAGAAAAAACTCTT
                    ************************************************************

P4HA1_204_9a__cds   TTGCCGCTACCATGATGGAAACCGTAATCCTAAATTTATTCTGGCTCCAGCTAAACAGGA
P4HA1_9a_OEvector   TTGCCGCTACCATGATGGAAACCGTAATCCTAAATTTATTCTGGCTCCAGCTAAACAGGA
                    ************************************************************

P4HA1_204_9a__cds   GGATGAATGGGACAAGCCTCGTATTATTCGCTTCCATGATATTATTTCTGATGCAGAAAT
P4HA1_9a_OEvector   GGATGAATGGGACAAGCCTCGTATTATTCGCTTCCATGATATTATTTCTGATGCAGAAAT
                    ************************************************************

P4HA1_204_9a__cds   TGAAATCGTCAAAGACCTAGCAAAACCAAGGCTGAGGCGAGCCACCATTTCAAACCCAAT
P4HA1_9a_OEvector   TGAAATCGTCAAAGACCTAGCAAAACCAAGGCTGAGGCGAGCCACCATTTCAAACCCAAT
                    ************************************************************P4HA1_9a

P4HA1_204_9a__cds   AACAGGAGACTTGGAGACGGTACATTACAGAATTAGCAAAAGTGCCTGGCTCTCTGGCTA
P4HA1_9a_OEvector   AACAGGAGACTTGGAGACGGTACATTACAGAATTAGCAAAAGTGCCTGGCTCTCTGGCTA
                    ************************************************************

P4HA1_204_9a__cds   TGAAAATCCTGTGGTGTCTCGAATTAATATGAGAATACAAGATCTAACAGGACTAGATGT
P4HA1_9a_OEvector   TGAAAATCCTGTGGTGTCTCGAATTAATATGAGAATACAAGATCTAACAGGACTAGATGT
                    ************************************************************

P4HA1_204_9a__cds   TTCCACAGCAGAGGAATTACAGGTAGCAAATTATGGAGTTGGAGGACAGTATGAACCCCA
P4HA1_9a_OEvector   TTCCACAGCAGAGGAATTACAGGTAGCAAATTATGGAGTTGGAGGACAGTATGAACCCCA
                    ************************************************************

P4HA1_204_9a__cds   TTTTGACTTTGCACGGAAAGATGAGCCAGATGCTTTCAAAGAGCTGGGGACAGGAAATAG
P4HA1_9a_OEvector   TTTTGACTTTGCACGGAAAGATGAGCCAGATGCTTTCAAAGAGCTGGGGACAGGAAATAG
                    ************************************************************
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P4HA1_204_9a__cds   AATTGCTACATGGCTGTTTTATATGAGTGATGTGTCTGCAGGAGGAGCCACTGTTTTTCC
P4HA1_9a_OEvector   AATTGCTACATGGCTGTTTTATATGAGTGATGTGTCTGCAGGAGGAGCCACTGTTTTTCC
                    ************************************************************

P4HA1_204_9a__cds   TGAAGTTGGAGCTAGTGTTTGGCCCAAAAAAGGAACTGCTGTTTTCTGGTATAATCTGTT
P4HA1_9a_OEvector   TGAAGTTGGAGCTAGTGTTTGGCCCAAAAAAGGAACTGCTGTTTTCTGGTATAATCTGTT
                    ************************************************************

P4HA1_204_9a__cds   TGCCAGTGGAGAAGGAGATTATAGTACACGGCATGCAGCCTGTCCAGTGCTAGTTGGCAA
P4HA1_9a_OEvector   TGCCAGTGGAGAAGGAGATTATAGTACACGGCATGCAGCCTGTCCAGTGCTAGTTGGCAA
                    ************************************************************

P4HA1_204_9a__cds   CAAATGGGTATCCAATAAATGGCTCCATGAACGTGGACAAGAATTTCGAAGACCTTGTAC
P4HA1_9a_OEvector   CAAATGGGTATCCAATAAATGGCTCCATGAACGTGGACAAGAATTTCGAAGACCTTGTAC
                    ************************************************************

P4HA1_204_9a__cds   GTTGTCAGAATTGGAATGA-------------------------------------------
P4HA1_9a_OEvector   GTTGTCAGAATTGGAATGAGGATCCACCGGATCTAGATAACTGATCATAATCAGCCATAC
                    *******************
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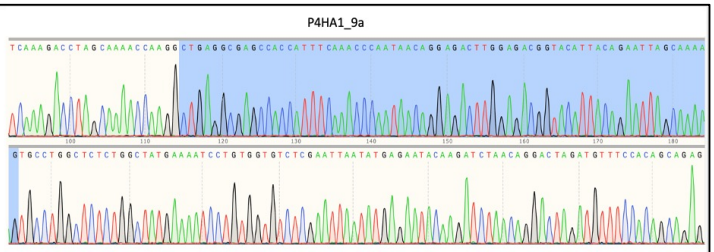

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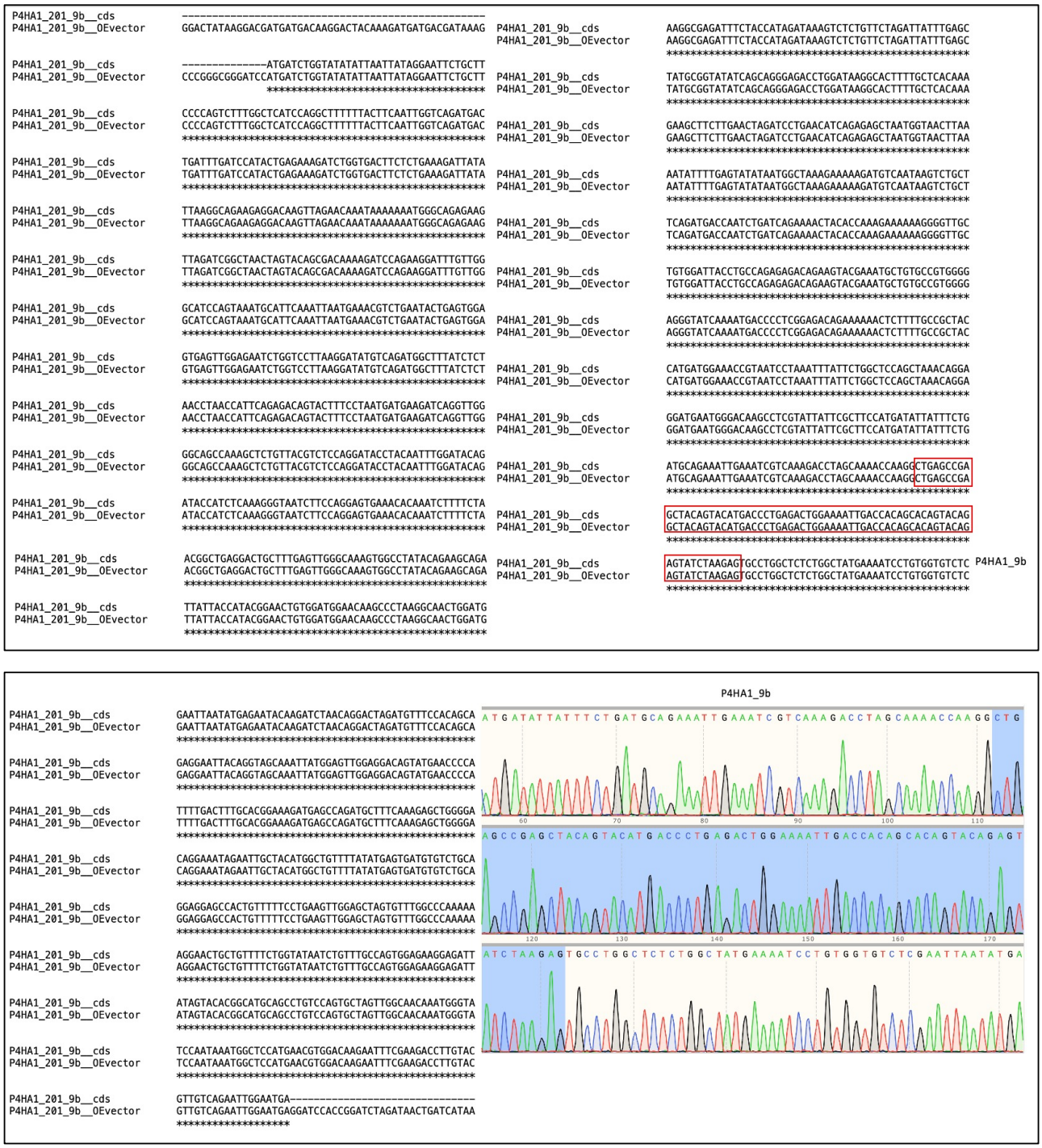

Figure S7. Sanger sequencing for confirming the sequences of A) pGL3_*ATF3*pro luciferase vector **B)** pGL3_*P4HA1*pro luciferase vector (confirmed sequencing results of *ATF3* and *P4HA1* promoter luciferase vectors were obtained after alignment (performed on Clustal Omega Multiple Sequence Alignment tool) with the promoter sequence of these genes

(obtained from Eukaryotic Promoter Database) The TSS has been marked within the sequences. Also, we have checked for the SDM and confirmed the mutated motifs in the SDM vectors, which have been marked within the sequences and shown in the chromatogram as well) **C)** pCMV3tag1A_*ATF3* overexpression vector **D)** egfp_*P4HA1_9a* overexpression vector and **E)** egfp_*P4HA1_9b* overexpression vector (confirmed sequencing results of pCMV3tag1A_*ATF3* and pegfp_*P4HA1* overexpression vectors were obtained after alignment (performed on Clustal Omega Multiple Sequence Alignment tool) with the coding sequences of these genes (obtained from Ensembl). To differentiate between the *P4HA1 9a* and *P4HA1 9b* sequences, we have marked the exons 9a and 9b within the sequences as well as shown in the chromatogram).