

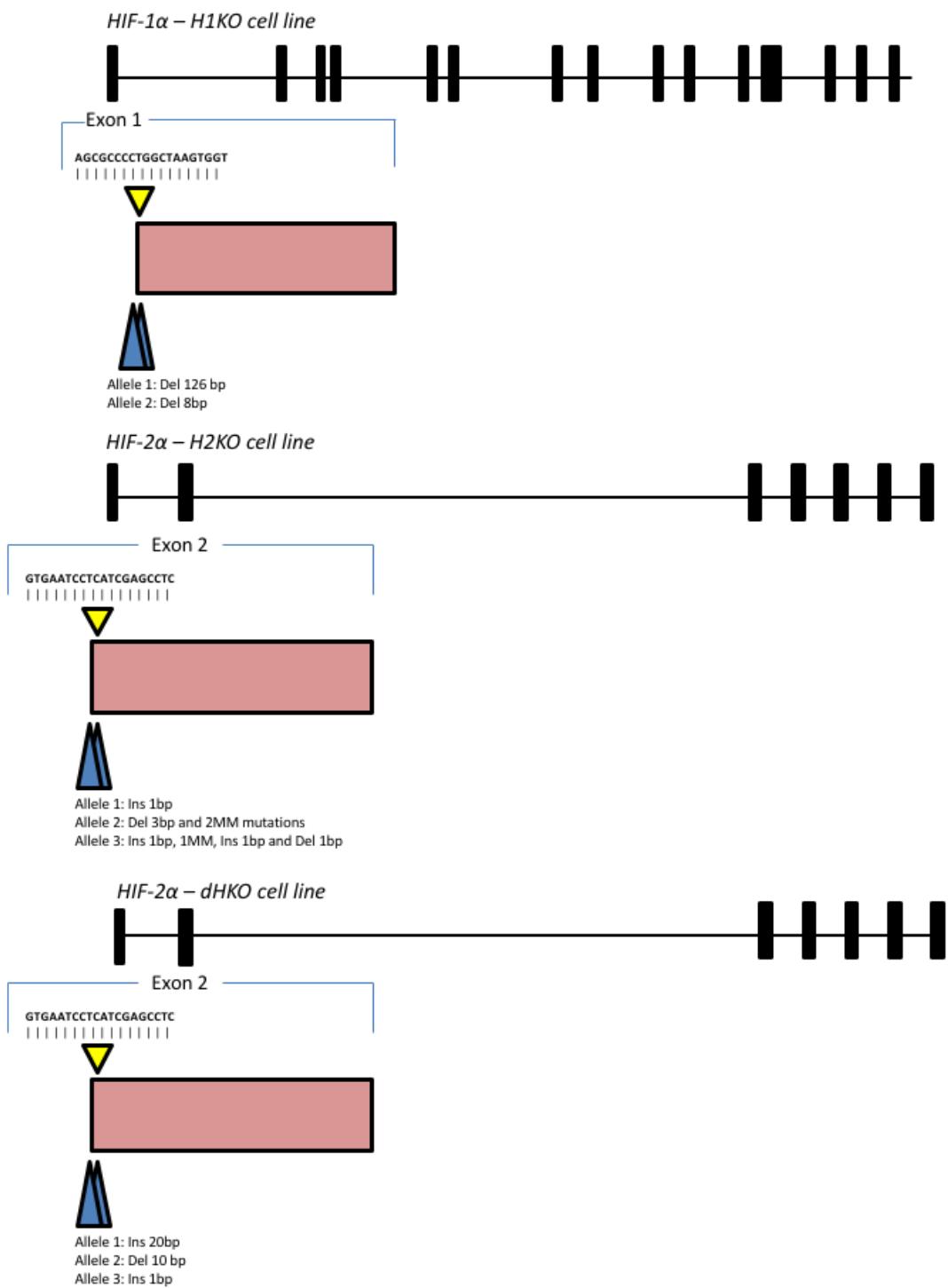
**SUPPLEMENTARY TABLE 1:** Antibodies used in this study

Antibody	Dilution	Vendor
HIF-1 $\alpha$	1:500	BD Biosciences
HIF-2 $\alpha$	1:1000	Novus Biologicals
HIF-1 $\beta$	1:1000	BD Biosciences
Lamin-A	1:1000	Sigma-Aldrich
pATM	1:1000	Abcam
pCHK2	1:1000	Bioke
CHK2	1:1000	Bioke

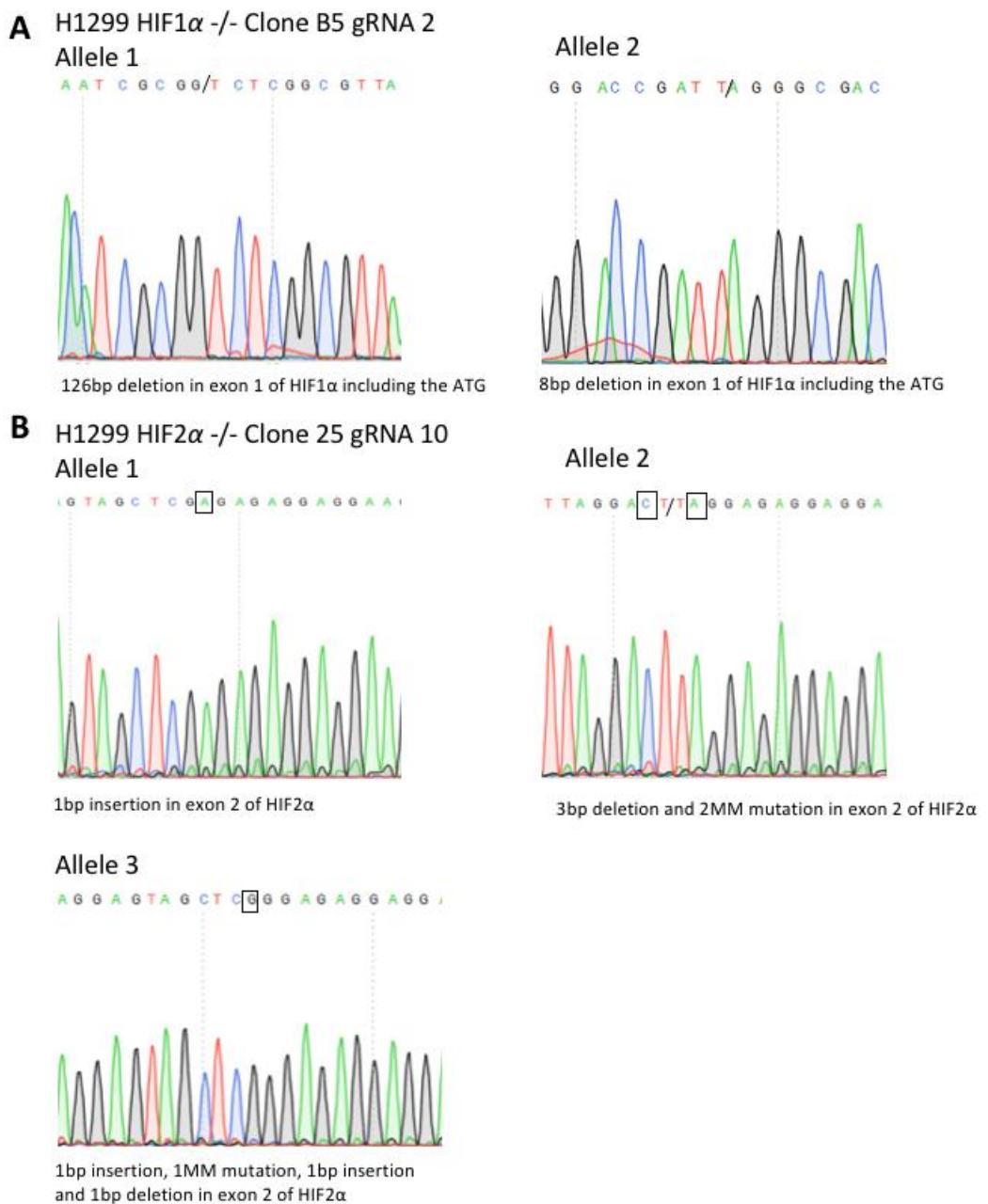
**SUPPLEMENTARY TABLE 2:** Primers used in this study

Genes	Primers	Sequence
CAIX	Forward	CATCCTAGCCCTGGTTTTGG
CAIX	Reverse	GCTCACACCCCCTTGGTT
GLUT1	Forward	GATTGGCTCCTTCTCTGTGG
GLUT1	Reverse	TCAAAGGACTTGCCCAGTTT
CITED2	Forward	ACGCCTTCAACGCCCTAATGG
CITED2	Reverse	ATGCCTGATGCCGCTCGTG
TWIST1	Forward	GGAGTCCGCAGTCTTACGAG
TWIST1	Reverse	TCTGGAGGACCTGGTAGAGG
MCT1	Forward	TATGGTGGAGGT CCTATCAGC
MCT1	Reverse	TGTACGGTGTACAGAAAGAAC
MCT4	Forward	TTTGTGCTTACGCCGTGG
MCT4	Reverse	CTGAAGAGGTAGACGGAGTAGG
HIF-2 $\alpha$	Forward	TGCTCCCACGGCCTGTAC
HIF-2 $\alpha$	Reverse	TTGTCACACCTATGGCATATCACA
HPRT	Forward	TATTGTAATGACCAGTCAACAG
HPRT	Reverse	GGTCCTTTCACCAAGCAAG

### Supplementary Figure 1

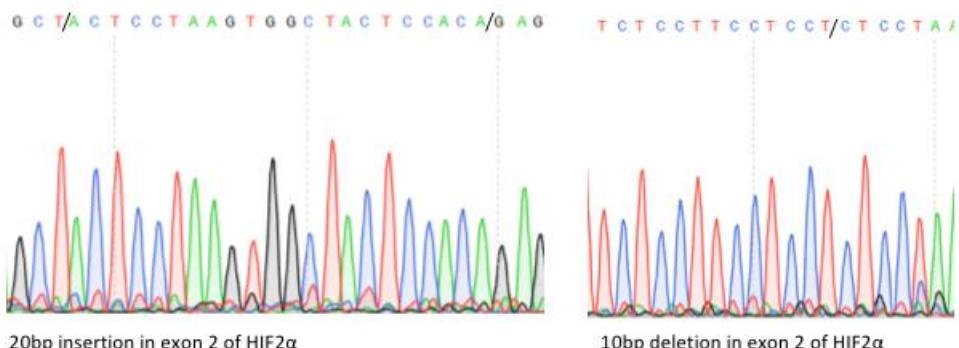


## Supplementary Figure 2

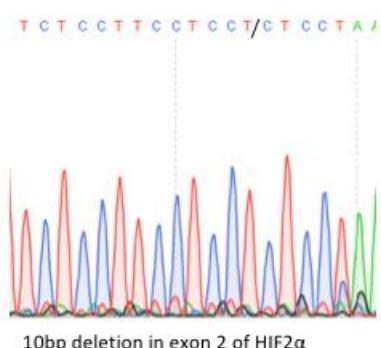


**C** H1299 HIF2 $\alpha$  -/- Clone 36.103 gRNA 10

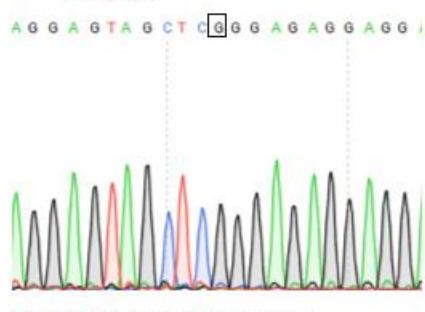
Allele 1



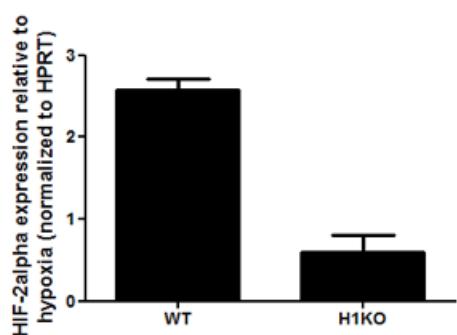
Allele 2



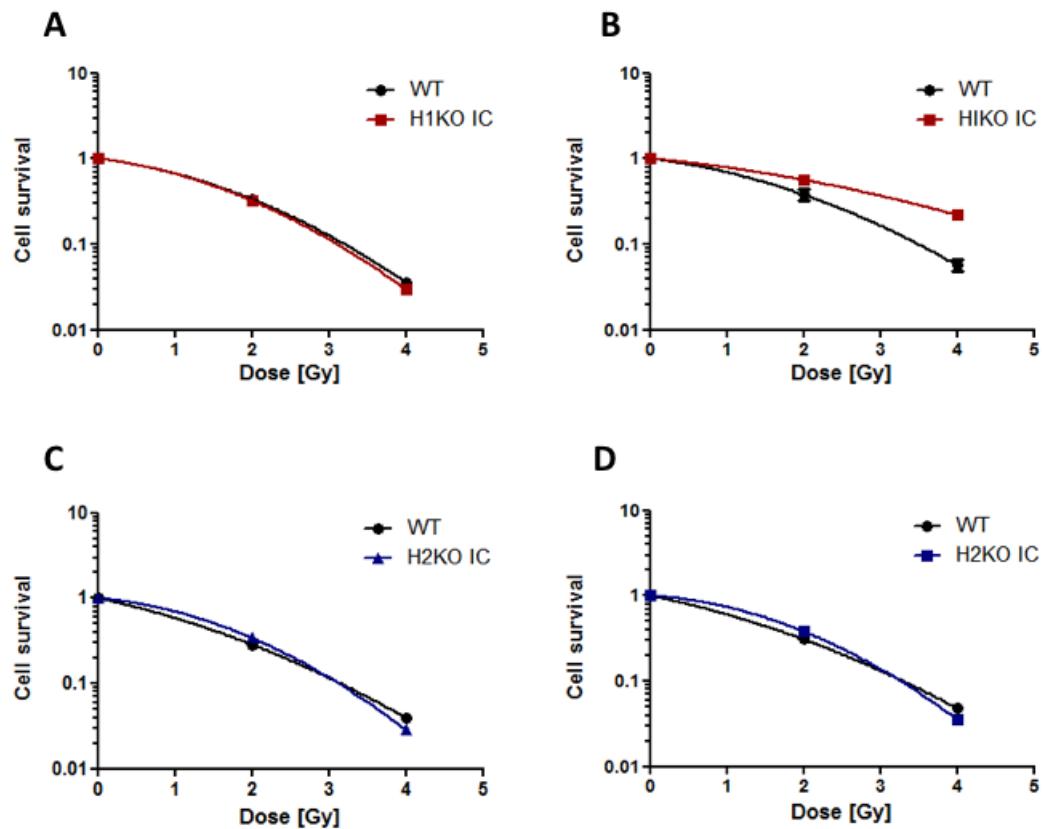
Allele 3



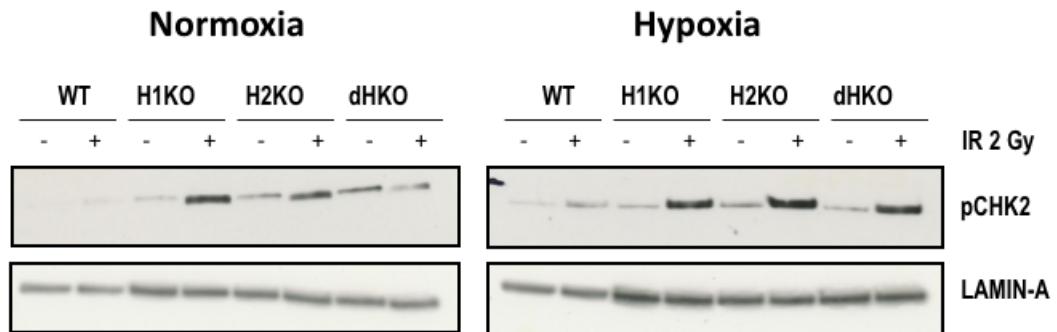
**Supplementary Figure 3**



**Supplementary Figure 4**



Supplementary Figure 5



Supplementary Figure 6

