

## **Supplementary Information**

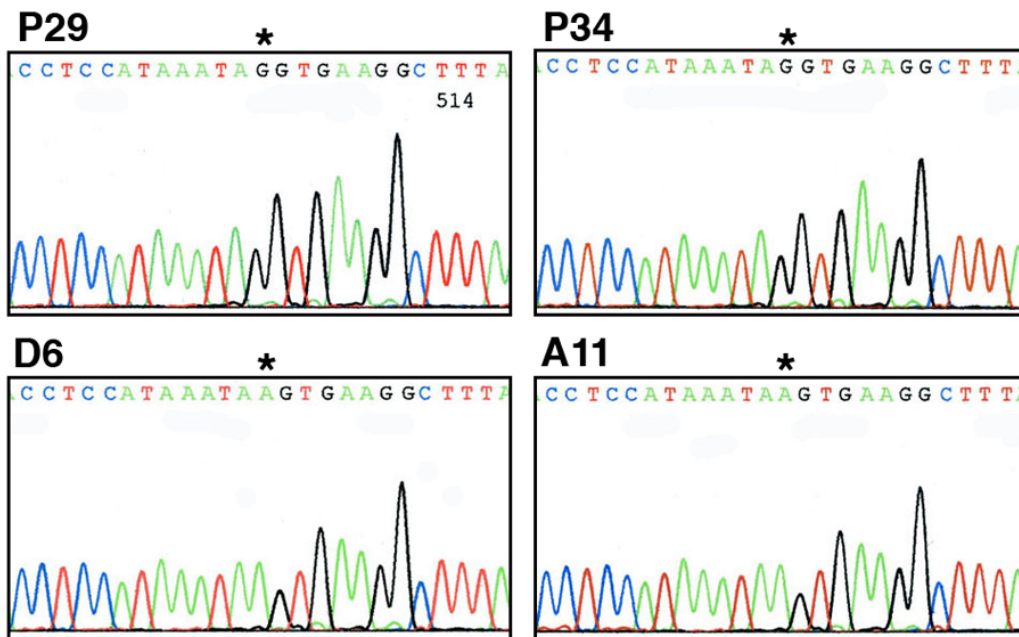
**ROS-GENERATING MITOCHONDRIAL DNA MUTATION UPREGULATES  
HYPOXIA-INDUCIBLE FACTOR-1 $\alpha$  GENE TRANSCRIPTION  
VIA PI3K-AKT/PKC/HDAC PATHWAY**

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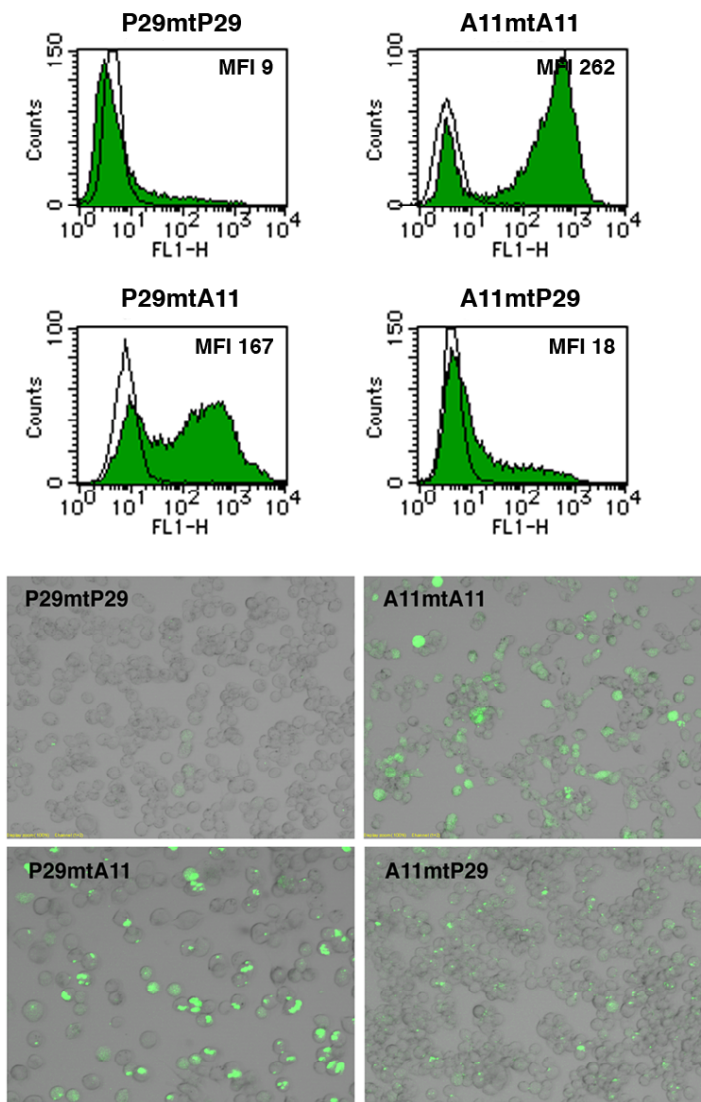
**Table S1 Alignment of amino acid sequence of ND6**

	10	20	25	30	40
<i>Mus musculus</i> (Mouse)	MNNYIFVLSS	LFLVGCLGLA	LKPS	P	IYGGL GLIVSGFVGC ~
P29 & P34 cells	MNNYIFVLSS	LFLVGCLGLA	LKPS	P	IYGGL GLIVSGFVGC ~
A11 & D6 cells	MNNYIFVLSS	LFLVGCLGLA	L	IYGGL GLIVSGFVGC ~	
<i>Homo sapiens</i> (Human)	MMYALFLLSV	GLVMGFVGF	SKPS	P	IYGGL VLIVSGVVG ~
<i>Bos taurus</i> (Bovine)	MMLYIVFILSV	IFVMGFVGF	SKPS	P	IYGGL GLIVSGGVGC ~
<i>Gallus gallus</i> (Chicken)	MTYFVIFLGI	CFMLGLAVA	SNPS	P	YGVV GLVVASVMGC ~
<i>Xenopus laevis</i> (Frog)	MIYMVSVSMM	VLVLGLVAVA	SNPS	P	FYAAL GLVLAAGAGC ~
<i>Danio rerio</i> (Zebra fish)	MAFYLSFLMA	ALVGGMIAIA	SNPA	P	YFAAF GLVVVAGVGC ~
<i>Drosophila melanogaster</i> (Fruit fly)	MIQLMLYS	LIITTSIIFL	NMIH	P	LALGL TLLIQTIFVC ~

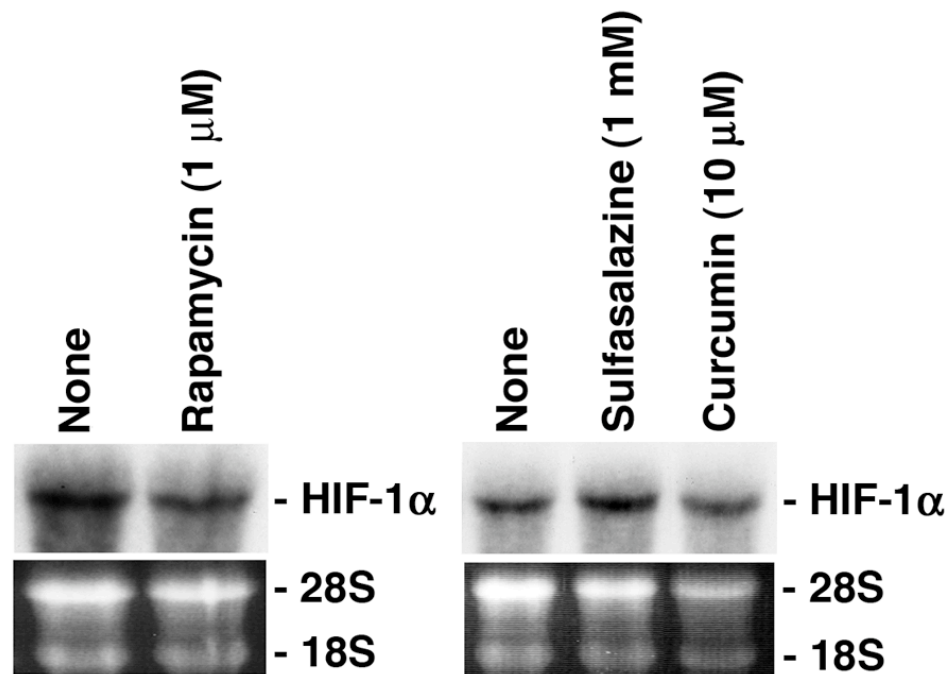
G13997A mutation in the *ND6* gene changes evolutionary conserved proline-25 to leucine.



**Figure S1. G13997A mutation in the *ND6* gene found in high-metastatic D6 and A11 cells.**  
The asterisk indicates the position of the mutation.



**Figure S2. ROS are overproduced in the cybrids with A11 mtDNA carrying a G13997A mutation in the *ND6* gene.** The cybrids were incubated with 10  $\mu$ M DCFH-DA for 10 min at 37°C in serum-free DMEM. ROS production was analyzed with a FACScan flow cytometer or visualized using a confocal laser microscope. Mean fluorescence intensity (MFI) was also shown.



**Figure S3. Rapamycin, sulfasalazine and curcumin do not inhibit the expression of *HIF-1α* mRNA in A11 cells.** A11 cells were treated with the reagents at the indicated concentration for 24 h. Total RNA was extracted and subjected to Northern blot analysis. The blots were hybridized with a <sup>32</sup>P-labeled *HIF-1α* cDNA. Ethidium bromide staining of the gel is also shown.