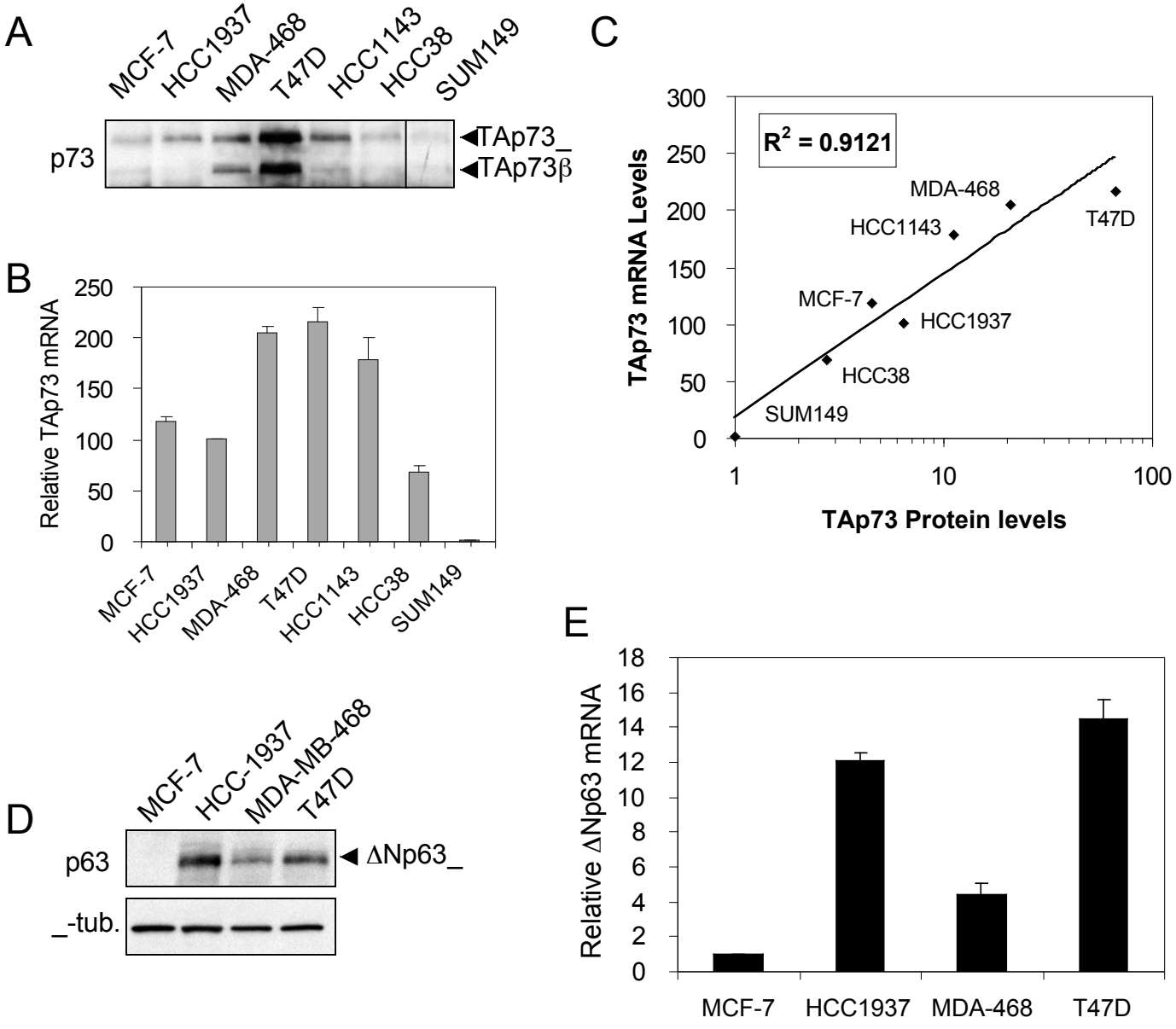
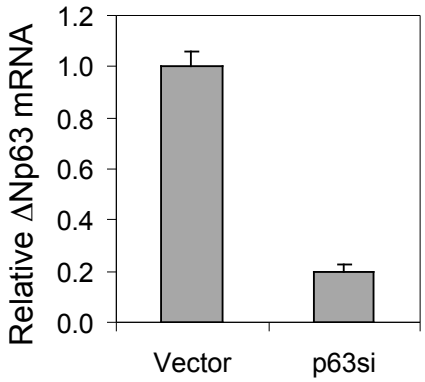
Supplementary Figure 1

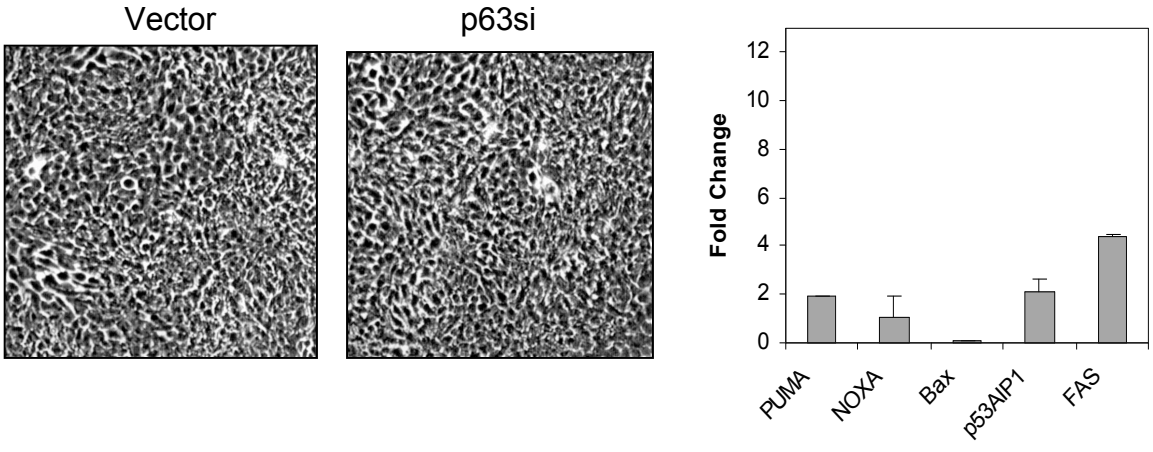


Supplementary Figure 2

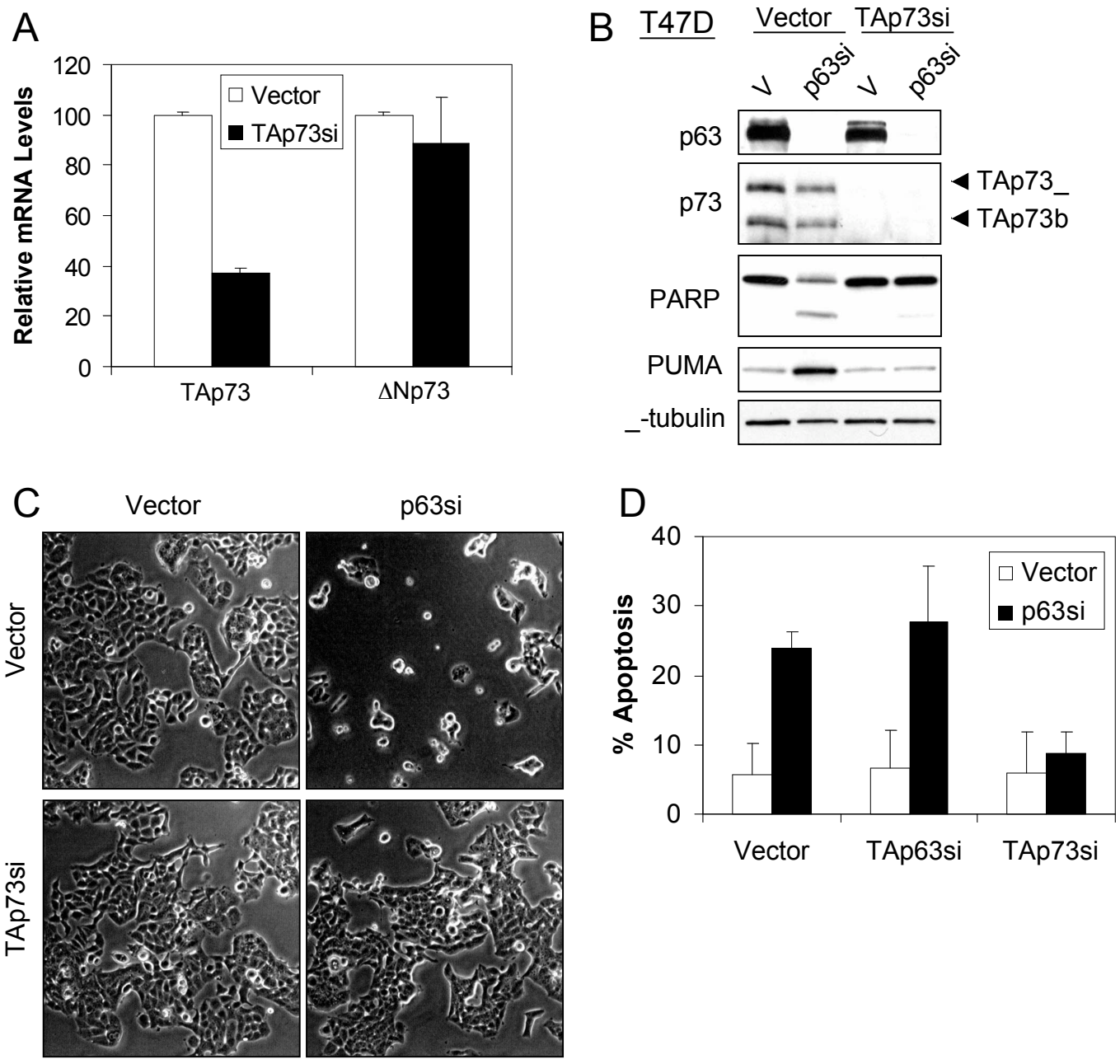
A



B MCF-7

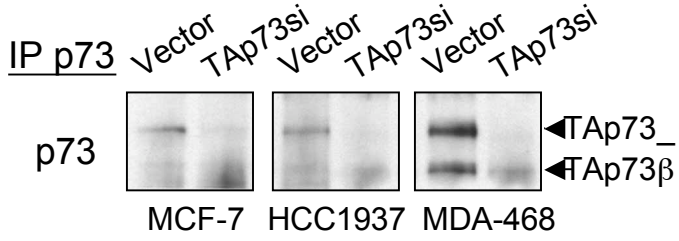


Supplementary Figure 3



Supplementary Figure 4

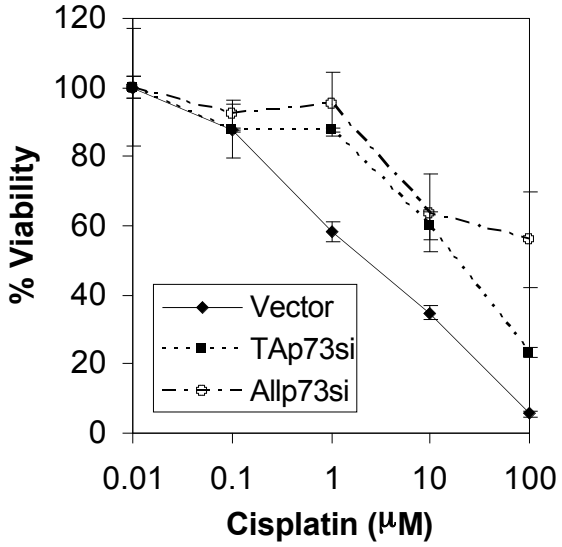
A



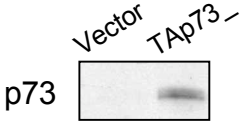
B

Cell Lines	Cisplatin (uM)	Doxorubicin (nM)	Paclitaxel (nM)
MCF-7			
Vector	6.00 ± 0.57	< 10.00	0.59 ± 0.04
TAp73si	9.22 ± 0.19	< 10.00	0.59 ± 0.06
HCC1937			
Vector	2.80 ± 1.48	40.14 ± 10.5	0.78 ± 0.08
TAp73si	43.75 ± 0.59	20.31 ± 9.26	0.53 ±0.50
MDA-MB-468			
Vector	1.15 ± 0.40	38.43 ± 7.70	0.56 ± 0.02
TAp73si	12.86 ± 3.10	69.28 ± 2.76	0.64 ± 0.06

C



D



E

MCF-10A	Cisplatin (μM)	Doxorubicin (nM)	Paclitaxel (nM)
Vector	6.06 ± 0.55	57.44 ± 2.73	8.23 ± 1.26
TAp73b	0.74 ± 0.03	73.29 ± 6.88	8.12 ± 0.15

Supplementary Figure Legends

Supplementary Figure 1 Correlation between p73 and p63 mRNA and protein levels in breast cancer cells. (**A**) TAp73 protein level by IP/Immunoblot of 2.5mg protein lysate from the indicated human breast cancer-derived cell lines. Little or no ΔNp73 is detected based on transfected isoform size controls and on isoform-specific QRT-PCR (not shown). (**B**) Quantitation of TAp73 by isoform-specific QRT-PCR, normalized to GAPDH. (**C**) Correlation of TAp73 mRNA and protein levels in breast cancer cells. (**D**) Expression of ΔNp63α protein by immunoblot. (**E**) Expression of ΔNp63 mRNA by isoform-specific QRT-PCR in the indicated cell lines. Error bars in **B** and **E** show SD for two experiments.

Supplementary Figure 2 Controls for apoptosis following p63 inhibition by lentiviral shRNA. (**A**) Knockdown of endogenous ΔNp63 mRNA by lentiviral p63-directed shRNA (p63si) in HCC-1937. RNA was prepared at 72 hours following lentiviral infection and assayed by isoform-specific QRT-PCR, normalized to GAPDH levels. (**B**) Neither gene induction nor apoptosis is observed in p63-negative MCF-7 cells. Left, photomicrographs (100X) taken at 72 hours post lentiviral shRNA infection. Right, QRT-PCR for the indicated genes. For gene expression graphs, error bars represent SD from two independent experiments performed in duplicate.

Supplementary Figure 3 Puma induction, PARP cleavage, and apoptosis following p63 knockdown are TAp73-dependent in T47D cells. (**A**) TAp73-directed shRNA targets TAp73 but not ΔNp73. Expression of endogenous TAp73 and ΔNp73 was assessed by QRT-PCR following lentiviral shRNA infection. Error bars indicate SD from three measurements. (**B**) Cells expressing a TAp73-directed shRNA or control were subsequently infected with a p63-directed lentiviral shRNA and harvested at 72 hours for immunoblot and IP/immunoblot (for p73). (**C**) Photomicrograph (100X) taken 72 hours post lentiviral infection as in **B** show that morphologic features of apoptosis correlate with Puma induction and PARP cleavage. (**D**) Rescue from apoptosis following ablation of TAp73 but not TAp63. Quantitation of apoptosis by Annexin/PI staining of cells

treated as in **B** and harvested 72 hours following p63 knockdown. Error bars show SD for 3 independent experiments.

Supplementary Figure 4 TAp73 mediates cisplatin sensitivity in breast cancer cells. (**A**) Knockdown of endogenous TAp73 protein by lentiviral shRNA in the indicated cell lines, assessed by IP/immunoblot. (**B**) IC_{50} values determined by cell viability (MTT) assay 5 days following treatment of control or TAp73-directed shRNA-expressing cells with the indicated agents. Values indicate the mean $\pm$ SD for 3 independent experiments. (**C**) Knockdown of TAp73 or All p73 isoforms induces cisplatin resistance in breast cancer cells. MTT assay performed as in **B**. (**D**) Stable retroviral expression of TAp73β in MCF-10A cells, assessed by immunoblot. (**E**) TAp73β expression in mammary epithelial cells conveys specific sensitivity to cisplatin. IC_{50} values determined and expressed as in **B**.

Supplementary Table 1. p53 Status in Clinical Breast Cancer Samples

Sample ID	ER Status	P53 Status	Codon 72 polymorphism	Codon nucleotide	Codon Amino Acid
282	Positive	WT	Pro		
432	Positive	WT	Pro		
481	Positive	WT	Pro		
480	Positive	WT	Pro		
398	Positive	WT	Pro		
298	Positive	WT	Pro		
469	Positive	WT	Pro		
436	Positive	WT	Pro		
477	Positive	WT	Pro		
426	Positive	WT	Pro		
430	Positive	WT	Pro		
242	Positive	WT	Pro		
356	Positive	WT	Pro		
253	Positive	WT	Pro		
588	Negative	WT	Unknown		
1274	Negative	Mutant	Pro	151 (G to T)	Stop
				152 (A to G)	E51G
164	Negative	Mutant	Arg	523 (C to G)	R175G
720	Negative	Mutant	Arg	639 (A to G)	R213R
209	Negative	Mutant	Arg	818 (G to A)	R273H
1196	Negative	Mutant	Pro	730 (G to A)	G244S
465	Negative	Mutant	Arg	Del (529-546)	
1322	Negative	WT	Arg		
1278	Negative	WT	Arg		
1106	Negative	WT	Arg		
222	Negative	WT	Unknown		
1321	Negative	WT	Arg		
715	Negative	Mutant	Pro	577 (C to T)	H193Y
999	Negative	WT	Arg		
158	Negative	WT	Arg		
489	Negative	Mutant	Pro	469 (G to T)	V157F
1502	Negative	WT	Arg		
289	Negative	WT	Pro		
1325	Negative	WT	Pro		
1273	Negative	Mutant	Pro	817 (C to T)	R273C
756	Negative	WT	Arg		
1509	Negative	WT	Pro		
488	Negative	WT	Pro		

Mutational status was determined based on bi-directional sequencing (exon 1-7), and was verified by the presence of nucleotide changes in both strands.

Supplementary Table 2. Primer sequences for QRT-PCR

Gene	Forward primer	Reverse primer	Product (bp)
ΔNp63	5′-GGAAAACAATGCCCAGACTC-3′	5′-GTGGAATACGTCCAGGTGGC-3′	294
TAp63	5′-AAGATGGTGCGACAAACAAG-3′	5′-AGAGAGCATCGAAGGTGGAG-3′	234
TAp73	5'-GCACCACGTTTGAGCACCTCT-3'	5′-GCAGATTGAACTGGGCCATGA-3'	168
ΔNp73	5'-CAAACGGCCCGCATGTTCCC-3'	5'-TTGAACTGGGCCGTGGCGAG-3'	232
Bax	5′-TGACATGTTTTCTGACGGCAAC-3′	5′-GGAGGCTTGAGGAGTCTCACC-3′	204
Noxa	5′-GAGATGCCTGGGAAGAAGG-3′	5′-ACGTGCACCTCCTGAGAAAA-3′	228
P53AIP1	5′-AGCTCACTCCGAAAGCCTCTGCTC-3′	5′-GCATCACCGAGAGGTTCTGGTCTC-3′	280
FAS	5′-GGGCATCTGGACCCTCCTAC-3′	5′-TCCTTTCACCTGGAGGACAG-3′	200
PUMA	5′-ACGACCTCAACGCACAGTACGAG-3′	5′-AGGAGTCCGCATCTCCGTCAGTG-3′	345
HER2	5′-AGCGGTGTGAAACCTGACC-3′	5′-TTGATGAGGATCCCAAAGACC-3′	224
B2M	5′- AGCTGTGCTCGCGCTACTCTC-3′	5′-CACACGGCAGGCATACTCATC-3′	286
GAPDH	5′-CACCCAGAAGACTGTGGATGG-3′	5′-GTCTACATGGCAACTGTGAGG-3′	587