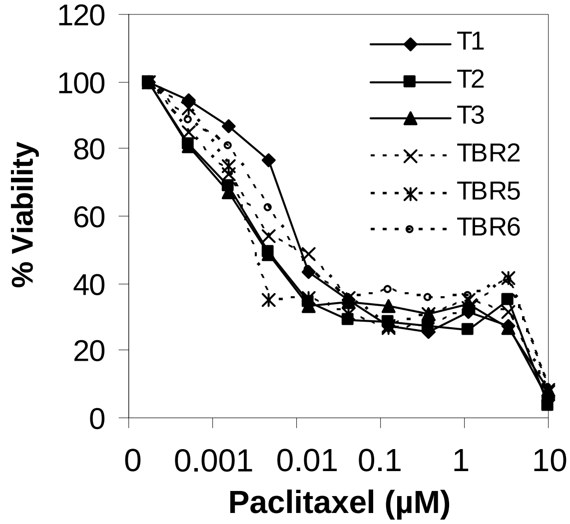
Supplementary Figure 1, Ibrahim et al

A

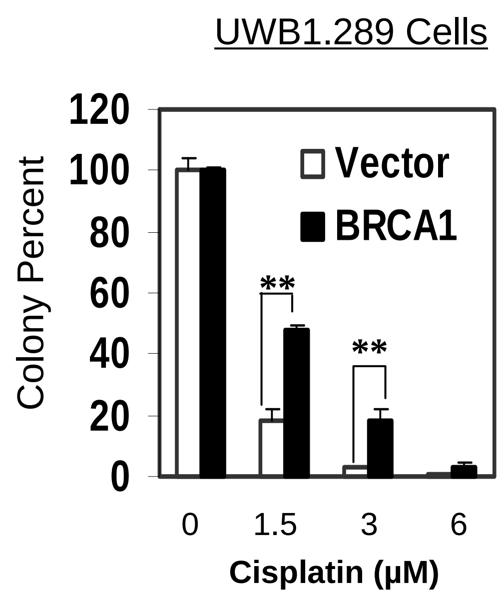


B

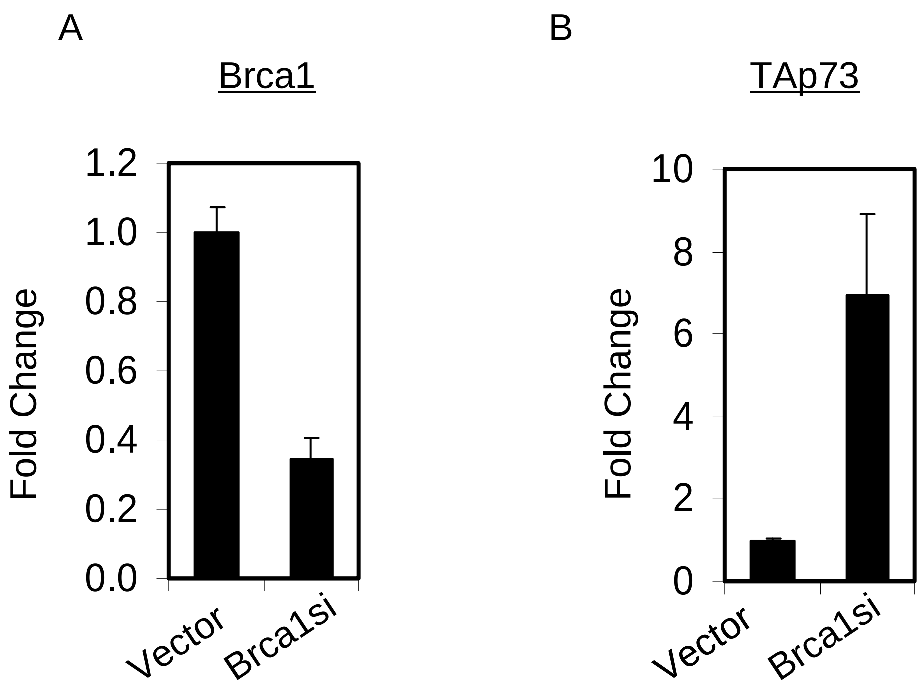
Cell lines	IC_{50}	
	Cisplatin (μM)	Paclitaxel (nM)
Murine		
T1	4.46 ± 0.43	11.94 ± 1.03
T2	3.58 ± 0.51	4.82 ± 1.35
T3	5.25 ± 0.68	4.93 ± 1.77
TBR2	0.18 ± 0.15	14.25 ± 4.44
TBR5	0.17 ± 0.05	3.84 ± 0.34
TBR6	0.26 ± 0.11	10.73 ± 1.82
Human		
UWB1.289 Vector	0.63 ± 0.14	N.D.
UWB1.289 Brca1	7.63 ± 1.44	N.D.

N.D. : Not determined

C



Supplementary Figure 2, Ibrahim et al

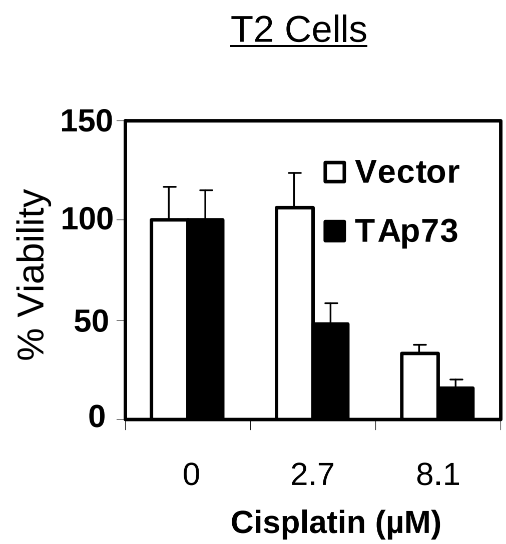


Supplementary Figure 3, Ibrahim et al

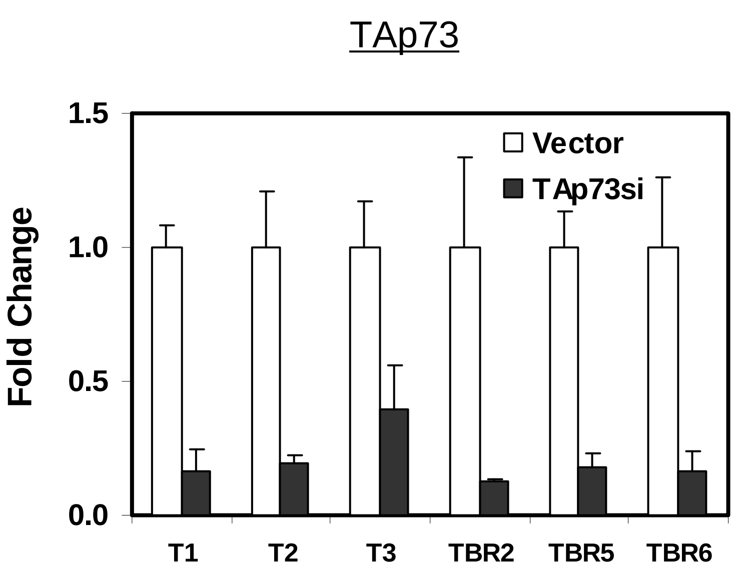
A

Cell lines	IC50 Cisplatin (μM) Vector	TAp73si
Mouse		
T1	1.73 ± 0.35	1.72 ± 0.28
T2	1.66 ± 0.47	1.54 ± 0.52
T3	1.82 ± 0.61	1.66 ± 0.42
TBR2	1.03 ± 0.50	2.35 ± 0.43
TBR5	0.25 ± 0.02	0.59 ± 0.18
TBR6	0.40 ± 0.12	1.69 ± 0.58
Human		
UWB1.289 Vector	0.49 ± 0.08	3.28 ± 0.39
UWB1.289 Brca1	6.43 ± 0.58	4.60 ± 0.96

C



B



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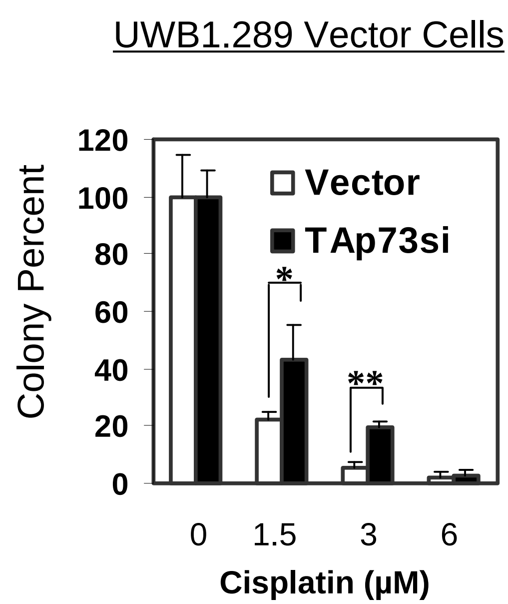
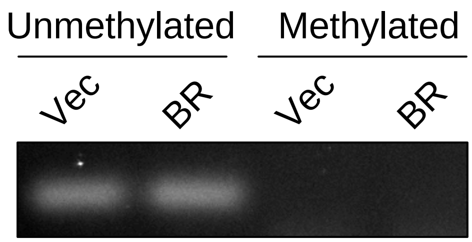
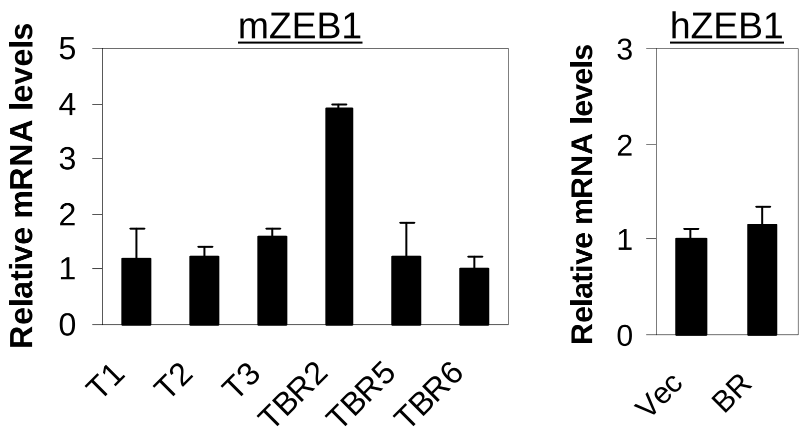


Supplementary Figure 4, Ibrahim et al



Supplementary Figure 5, Ibrahim et al



Supplementary Figure Legends

Figure S1. Cisplatin sensitivity of BRCA1-deficient cells. (A) No difference in paclitaxel sensitivity is observed in murine BRCA1 wild-type (T) versus BRCA1-deficient (TBR) lines, assessed by quantitative dose response (MTT) assay at 72 hours. (B) Consistently increased sensitivity to cisplatin, but not paclitaxel, in human and murine BRCA1-deficient ovarian carcinoma cells. UWB1.289 Vector cells are BRCA1-deficient, while the matched UWB1.289 Brca1 cells are reconstituted with BRCA1. IC_{50} values were determined by quantitative dose-response curve as in (A). (C) Cisplatin sensitivity of BRCA1-deficient cells is confirmed in a clonogenic assay. Cells were treated with the indicated doses of cisplatin for 1 hour, then plated at clonal density and colonies were counted at 2 weeks. Error bars show SEM for three independent plates. ** $P < .01$

Figure S2. BRCA1-dependent induction of TAp73 in p53-deficient cells. (A) Homozygous p53-null MEFs were transduced with a lentivirus expressing a control (Vector) or BRCA1-targeted shRNA (BRCA1si), then selected with puromycin (0.5 μg/ml) for 72 hours prior to (B) treatment with doxorubicin (0.4μg/ml, 16 hours) or control. RNA was analyzed for BRCA1 and TAp73 by QRT-PCR. Error bars show SEM for triplicate plates from a representative experiment.

Figure S3. TAp73 is a contributor to cisplatin sensitivity. (A) Ablation of TAp73 induces cisplatin resistance in murine and human BRCA1-deficient, but not BRCA1-expressing, ovarian carcinoma cells. BRCA1 wild-type (T1,2,3; UWB1.289 Brca1) or BRCA1-deficient (TBR2,5,6; UWB1.289 Vector) lines were transduced with lentivirus expressing a control (Vector) or TAp73-directed shRNA (TAp73si), followed by quantitative dose response (MTT) assay at 72 hours. Note that TAp73 knockdown induces resistance comparable to that observed in BRCA1-expressing cells. Note also that independent hairpins were used for TAp73 knockdown in human and murine cells. (B) Knockdown of TAp73 mRNA in murine ovarian carcinoma cells as described in (A). (C) TAp73 overexpression induces cisplatin sensitivity in BRCA1-proficient cells.

Murine T2 ovarian carcinoma cells were transduced with a TAp73β-expressing retrovirus, followed by treatment with cisplatin (48h) at the indicated concentrations and assessment of viability by MTT assay. (D) Cisplatin resistance induced by TAp73 knockdown in BRCA1-deficient cells is confirmed in a clonogenic assay, performed as in Figure S1. Error bars show SEM for three independent plates. * $P < .05$; ** $P < .01$

Figure S4. Absence of differential promoter methylation in human UWB1.289 cells. Bisulfite modified genomic DNA was subjected to semi-quantitative PCR. No differences were observed in amplification of the methylated or unmethylated product in BRCA1-deficient (Vec) or BRCA1-reconstituted (BR) cells. The primers used are listed in Table S6.

Figure S5. ZEB1 expression in ovarian tumor lines is independent of BRCA1. Levels of ZEB1 were determined by QRT-PCR in murine (left) or human UWB1.289 (right) BRCA1-deficient (TBR2, 5, 6; Vec) and BRCA1-expressing (T1,2,3; BR) ovarian carcinoma cells.

Supplementary Table 1, Ibrahim et al

QRT-PCR primer sequences

Target	Forward (5’ → 3’)	Reverse (5’ → 3’)
Human		
TAp73	GCACCACGTTTGAGCACCTCT	GCAGATTGAACTGGGCCATGA
NOXA	GAGATGCCTGGGAAGAAGG	ACGTGCACCTCCTGAGAAAA
PUMA	ACGACCTCAACGCACAGTACGAG	AGGAGTCCGCATCTCCGTCAGTG
P53AIP1	AGCTCACTCCGAAAGCCTCTGCTC	GCATCACCGAGAGGTTCTGGTCTC
ZEB1	ACTGCTGGGAGGATGACAGAAA	AACTGCACAGGGAGCAACTAAA
GAPDH	CACCCAGAAGACTGTGGATGG	GTCTACATGGCAACTGTGAGG
Mouse		
TAp73	TCGAGCACCTGTGGAGTTCTCT	CTGGTCCATGGCACTGCTGA
DNp73	CTCGCCACGGCCCAGTTC	CGGTCACATGCTCTGCCTTC
NOXA	GGGCAGAGCTACCACCTGAG	CACTCGTCCTTCAAGTCTGCTG
ZEB1	GGCAAGACAACGTGAAAGACAA	TCACAATACGGGCAGGTGAG
GAPDH	GGGAAGCCCATCACCATCTT	GCCTTCTCCATGGTGGTGAA
BRCA1	CCCAAAGATGAGCTGGAGAG	GTCCCACATCACAAGACGTG

Supplementary Table 2, Ibrahim et al

shRNA targeted sequences

Target	Sequence (5’ → 3’)
Human TAp73	5′-GGATTCCAGCATGGACGTCTT-3′
Mouse TAp73	5′-GCCAGACAGCACCTACTTTGA-3′
Human ZEB1si-1	5′-CCTCTCTGAAAGAACACATTA-3′
Human ZEB1si-2	5′-GCTGTTGTTCTGCCAACAGTT-3′
Mouse BRCA1	5′-CCACAGGTAAATCAGGAATTT-3′
Mouse ZEB1si-1	5′-CCATAAACATTGCTATTCCTA-3′
Mouse ZEB1si-2	5′-GCATCATTTGATTGAGCACAT-3′

Supplementary Table 3, Ibrahim et al

Primer sequences for ChIP

Target	Forward (5' → 3')	Reverse (5' → 3')
Human		
H1 (-1550 to -1137)	ATGCACACCCTCAGCTCCAC	TGGAACCTGTCGTTTTTGTCC
H2 (-1275 to -839)	CTGCTTGTCCCAGGCCATC	CCGCTGGTCTTTGTCTCCAC
H3 (-943 to -519)	CTGTGCTCTGCCTGGACACT	GGTTTGGGGTCTCCCTGATG
H4 (-597 to -136)	TCACACACGCTGTTCCCAAG	CCTGTGCCCTCTCCACTGTC
H5 (-322 to +88)	AGGAGCGGGTGTTGCTGTC	CAGAGGTGCTCAAACGTGGT
Mouse		
M1 (-1550 to -1127)	CCTCTTGGGTCTCAGGGTGT	GGCCAGTAAAAGGGGACCAG
M2 (-1174 to -729)	CCCCACCCCACTCTCTACCT	GCCCCAGCTAGTACCCACAAC
M3 (-771 to -287)	TGAGGAAATCGTGGGGAAAG	GCCAGAAAACGGGTAAGAAGG
M4 (-379 to +69)	AAAAACTGACCCAAGACCACAAA	CCACAGGTGCTCGAAGGTG

Supplementary Table 4, Ibrahim et al

Primer sequences for methylation analysis

Target Region	Forward (5' → 3')	Reverse (5' → 3')
P73 promoter: Methylation-specific primer (MSP) and Unmethylated-specific primer (USP)		
MSP	GGACGTAGCGAAATCGGGGTTC	ACCCCGAACATCGACGTCCG
USP	AGGGGATGTAGTGAAATTGGGGTTT	ATCACAACCCCAAACATCAACATCCA
P73 intron 1 (numbers relative to exon 2)		
MSP (-658 to -551)	TGTAGTAGTGGGTATAGTTAGGTTTTAGTC	AAACCTAAAAATAACTCCGATCCCGATCAC
USP (-654 to -548)	GTAGTGGGTATAGTTAGGTTTTAGTTGG	AAACCTAAAAATAACTCCAATCCCAAT
P73 bisulfite sequencing primers(relative to exon 2)		
(-754 to -509)	TTAACGTTTTAGTTTTGTTAGGTTTTTTTG	ATACAACCAAATTTAAAATCTCCCTAATAC
(-665 to -499)	TGTGTTTTGTAGTAGTGGGTATAGTTAGGT	CTAAAAAATACAACCAAATTTAAAATCTCC
(-539 to -246)	GTATTAGGGAGATTTTAAATTTGGTTGTAT	TAAAAATACCCTAAACAAACAAAAACTTC
(-367 to -85)	GTATTTTAAAGAGTTTGTTTTTTTGAAGG	AATAAACCTACCTAAAACATCCCTAAAAC
(-154 to +196)	ATAGTGAGGGTATAGGGAGGGTAAG	ATTCCAAAAAACTCCAAAAATACTCAAAC
P73 sequencing primers for HpaII/MspI analysis		
Human	ATGCACACCCTCAGCTCCA	GCTCCAGAGGTGCTCAAAC
Mouse	TCCTCTTGGGTCTCAGGGTGT	CTCCACAGGTGCTCGAAGGT

Supplementary Table 5, Ibrahim et al

Clinical characteristics of unselected ovarian carcinoma cases

Cases	First Remission (Years)	Grade	Histology
Responsives			
115	1.17	3	Serous
126	>2.67	3	Serous and Transitional
134	1.86	3	Serous
141	1.50	not specified	Serous
147	1.35	3	Transitional
148	1.36	3	Serous
153	>2.30	3	Serous
163	>2.16	3	Serous and Transitional
182	1.08	2	Serous
216	>1.30	3	Serous
Non-Responsives			
112	0.42	3	Serous
125	0.42	2-3	Serous
132	0.00	2-3	Serous
143	0.33	3	Serous
156	0.31	3	Serous
158	0.12	not specified	Poorly differentiated
167	0.40	3	Serous
204	0.50	3	Serous

Supplementary Table 6, Ibrahim et al

Clinical characteristics of wild-type (WT) and BRCA1-deficient ovarian carcinoma cases. All tumors were stage III or IV.

Cases	Histology
WT	
168	Serous
245	Serous
246	Serous
248	Clear cell
257	Serous
261	Serous
298	Serous
313	not accessible
BRCA1 deficient	
A1	Serous
B2	Serous
C1	Serous
175	not accessible