# <u>Appendix</u>

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	Image	Scattergram	Pearson's Coefficient (Rr)
GFP-Bax			0.644
GFP-Bax S184A			0.607
GFP-Bax S184E			0.206

Appendix Figure S1. Colocalization analysis of images from Figure 2C. MDA-MB-468 cells were transfected with plasmids encoding GFP-Bax, GFP-Bax S184A or GFP-Bax S184E. Cells were co-stained with MitoTracker Red CMXRos (mitochondria) and DAPI (nucleus). Whole image Pearson's correlation coefficients between MitoTracker and GFP for the single image shown above were calculated using CoLocalizer Pro software for Mac.

#### **Appendix Table S1**

	MBA-MB-468				MBA-MB-435				ZR-75-1				MCF-7			
	LY294002	Deguelin	MK- 2206	A- 443654	LY294002	Deguelin	MK- 2206	A- 443654	LY294002	Deguelin	MK- 2206	A- 443654	LY294002	Deguelin	MK- 2206	A- 443654
Bid	0.0333	0.0016	<0.000 1	<0.0001	ns	ns	ns	ns	0.0004	0.0024	<0.0001	<0.0001	ns	ns	ns	ns
Bim	ns	0.0183	0.0008	0.0002	ns	ns	ns	ns	<0.0001	0.0003	<0.0001	<0.0001	ns	ns	ns	ns
Bad	ns	ns	0.0031	0.0203	ns	ns	ns	ns	ns	<0.0001	<0.0001	<0.0001	ns	ns	ns	ns
Puma	ns	ns	0.0002	0.0017	ns	ns	ns	ns	0.0145	0.0422	<0.0001	<0.0001	ns	ns	ns	ns
Bmf	ns	ns	0.0064	0.0432	ns	ns	ns	ns	<0.0001	0.0128	<0.0001	0.0003	ns	ns	ns	ns

**Related to Figure 4A.** Two-way ANOVA was conducted on the influence of two independent variables (BH3 peptide, drug) on cytochrome *c* release of isolated mitochondria for each cell-line. BH3 peptide included Bid, Bim, Bad, Puma and BMF. Drug included LY294003, Deguelin, MK-2206 and A-443654. Each drug treatment was statistically compared to DMSO control within each peptide group using t-tests with Bonferroni correction for multiple comparisons. Table indicates p-values for each comparison (ns=not significant). Data are located in Figure 4A.

#### **Appendix Table S2**

	MDA-MB 468 S100										ZR-75-1 S100			
	MDA-MB 468 S100	LY294002 pretreated S100	Deguelin pretreated S100	MK-2206 pretreated S100	A-443654 pretreated S100	Akt depleted S100	IgG pretreated S100	ZR-75-1 S100	LY294002 pretreated S100	Deguelin pretreated S100	MK-2206 pretreated S100	A-443654 pretreated S100	Akt depleted S100	IgG pretreated S100
Bid	0.0031	ns	ns	ns	0.0324	ns	0.0432	0.0004	ns	ns	ns	ns	ns	0.003
Bim	0.0003	ns	ns	ns	ns	ns	0.0027	<0.0001	ns	ns	ns	ns	ns	0.0003
Bad	0.0013	ns	ns	ns	ns	ns	0.0002	0.0316	ns	ns	ns	ns	ns	0.0026
Puma	<0.0001	ns	ns	ns	ns	ns	0.001	0.0014	ns	ns	ns	ns	ns	0.0001
Bmf	ns	ns	ns	ns	0.0044	ns	ns	0.0053	ns	ns	ns	ns	ns	0.0013

Related to Figure 4C and EV2B. Two-way ANOVA was conducted on the influence of two independent variables (BH3 peptide, treatment) on cytochrome *c* release of isolated mitochondria from ABT-737 sensitive MDA-MB-435 cells that were treated with the S100 fraction isolated from ABT-737 resistant MDA-MB-468 or ZR-75-1 cells. BH3 peptide included Bid, Bim, Bad, Puma and BMF. Treatment included S100, LY294003 pretreated S100, Deguelin pretreated S100, MK-2206 pretreated S100, A-443654 pretreated S100, Akt depleted S100 and IgG pretreated S100. Each treatment was statistically compared to control within each peptide group using t-tests with Bonferroni correction for multiple comparisons. Table indicates p-values for each comparison (ns=not significant). Data for Bid MDA-MB-468 S100 treatments are in Figure 4C and the rest of the data are located in Figure EV2B.

### **Appendix Table S3**

			AKT1		AKT2		PIK3CA		PIK3R1		PTEN
		CNA	mRNA								
Pan Cancer	<i>BAX</i> gain	1.00E-05	1.00E-02	1.00E-53	1.00E-37	NS	1.00E-06	1.00E-06	1.00E-13	NS	NS
Fan Cancer	High BAX mRNA expression	NS	1.00E-08	NS	1.00E-04	NS	1.00E-95	NS	1.00E-80	NS	1.00E-30
Breast Invasive	<i>BAX</i> gain	2.00E-68	NS	4.00E-13	8.00E-14	NS	NS	2.00E-08	1.00E-03	NS	NS
Carcinoma	High BAX mRNA expression	NS	8.00E-22	7.00E-03	1.00E-09	9.00E-03	4.00E-54	NS	4.00E-36	NS	3.00E-44
Pan Cancer	<i>BAK1</i> gain	NS	NS	4.00E-05	NS	NS	NS	NS	NS	1.00E-10	NS
	High BAK1 mRNA expression	NS	2.00E-03	NS	NS	NS	NS	NS	1.00E-58	NS	5.00E-06
Breast Invasive	<i>BAK1</i> gain	NS	NS	4.00E-04	NS	8.00E-06	NS	1.00E-16	4.00E-04	NS	2.00E-03
Carcinoma	High BAK1 mRNA expression	NS	NS	NS	4.00E-06	NS	NS	2.00E-16	1.00E-08	2.00E-04	1.00E-18

Related to Figure 6C and EV5B. TCGA database was probed for significant associations between the row heading (e.g *BAX* gain) and copy number (CNA) gain/loss (red/blue) or mRNA up/downregulation (red/blue) of the indicated genes (AKT1, AKT2, PIK3CA, PIK3R1, PTEN). The p-values are indicated for each analysis. This data was used to generate Figure 6C and EV5B. NS = non-significant p-value for positive/negative associations.