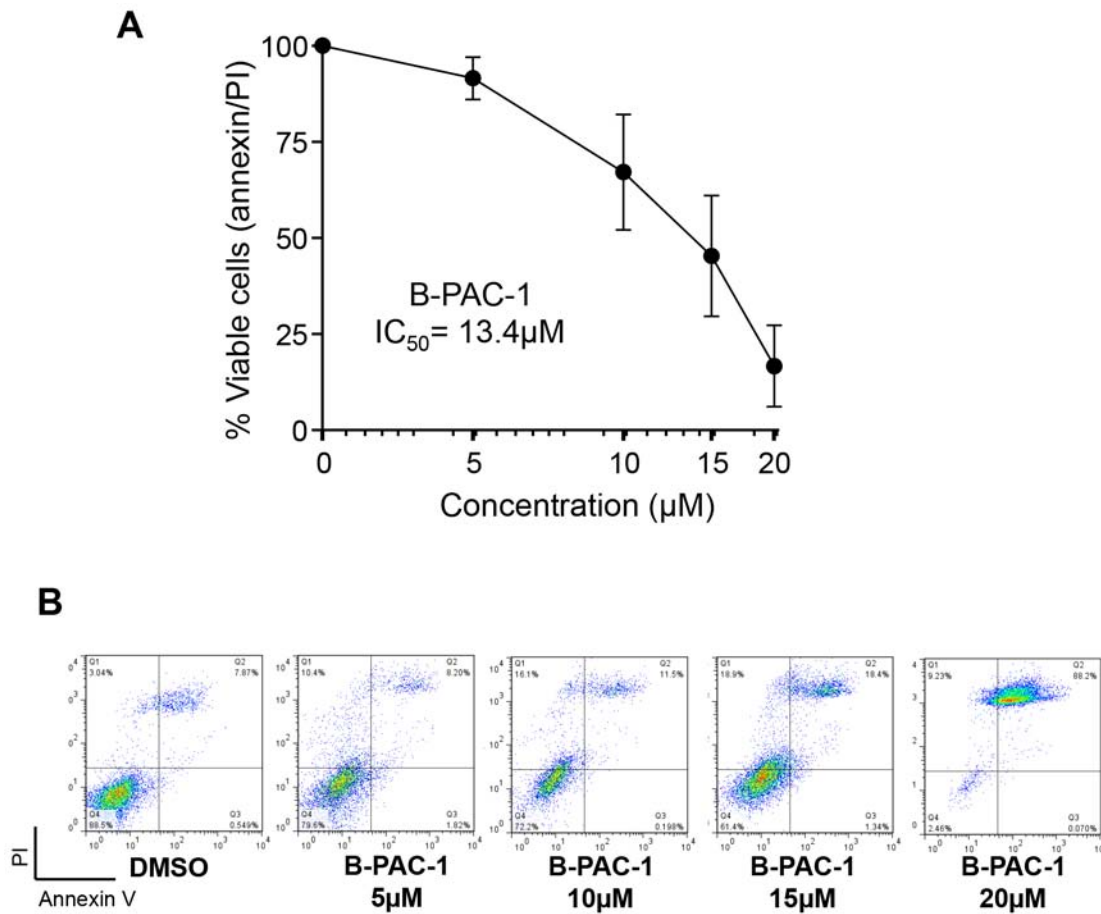
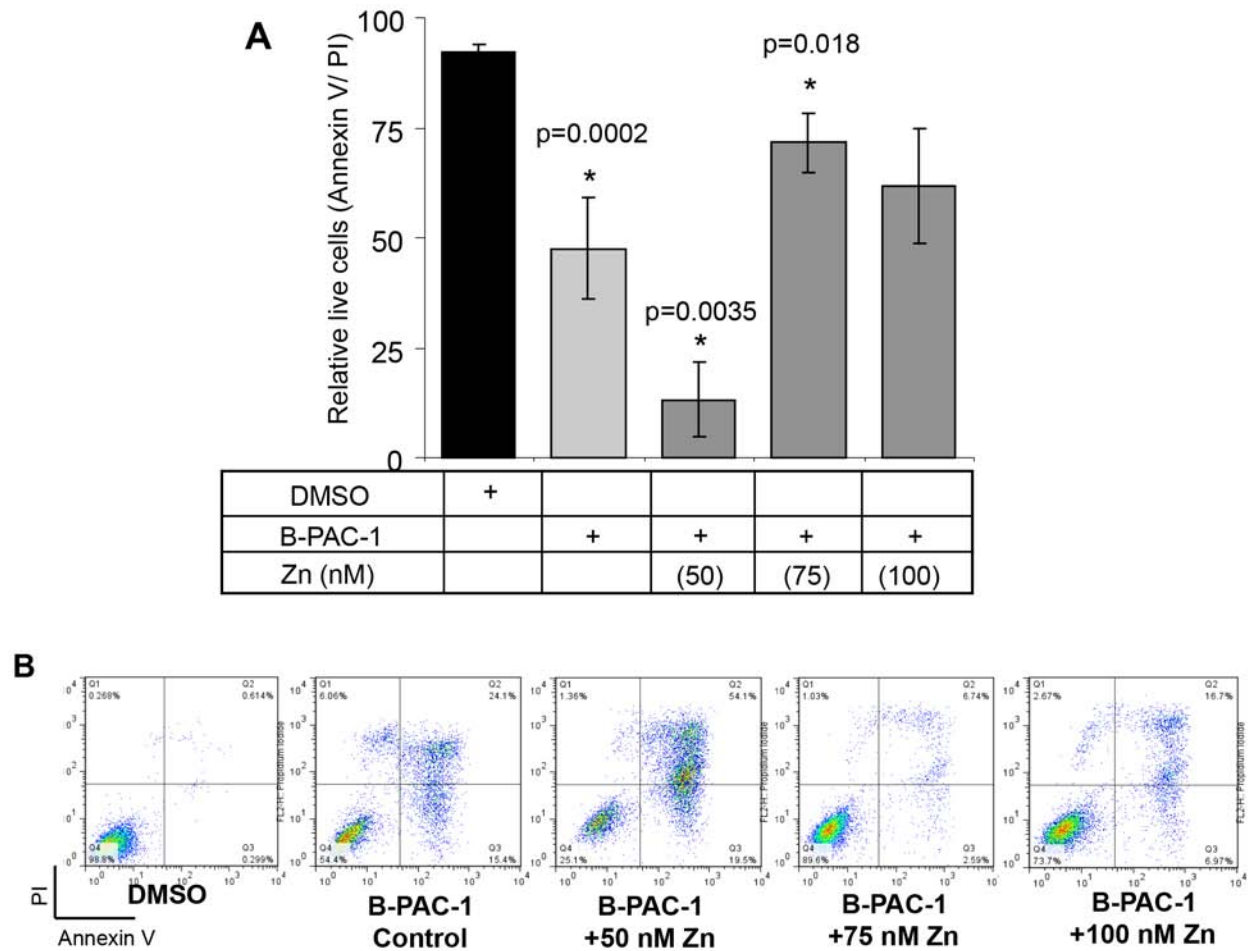


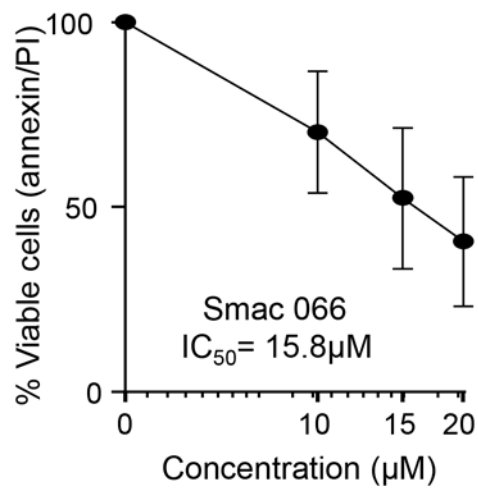
SUPPLEMENTARY FIGURES AND TABLES



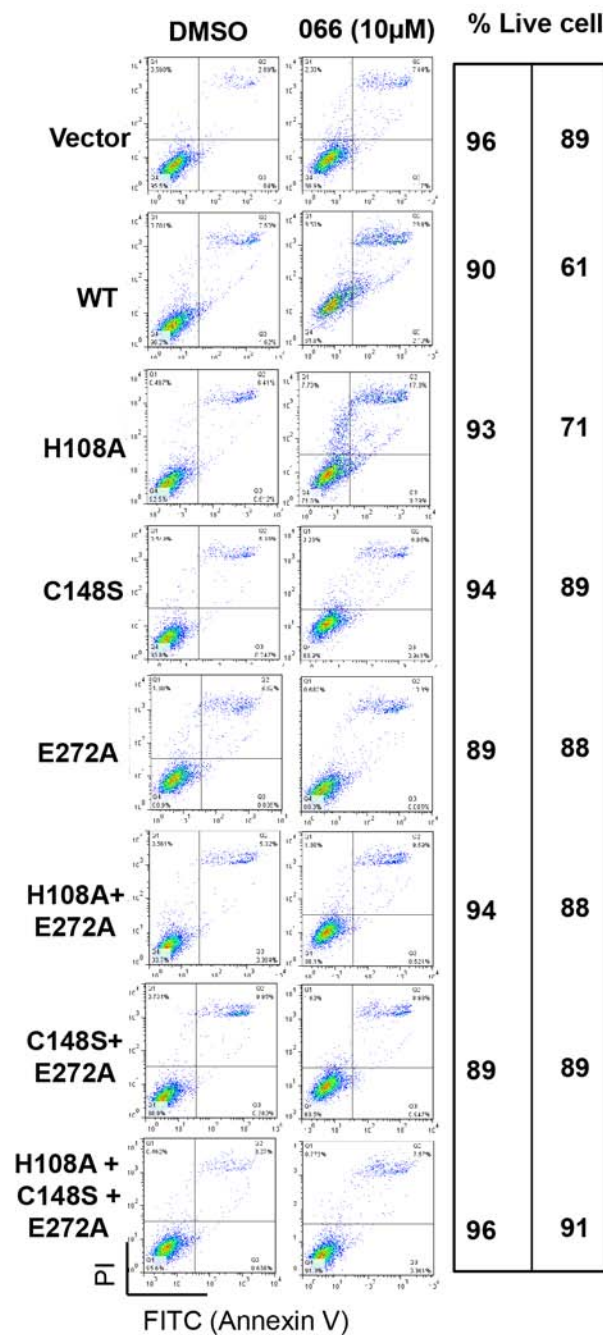
Supplementary Figure S1: A. Dose dependent cell death by B-PAC-1 in MEF cells stably over-expressed with WT Casp3 construct. 0.5×10^6 cells were treated with 5, 10, 15 or 20 µM B-PAC-1 for 24 hr. Cells were harvested and stained with Annexin V and PI and the amount of apoptosis was measured compared with DMSO control. Mean \pm SE ($n = 7$); IC₅₀ value was determined as shown in the inset (13.4 µM). B. Representative Annexin V-PI FACS analysis showing dose dependent induction of apoptosis induced by B-PAC-1



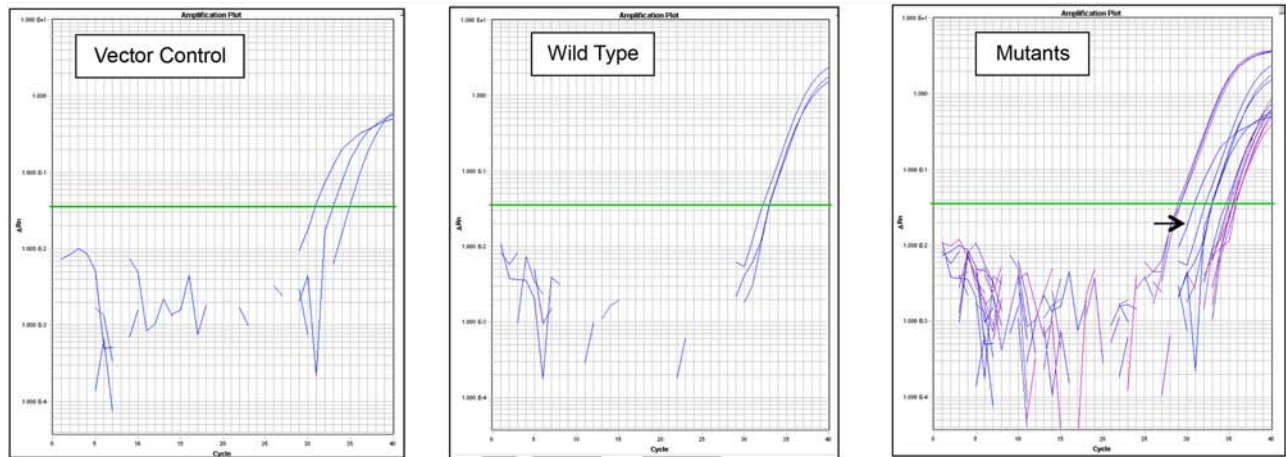
Supplementary Figure S2: A. Dose dependent inhibition of B-PAC-1 induced apoptosis of WT Casp3 expressing MEF cells by exogenous Zn. Stably over-expressed WT Casp3 (0.5×10^6 /well) MEF cells were treated with $15 \mu\text{M}$ B-PAC-1 either alone or in combination with Zn in the indicated amount for 24 hr. Cell were harvested and stained with Annexin V and PI and the amount of apoptosis was measured. Mean \pm SE ($n = 5$); *significant difference from DMSO treated cells. Maximum protection was calculated as 90 nM of Zn. **B.** Representative Annexin V-PI FACS analysis showing dose dependent Zn inhibition of apoptosis induced by B-PAC-1.



Supplementary Figure S3: Dose dependent cell death by 066 in MEF cells stably over-expressed with WT Casp3. 0.5×10^6 cells were treated with 10, 15 or 20 μM 066 for 24 hr. Cells were harvested and stained with Annexin V and PI and the amount of apoptosis was measured compared with DMSO control. Mean \pm SE ($n = 5$); IC_{50} value was determined as shown in the inset (15.8 μM)



Supplementary Figure S4: Representative Annexin V-PI FACS analysis of smac mimetic 066 induced cell death. MEF cells stably over-expressed with indicated plasmids were seeded into 6 well plate (0.5 ± 10^6 /well) and treated with 10 µM 066 for 24 hr. Cells were harvested and stained with Annexin V and PI and the amount of apoptosis was measured



Supplementary Figure S5: qRT-PCR expression of Casp3 in vector control, WT and Zn-Casp3 mutant MEFs. Representative snapshot of results of SDS 2.3 software showing amplification curve. Black arrow showed the amplification curves of vector control compared to other MEFs

Supplementary Table S1: List of antibodies and reagents used.

Antibodies/reagents	Source and Catalog #
Casp3	Cell Signaling, 9665
Casp9	Cell Signaling, 9502
Casp6	Cell Signaling, 9762
Casp7	Cell Signaling, 9492
cIAP2	Epitomics, S2700
cIAP1	Abcam, ab2399
Mcl-1	Santa Cruz, S-19
ATM	EMD Millipore, PC116
Smac (DIABLO)	BD Biosciences, 612246
XIAP	BD Biosciences, 610762
Poly (ADP-ribose) polymerase	Enzo Life Sciences, BML-SA250
Cleaved Poly (ADP-ribose) polymerase	Cell Signaling, 9541
Rabbit HA	Bethyl Lab., A190-108P
Mouse FLAG	Sigma-Aldrich, F1804
GAPDH	Sigma-Aldrich, G8795
Staurosporine	LC Laboratories
Bendamustine	Selleckchem
MK2206	Selleckchem
ABT199	Xcessbio, CA
Annexin V fluorescein isothiocyanate (FITC),	BD Biosciences
Hoechst 33258	Invitrogen
Zinc sulfate heptahydrate (Zn. 7H ₂ O)	Sigma-Aldrich
Geneticin® (G418 Sulfate) (50 mg/mL)	Life Technologies (10131-035)
FuGENE6	Promega Inc
cycloheximide	Sigma-Aldrich