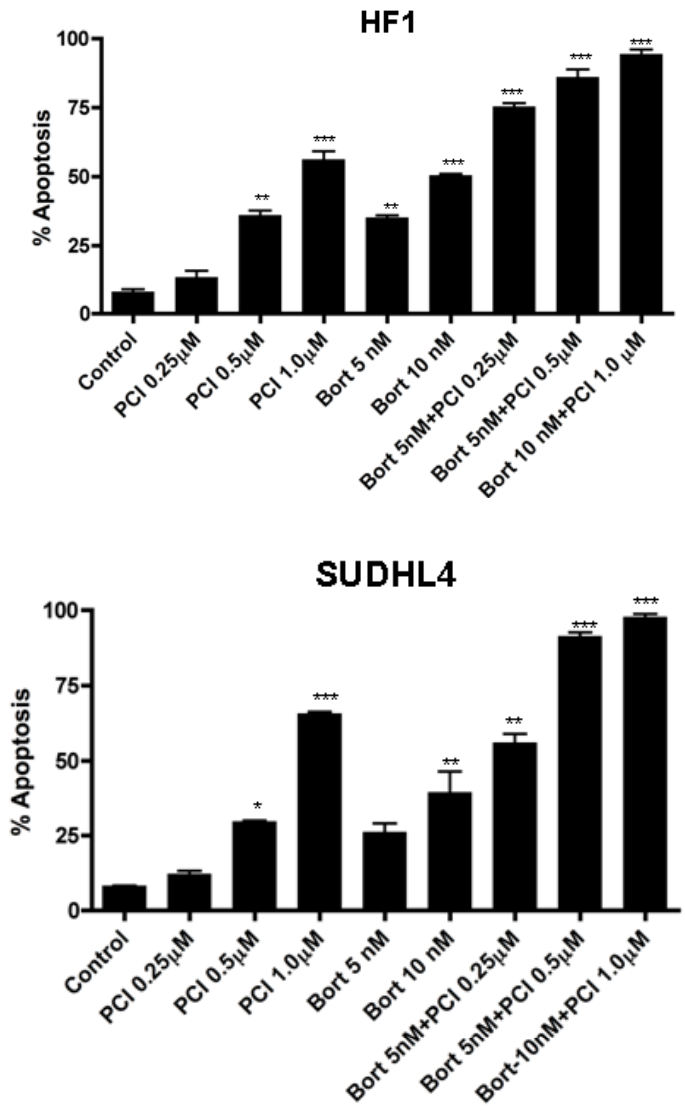
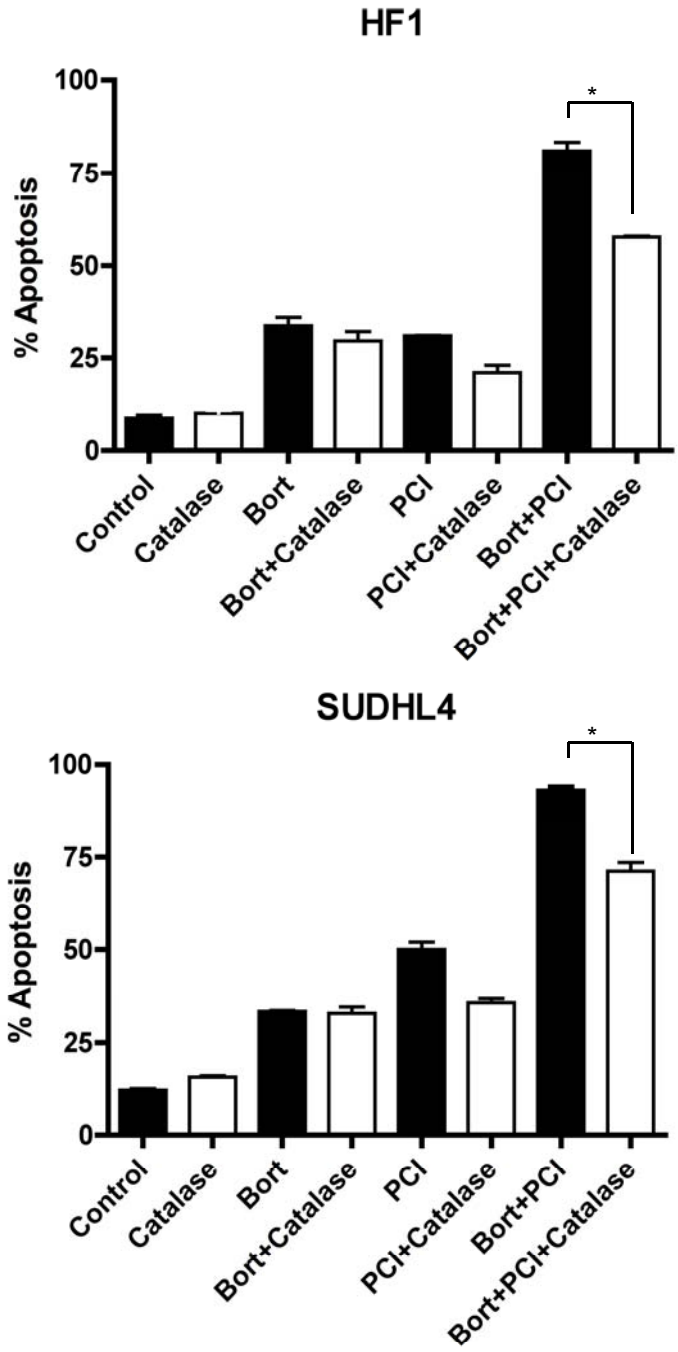
Supplementary Figure S1



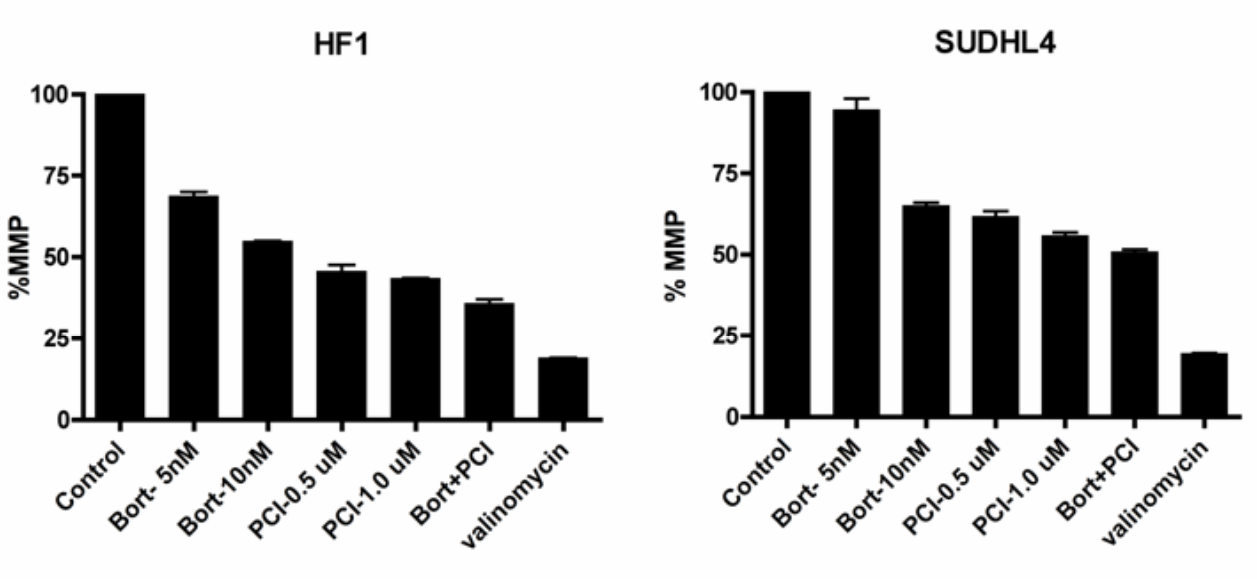
Supplementary Figure S1: Co-treatment with bortezomib enhanced PCI-24781-related apoptosis.HF1 and SUDHL4 cell lines were treated with varying concentrations of PCI-24781 (0.25μM to 1.0μM) and bortezomib (5nM to 10nM) either alone or in combination as indicated for 48 hours. Percentage of apoptotic cells was measured by flow cytometry after Annexin-V/propidium iodide (PI) staining

Supplementary Figure S2



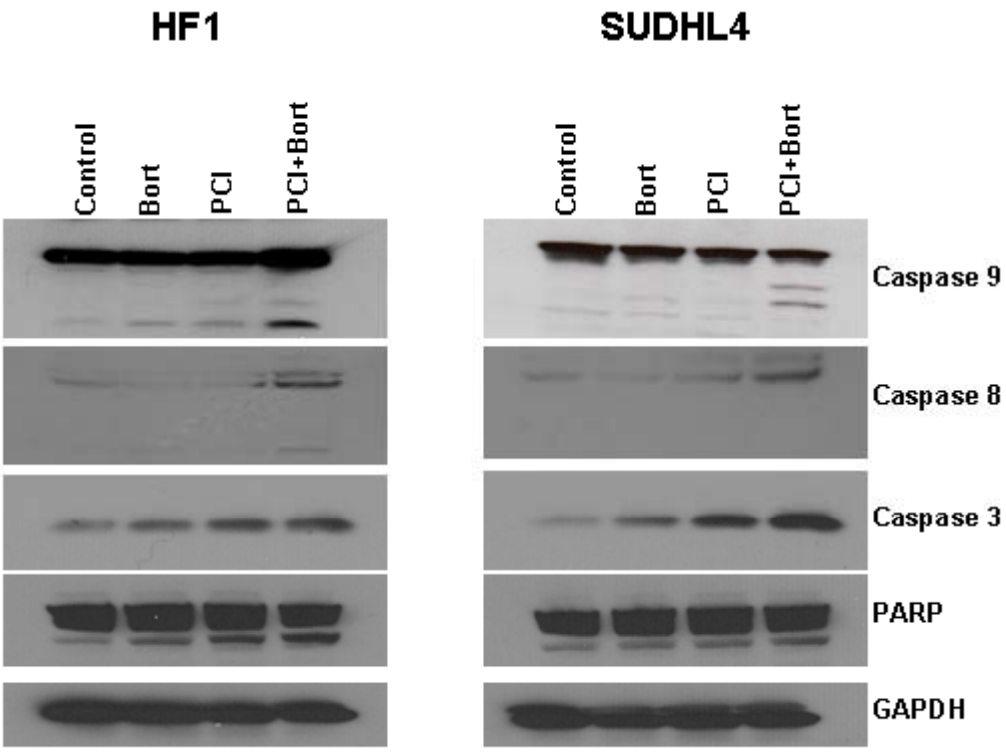
Supplementary Figure S2: Catalase partially inhibited bortezomib and PCI-24781-induced apoptosis in HF1 and SUDHL4 cells. Cells were treated with 4000 units of catalase for 2 hours following incubation with the 5nM bortezomib or 0.5μM PCI-24781 or combination bortezomib/PCI for 48 hours. The percentage of apoptotic cells was determined by annexinV/PI staining followed by flow cytometric analysis. $P<0.05$ for bort/PCI plus catalase as compared to bort/PCI.

Supplementary Figure S3



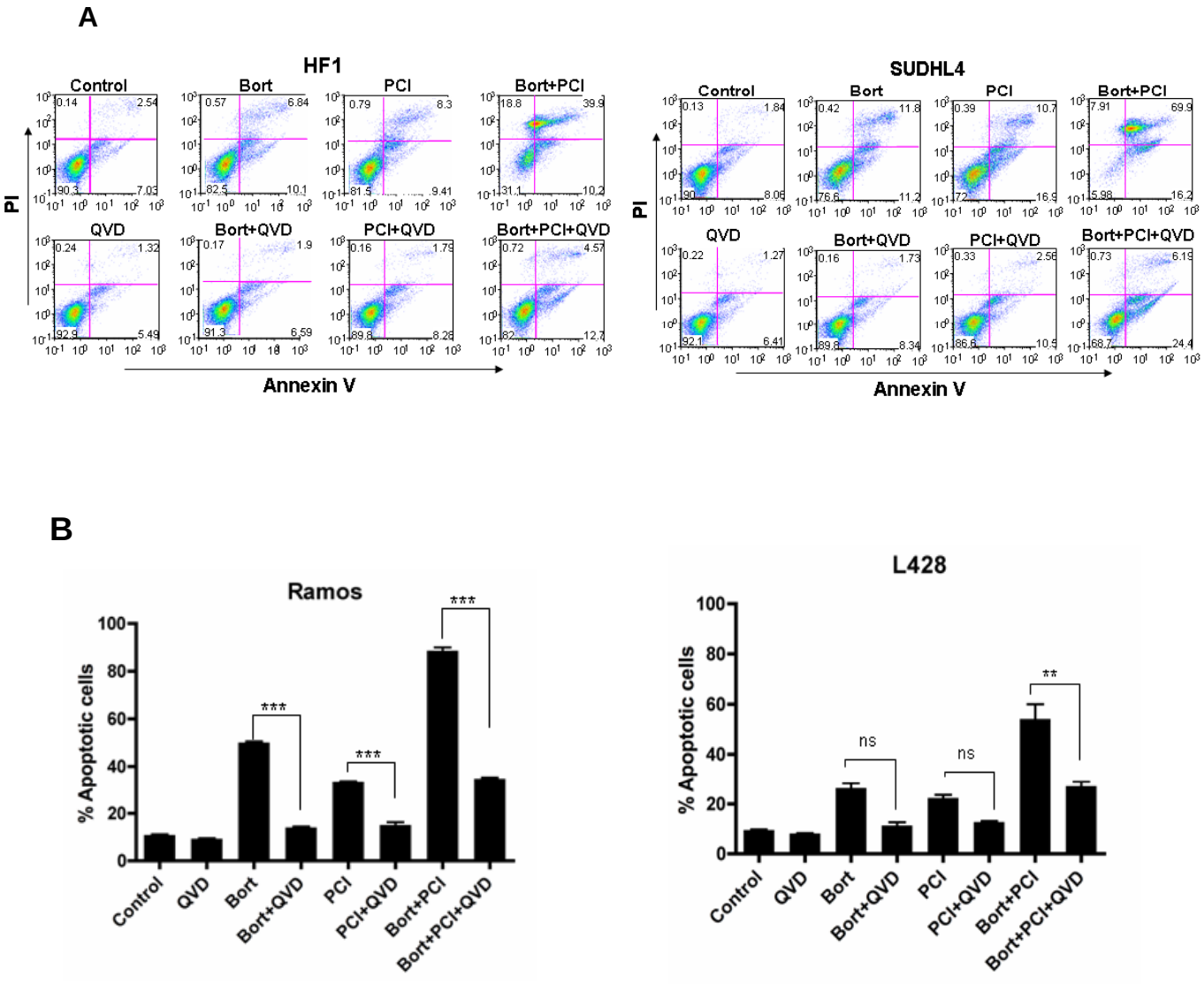
Supplementary Figure S3: HF1 and SUDHL4 cells were treated with indicated concentrations of bortezomib and PCI-24781or combination (5nM bortezomib and 0.5μM PCI) for 24 hours. The percentage of cells exhibiting loss of mitochondrial membrane potential ($\Delta\Psi m$) was determined by JC-1 staining followed by flow cytometric analysis. $P < 0.01$ for PCI/bortezomib combinations as compared to control as well as 5nM bortezomib in HF1 as well as in SUDHL4 cells

Supplementary Figure S4



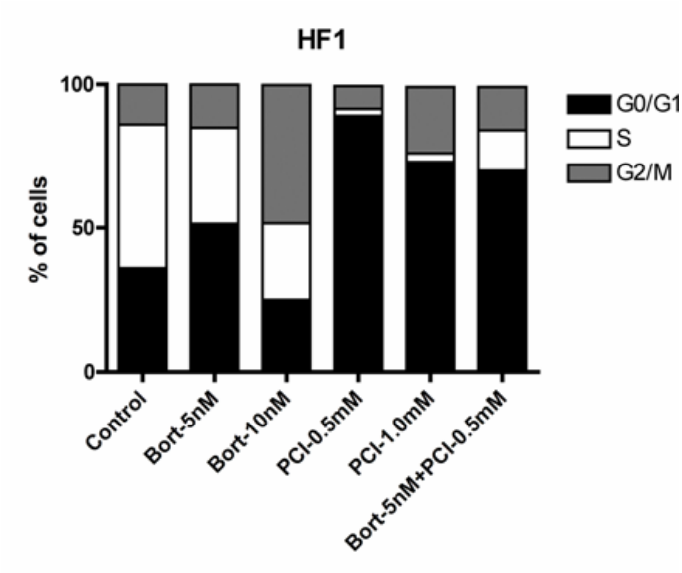
Supplementary Figure S4: Western blot analysis of caspases 3, 9, 8, and PARP activation in HF1 and SUDHL4 cells. Cells were treated with the 5nM bortezomib or 0.5μM PCI-24781 or combination bortezomib/PCI for 24 hours. GAPDH was used as internal control for all Western blots. PCI, PCI-24781; Bort, bortezomib

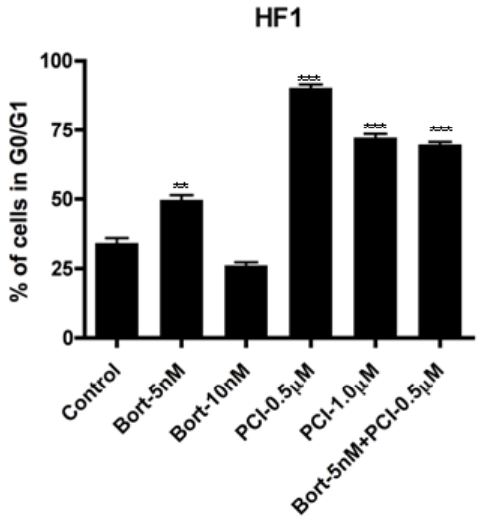
Supplementary Figure S5

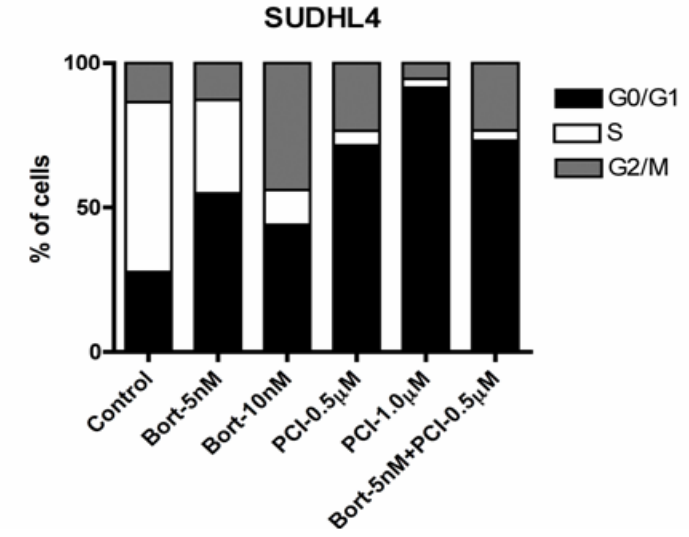


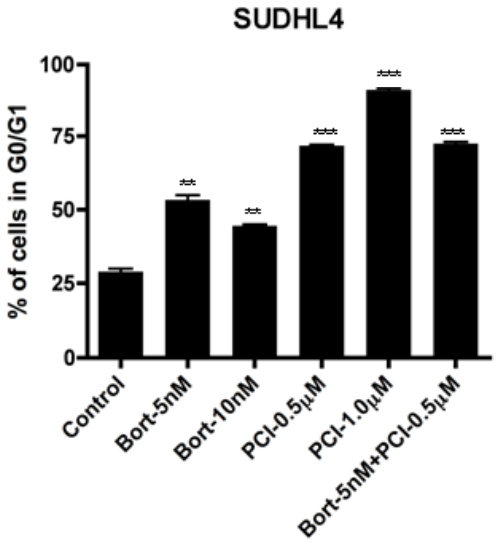
Supplementary Figure S5: The pan-caspase inhibitor, Q-VD-OPh, inhibited bortezomib/PCI-24781-induced apoptosis in HF1,SUDHL4 cells **(A)** and Ramos and L428 cells **(B)** . Cells were treated with either 5 nM bortezomib or 0.5μM PCI or combined bortezomib/PCI-24781 (5nM bortezomib and 0.5μM PCI-2478i) for 48 hours alone (control) or with 4-hour pretreatment with 50μM Q-VD-OPh. Apoptotic cells were detected by annexinV/propidium iodide staining and measured by flow cytometry. *P<0.05, **P<0.01, and ***P<0.001. Unless designated, P values for single-agents reflect bortezomib or PCI-24781 vs control; P values for combinations reflect bortezomib/PCI-24781 vs matching single-agent concentrations. PCI, PCI-24781; Bort, bortezomib. P<0.05

Supplementary Figure S6



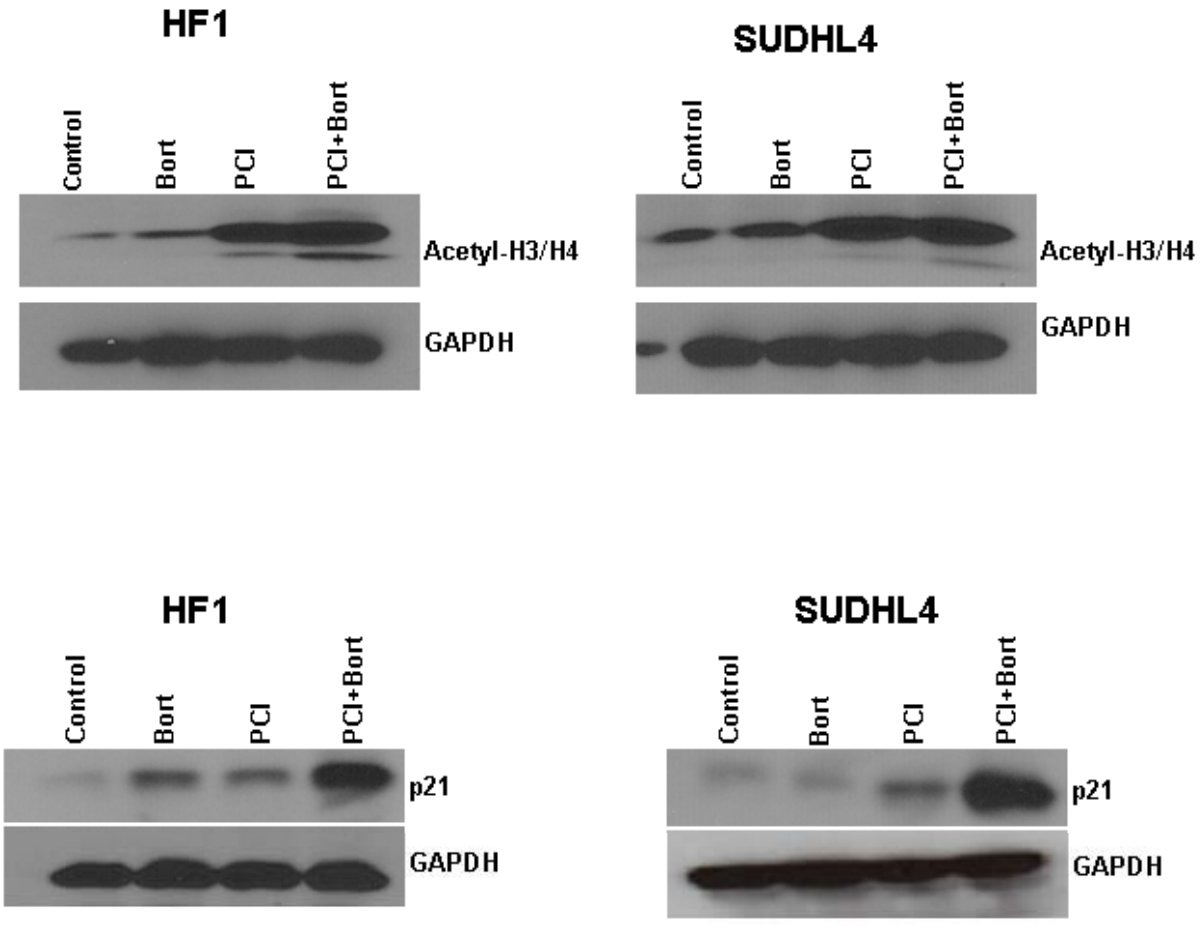






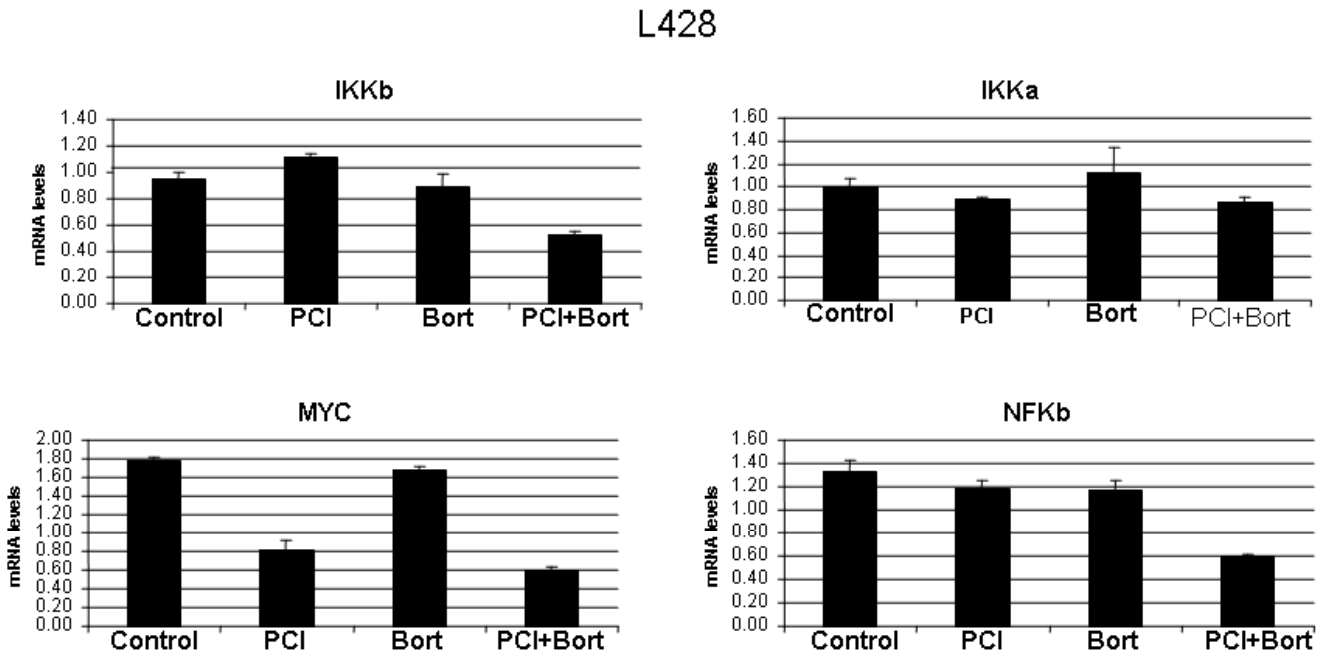
Supplementary Figure S6: HF1 and SUDHL4 cells were treated with the indicated concentrations of bortezomib or PCI-24781 and the combination for 24 hours and then stained with propidium iodide and their cell cycle profiles were examined by flow cytometry.

Supplementary Figure S7



Supplementary Figure S7: Western blot showing histone hyperacetylation and P21 upregualtion in HF1 and SUDHL4 cells. Cells were treated with 5nM of bortezomib and 0.5μM of PCI-24781 or the combination bort/PCI for 16 hours.The level of acetyl histone H3/H4 and p21 protein was measured using antibody as described in the Methods. GAPDH was used as internal control for all Western blots. PCI, PCI-24781; Bort, bortezomib.

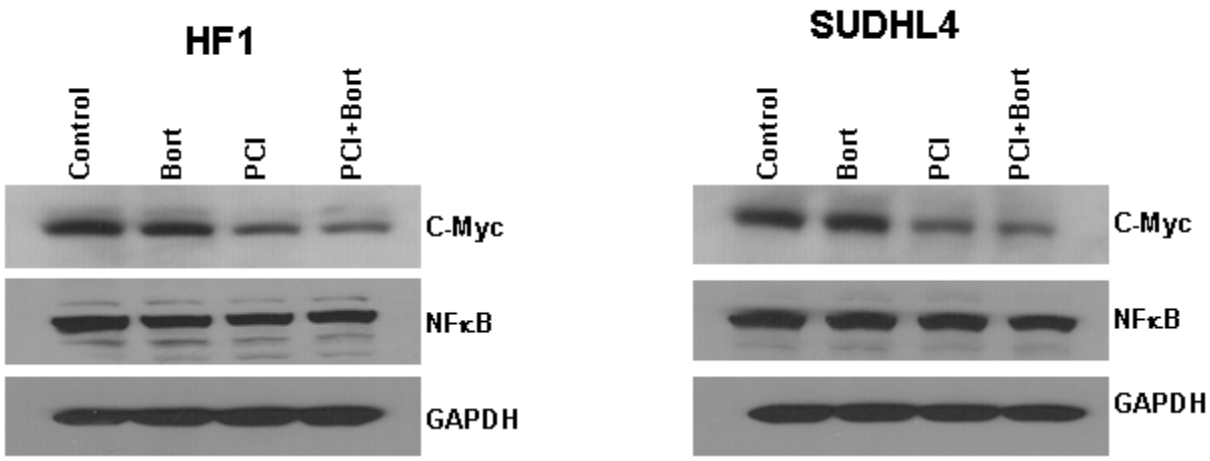
Supplementary Figure S8



P<0.01 for the combination PCI/Bort as compared to control as well as single agent bortezomib and PCI for NFkB and IKKb and MYC. P<0.05 for combination as compared to control and bortezomib for IKKa.

Supplementary Figure S8: NF-κB1 (p105), c-Myc, IKKα, and IKKβ mRNAs were quantified by RT-PCR. L428 cells were treated with 10 nM bortezomib or 1μM PCI-24781 or the combination for 24 hours.

Supplementary Figure S9



Supplementary Figure S9: Western blot of c-Myc and NF-κB p65 (RelA) protein expression. HF1 and SUDHL4 cells were treated with 5nM of bortezomib and 0.5μM of PCI-24781 or the combination bort/PCI for 16 hours. The level of c-Myc and NF-κB protein was measured using antibody as described in the Methods. GAPDH was used as internal control for all Western blots. PCI, PCI-24781; Bort, bortezomib.