Titles and legends to supplementary figures

Supplentary Figure 1. Fenretinide, bortezomib and thapsigargin induce caspase 3 activity. SH-SY5Y, A375 and SK-MEL-28 cells were treated with fenretinide (SH-SY5Y 5 μM; A375/SK-MEL-28 10 μM), bortezomib (SH-SY5Y 5 nM; A375/SK-MEL-28 30 nM) or thapsigargin (SH-SY5Y 1.5 μM; A375/SK-MEL-28 7.5 μM) for 24 hr. Data are expressed relative to control untreated cells; each point is the mean ± S.E.M, n ≥ 3.

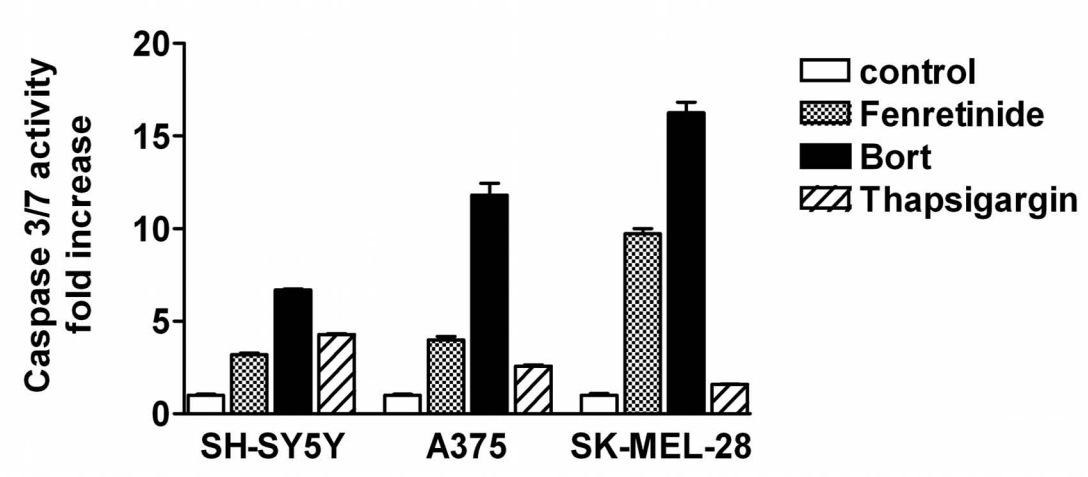
Supplementary Figure 2. A375 cells were transfected with the ATF4 expression vector (pATF4) or control vector (pXL4) prior to treatment with fenretinide (FenR; 15 μM), bortezomib (Bort; 50 nM), or thapsigargin (Thap; 10 μM) for 24 hr. ATF4 and β-actin expression were determined by western blotting, and apoptosis was measured by flow cytometry of propidium iodide stained cells to determine the sub-G1 fraction. Data are expressed as fold change relative to control untreated cells; each point is the mean ± S.E.M, n ≥ 3.

Supplementary Figure 3. Role of c-myc and ATF3 on fenretinide- or bortezomib-induced Noxa expression. *A,* top panel, SK-MEL-28 cells were transfected with siRNAs for c-myc or with a non-silencing control siRNA (ctrl) prior to treatment with fenretinide (FenR; 10 μM) or bortezomib (Bort; 30 nM) for 6 hr. Bottom panel, SH-SY5Y or A375 cells were treated with fenretinide (SH-SY5Y 5 μM; A375 10 μM), bortezomib (SH-SY5Y 5 nM; A375 30 nM) or thapsigargin (SH-SY5Y 1.5 μM; A375 7.5 μM) for 6-24 hr. c-myc, Noxa and β-actin expression were determined by western blotting. *B,* A375 cells were transfected with siRNAs for ATF3, or with a non-silencing control siRNA (ctrl) prior to treatment with fenretinide (FenR; 15 μM), bortezomib (Bort; 50 nM), or thapsigargin (Thap; 10 μM) for 24 hr. Apoptosis was measured by flow cytometry of propidium iodide stained cells to determine the sub-G1 fraction. Data are expressed as percentage total population; each point is the mean ± S.E.M, n ≥ 3. *C,* A375 cells were transfected with siRNAs for ATF3, or with a non-silencing control siRNA (ctrl) prior to treatment with fenretinide (FenR; 10 μM), bortezomib (Bort; 30 nM), or thapsigargin (Thap; 7.5 μM) for 6 hr. ATF3, Noxa and β-actin expression were determined by western blotting. Noxa mRNA was measured by real-time PCR, relative to β-actin as an internal control.

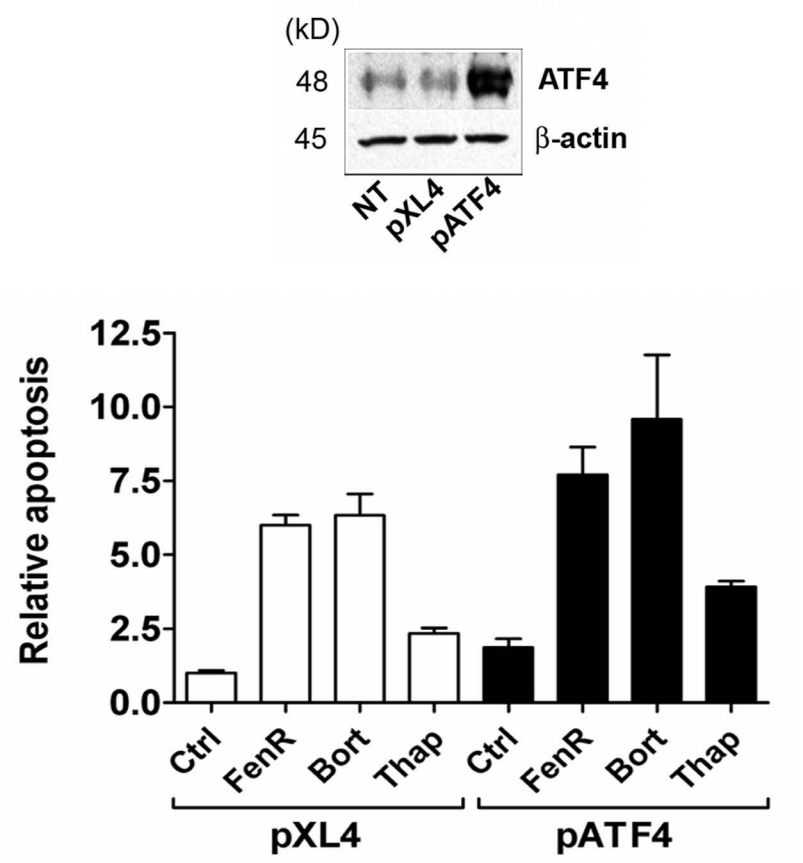
Supplementary Figure 4. Effect of IRE1 or GADD153 knockdown on fenretinide- and bortezomib-induced cell death. *A,* A375 cells were transfected with siRNAs for IRE1, GADD153 (1), or with a non-silencing control siRNA (ctrl) prior to treatment with fenretinide (FenR; 15 μM), bortezomib (Bort; 50 nM), or thapsigargin (Thap; 10 μM) for 24 hr. Apoptosis was measured by flow cytometry of propidium iodide stained cells to determine the sub-G1 fraction. Data are expressed as percentage total population; each point is the mean ± S.E.M, n ≥ 3. *B,* A375 cells were transfected with siRNAs for IRE1, or with a non-silencing control siRNA (ctrl) prior to treatment with fenretinide (FenR; 10 μM), bortezomib (Bort; 30 nM), or thapsigargin (Thap; 7.5 μM) for 6 hr. IRE1α, XBP-1s, Noxa and β-actin expression were determined by western blotting. *C,* A375 cells were transfected with siRNAs for GADD153 (1), GADD153 (2), or with a non-silencing control siRNA (ctrl) prior to treatment with fenretinide (FenR; 10 μM), bortezomib (Bort; 30 nM), or thapsigargin (Thap; 7.5 μM) for 6 hr. GADD153, Noxa and β-actin expression were determined by western blotting. GADD153 and Noxa mRNA were measured by real-time PCR, relative to β-actin as an internal control.

Supplementary Figure 5. Effect of p8 knockdown on the induction of ATF4 by fenretinide and bortezomib. *A,B* A375 cells were transfected with siRNAs for p8, or with a non-silencing control siRNA (ctrl) prior to treatment with fenretinide (FenR; 10 μM), bortezomib (Bort; 30 nM), or thapsigargin (Thap; 7.5 μM) for 6 hr. p8 and ATF4 mRNA were measured by real-time PCR, relative to β-actin as an internal control.

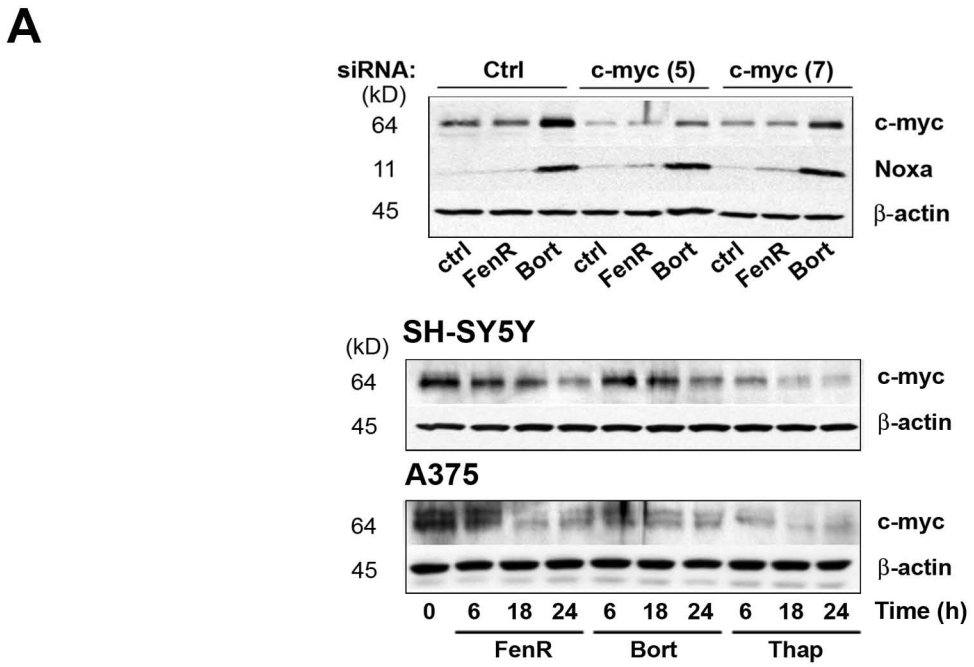
Supplementary Figure 1

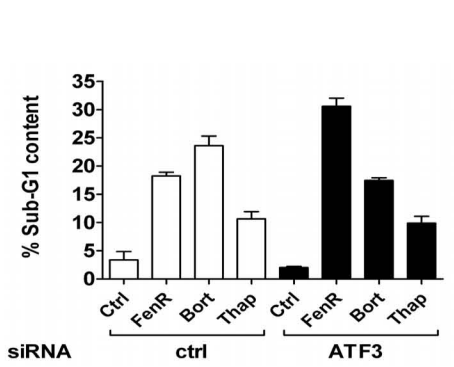


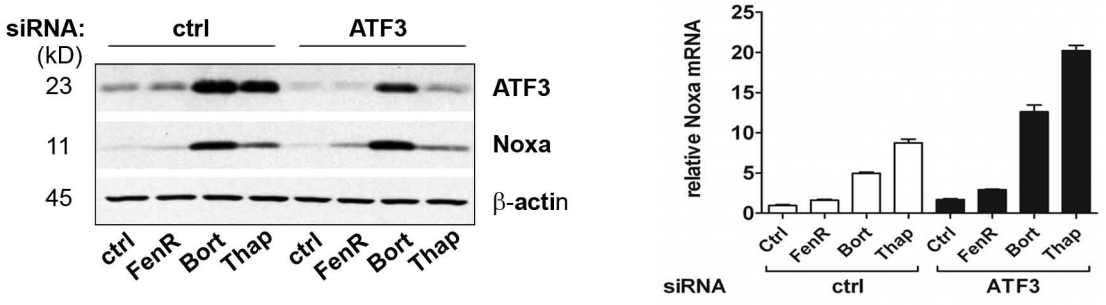
Supplementary Figure 2



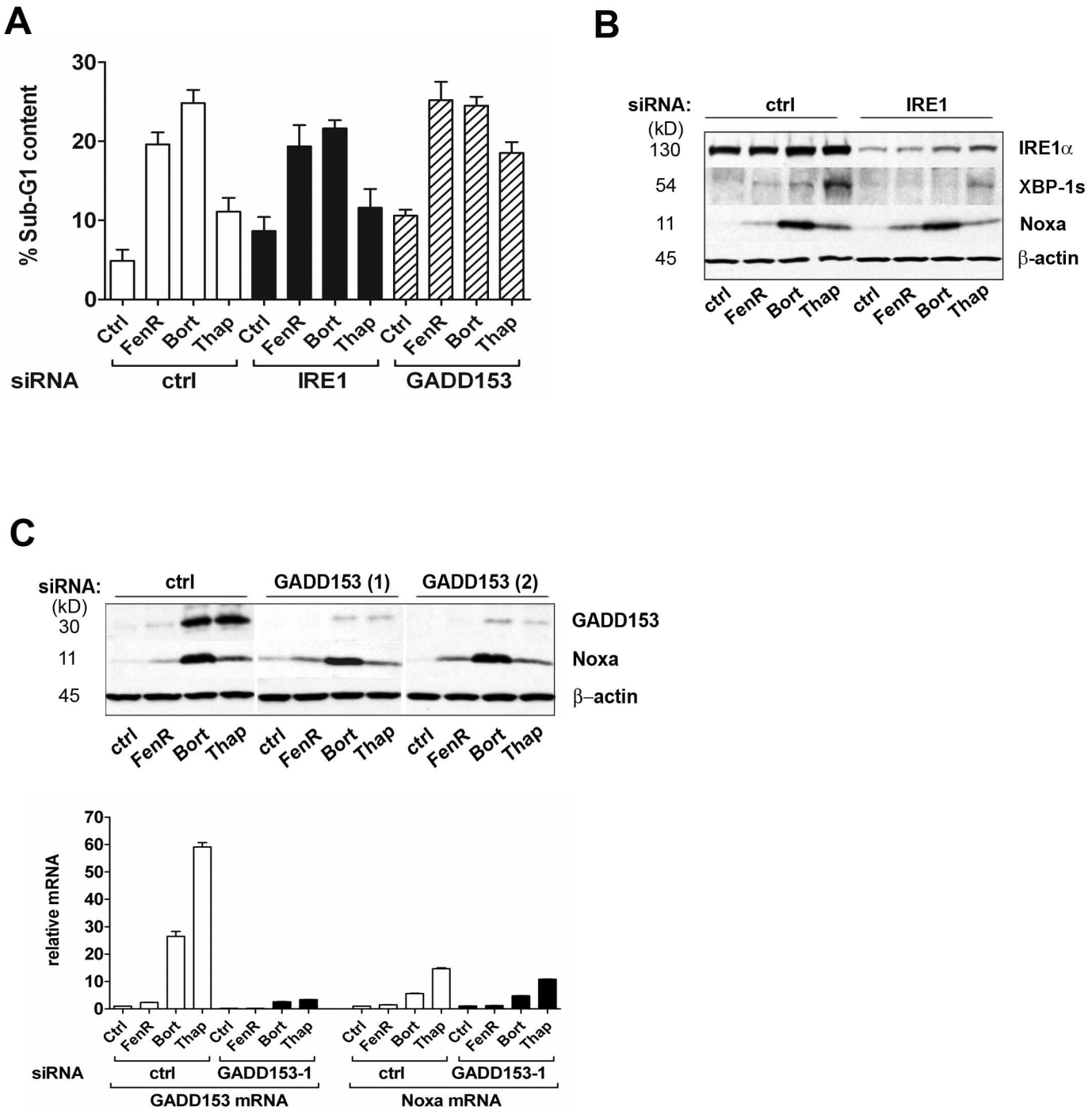
Supplementary Figure 3







Supplementary Figure 4



Supplementary Figure 5