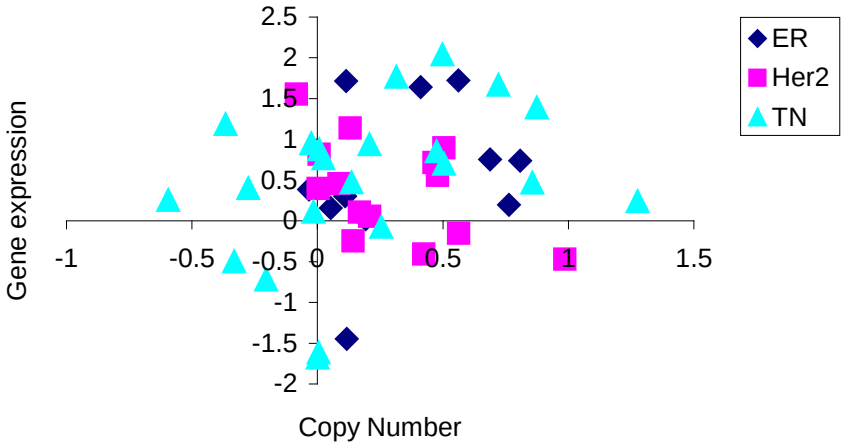
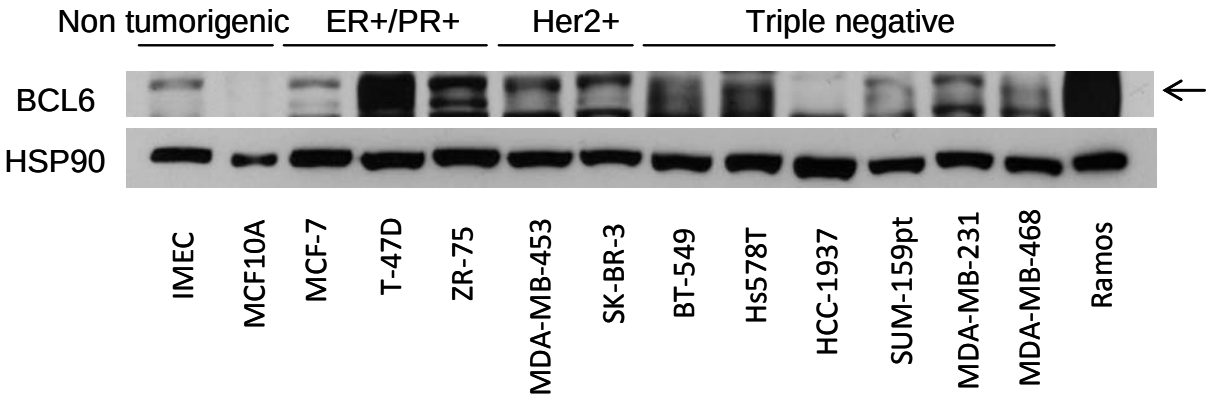
Supplemental Figure 1

A.

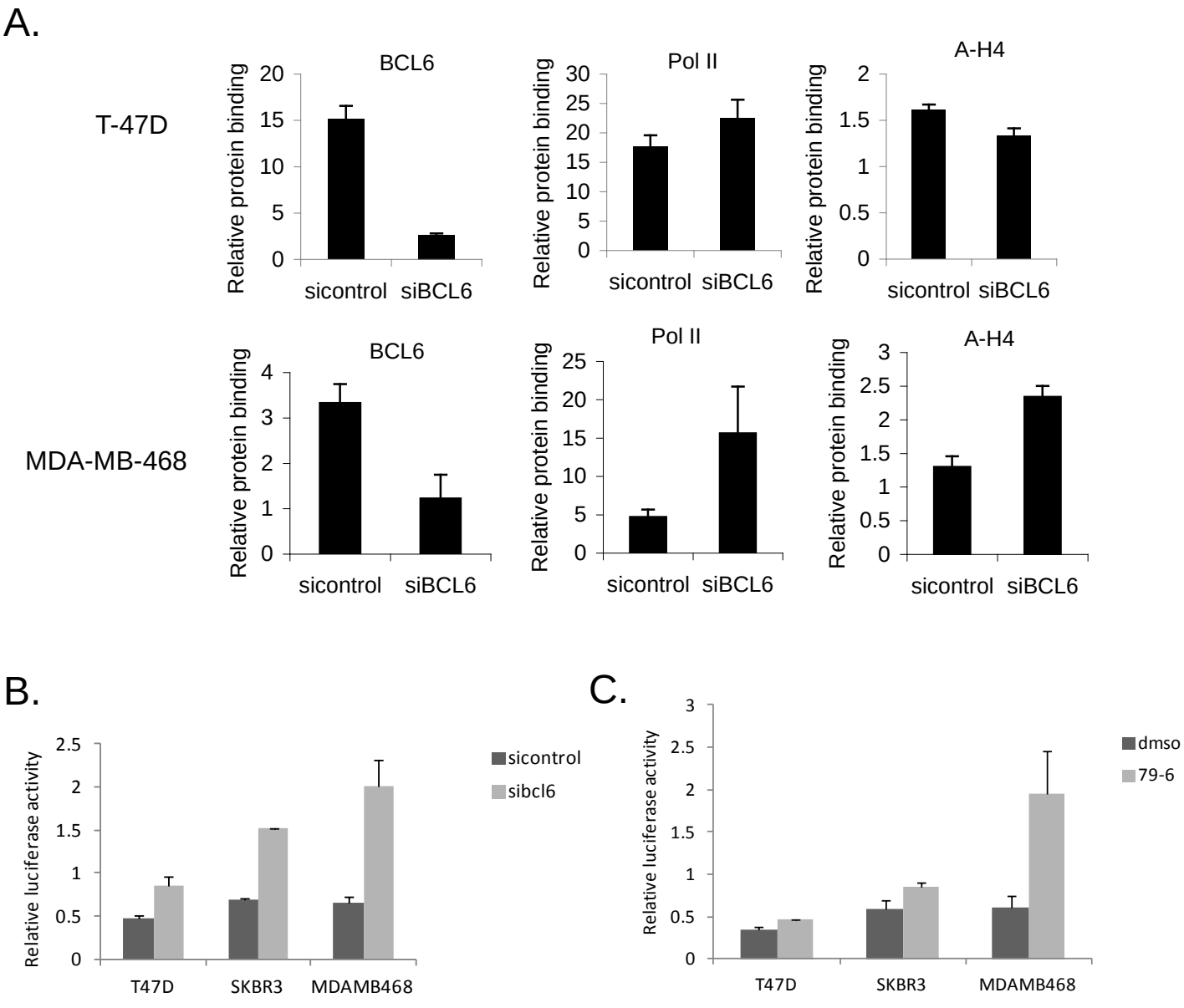


B.



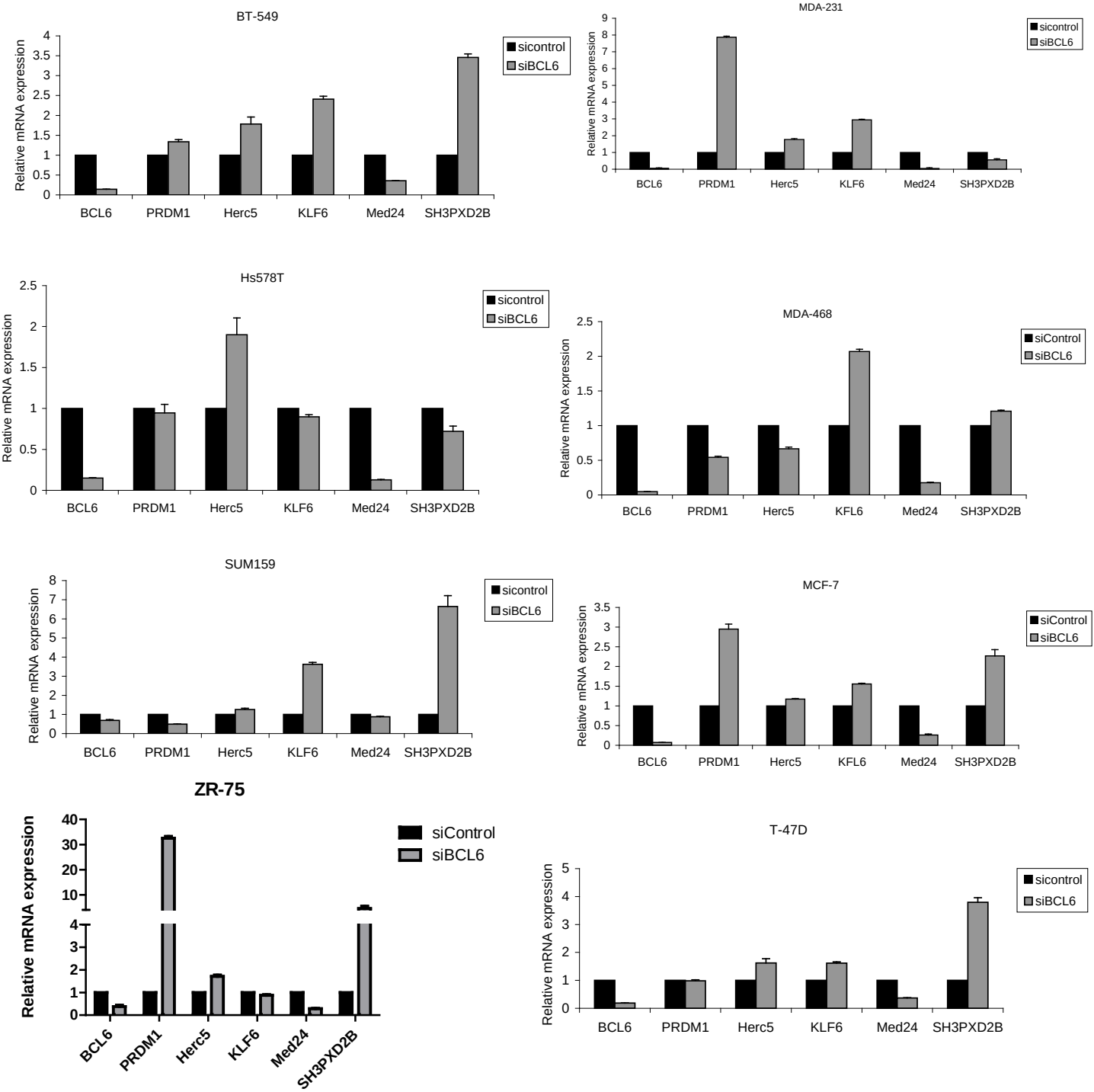
Supplementary Figure 1. BCL6 is amplified in breast cancer cell lines. (A) The BCL6 locus was analyzed for changes in copy number of breast cancer cell lines in the Cancer Cell Line Encyclopedia compared to BCL6 gene expression. Cell lines were separated based on tumor subtype. (ER=ER/PR, Her2, TN=Triple Negative). (B) Eleven breast cancer cell lines, comprising the three major types of breast cancer and two non-tumorigenic breast cell lines were analyzed for BCL6 protein expression by immunoblot. Ramos cell lysates served as a control for BCL6 expression. HSP90 served as a loading control.

Supplementary Figure 2



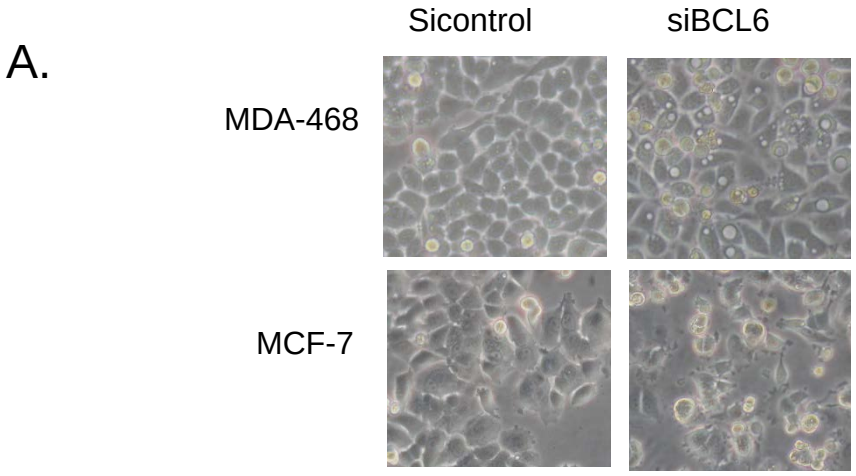
Supplementary Figure 2. BCL6 modulates gene expression in breast cancer cells. (A) T-47D and MDA-MB-468 cells were transfected with siRNA to BCL6 (or control). Cells were then analyzed by ChIP for binding of BCL6, RNA polymerase II, and acetylated histone H4 (A-H4) to region B of the BCL6 gene. Binding is relative to a nonbinding control region. (B) Breast cancer cells were reverse transfected with siRNA to BCL6 (or control) and then transfected with a BCL6-responsive (repressed) luciferase reporter. Luciferase activity was measured 24 hours after plasmid transfection. (C) Breast cancer cells transfected with the BCL6-responsive reporter were treated with vehicle (DMSO) or the BCL6 small molecule inhibitor 79-6 for 16 hour and luciferase activity was measured.

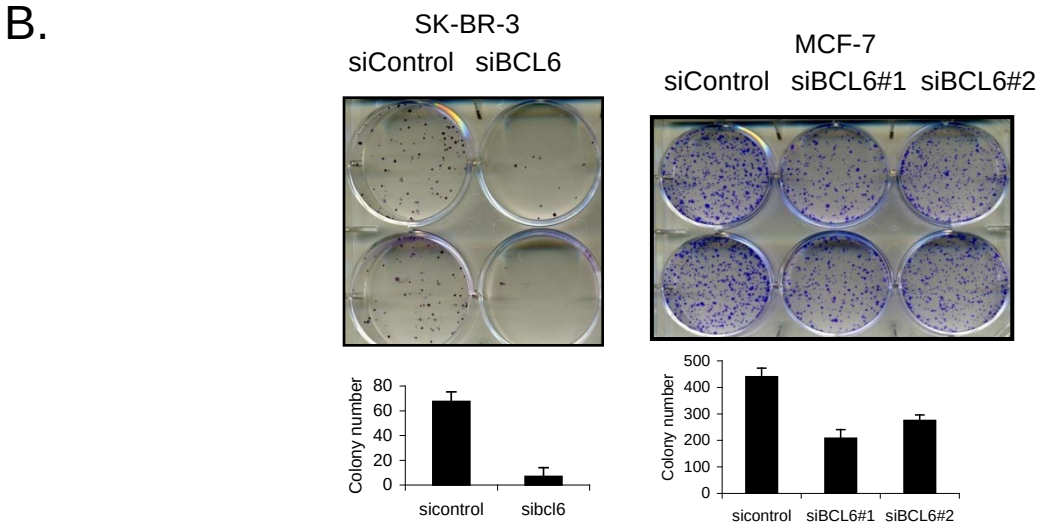
Supplementary Figure 3



Supplementary Figure 3. BCL6-regulated gene expression is similar among breast cancer cell lines. The indicated breast cancer cells were transfected with siRNA to BCL6 and the expression of the indicated genes was analyzed by qRT-PCR. Target gene expression was normalized to HPRT or actin.

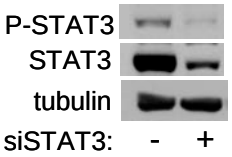
Supplementary Figure 4

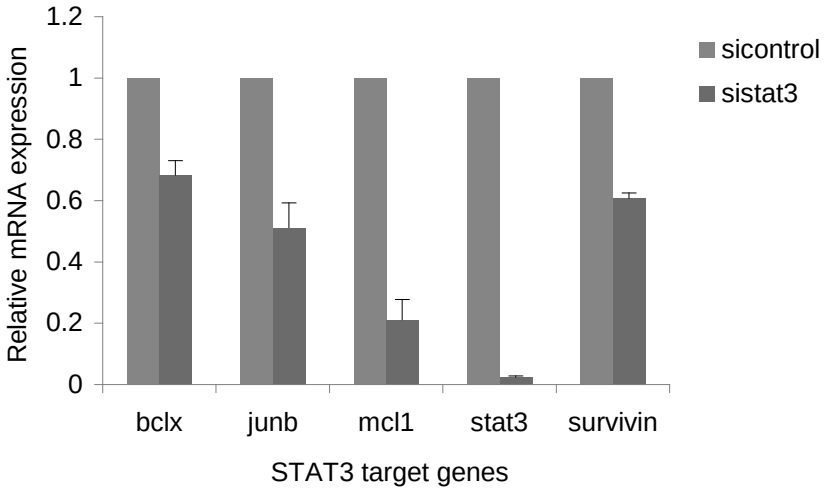




Supplementary Figure 4. BCL6 depletion inhibits breast cancer growth and survival. (A) Breast cancer cells transfected with siRNA to BCL6 were photographed at 48 (MCF-7) and 72 (MDA-MB-468) hours after transfection. (B) Breast cancer cells transfected with siRNA to BCL6 were replated at low density 24 hours after transfection to measure colony formation (top). Quantitation of colony numbers in a representative experiment is shown (bottom).

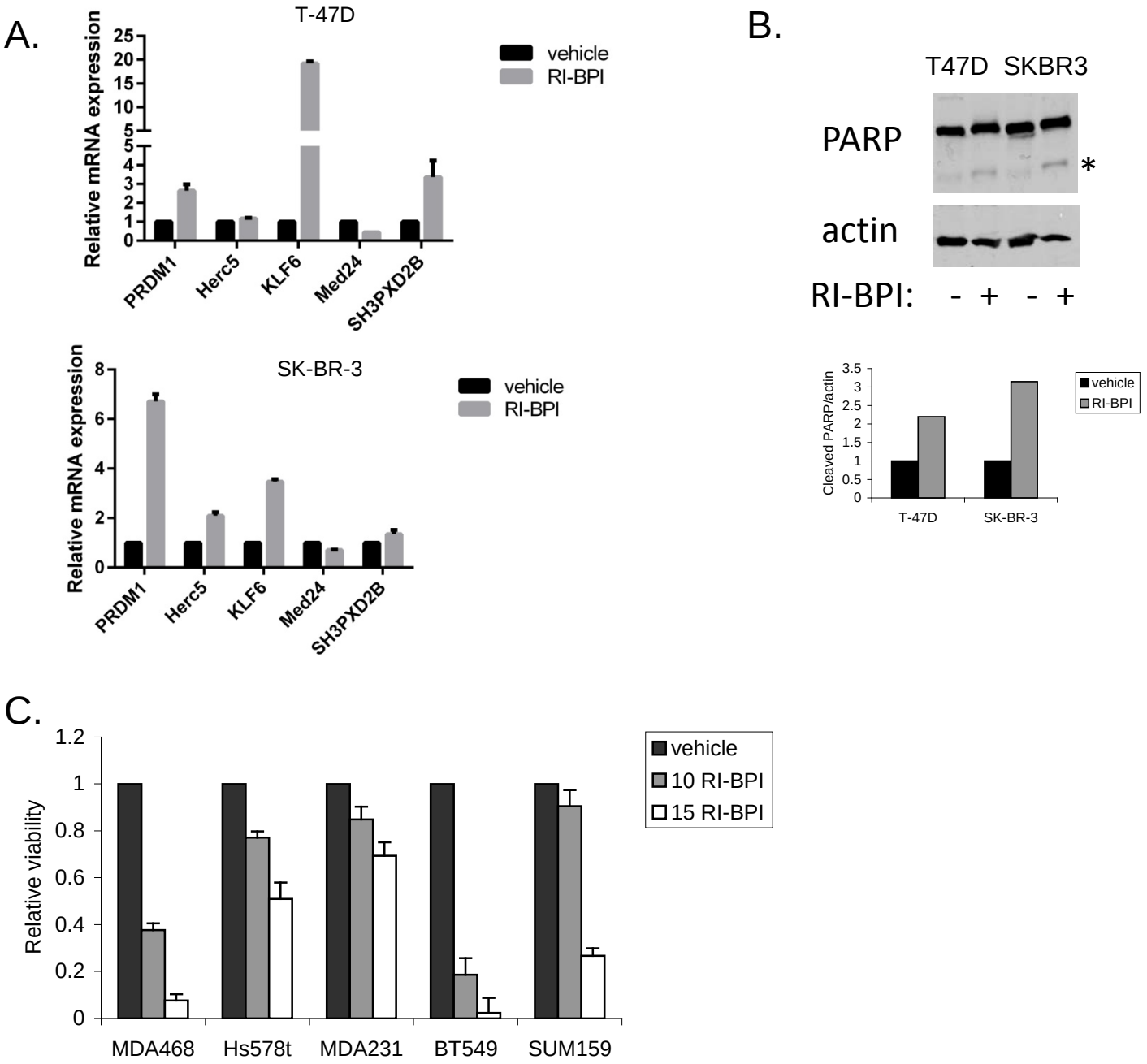
Supplementary Figure 5





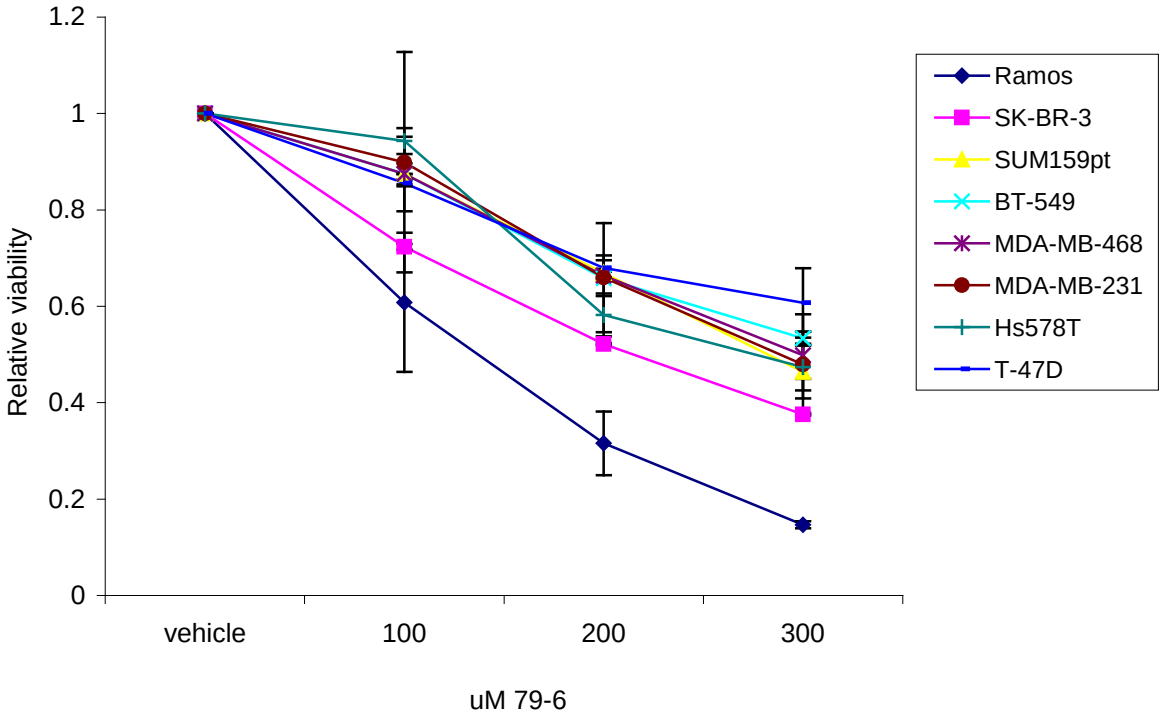
Supplementary Figure 5. MDA-MB-468 cells contain activated STAT3. MDA-MB-468 cells were transfected with siRNA to STAT3. Forty-eight hours after transfection, cells were analyzed for STAT3 activation and expression by immunoblot (left) and STAT3 target genes were analyzed by qPCR (right).

Supplementary Figure 6



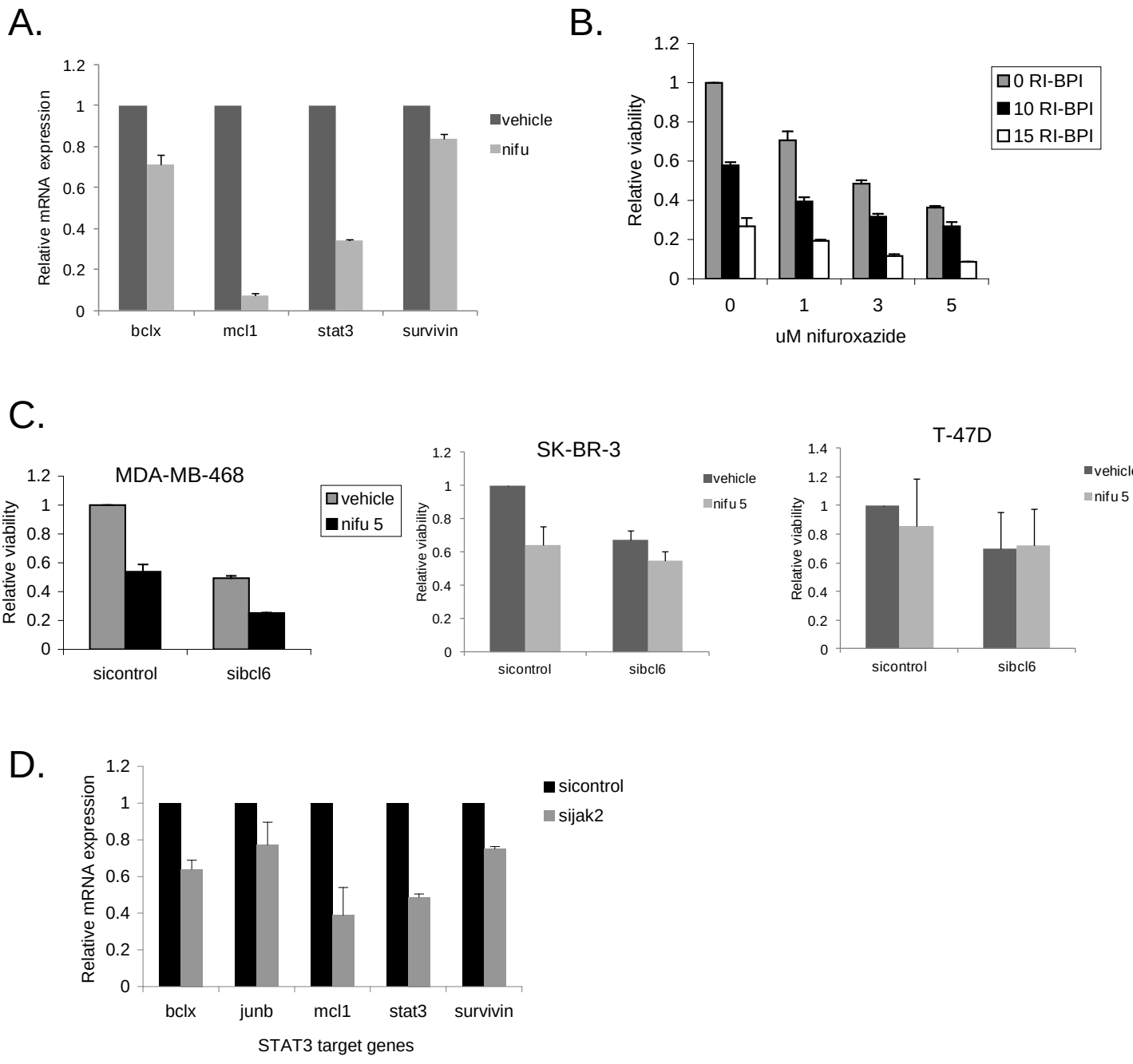
Supplementary Figure 6. The BCL6 peptidomimetic RI-BPI inhibits BCL6 target gene expression and kills breast cancer cells. (A) Breast cancer cells were treated with RI-BPI for 12 hours and BCL6 target genes were analyzed by qPCR. (B) Breast cancer cells were treated with RI-BPI for 48 hours and apoptosis was assessed by analyzing PARP cleavage by immunoblot (top). Actin served as a loading control. Cleaved PARP was quantitated compared to actin (bottom). (C) Triple negative breast cancer cells were treated with the indicated doses of RI-BPI for 48 hours and cell viability was measured by ATP dependent luminescence.

Supplementary Figure 7



Supplementary Figure 7. The BCL6 small molecule inhibitor 79-6 reduces cell viability. Breast cancer cells or Ramos B cell lymphoma cells were treated with the indicated doses of 79-6 for 48h. Cell viability was measured by ATP-dependent luminescence.

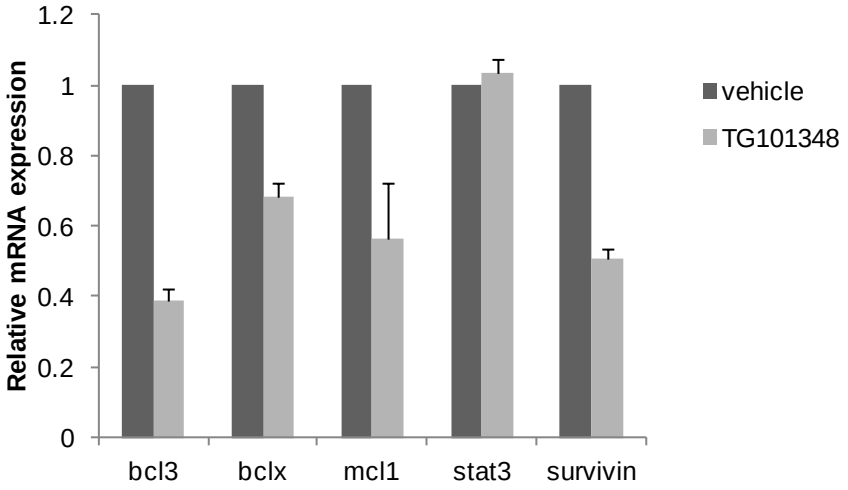
Supplementary Figure 8



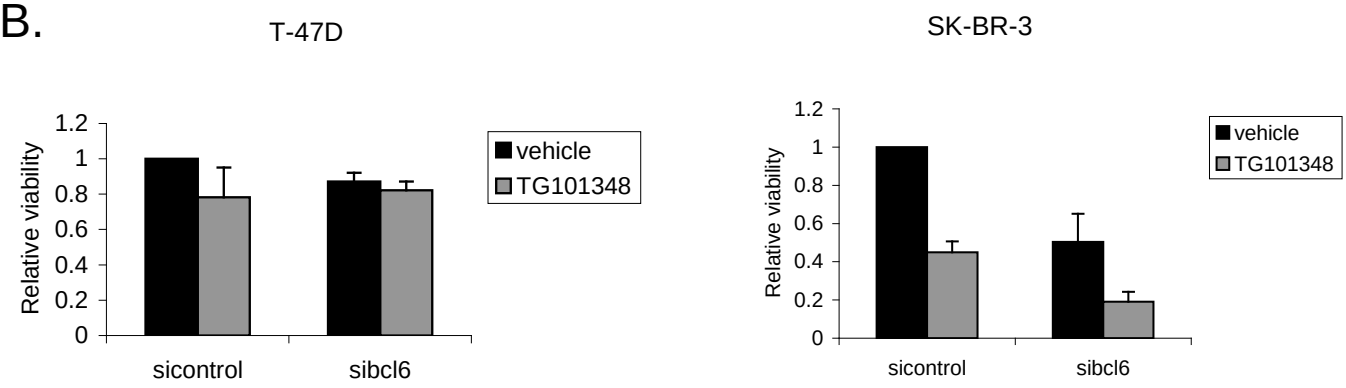
Supplementary Figure 8. STAT3 inhibition combines with BCL6 inhibition to reduce the viability of triple negative breast cancer cells. (A) MDA-MB-468 cells were treated with 5 μM nifuroxazide for 24 hours and STAT3 target gene was assessed by qPCR. (B) MDA-MB-468 cells were treated with RI-BPI, nifuroxazide, or the combination for 48 hours and viable cell number was measured. (C) The indicated breast cancer cells treated with control or BCL6-targeted siRNA were treated with 5 μM nifuroxazide for 48 hours and viable cell number was measured. (D) MDA-MB-468 cells were transfected with siRNA to Jak2 or control for 48 hours after which STAT3 target gene expression was analyzed by qPCR.

Supplementary Figure 9

A.



B.



Supplementary Figure 9. Inhibition of Jak2 combines with inhibition of BCL6 to reduce the viability of cancer cells. (A). MDA-MB-468 cells were treated with 3 μM TG101348 for 24 hours and STAT3 target genes were analyzed by qPCR . (B) Breast cancer cells transfected with siRNA to BCL6 (or control) were treated with 3 μM TG101348 for 48 hours and cell viability was measured by ATP-dependent bioluminescence.