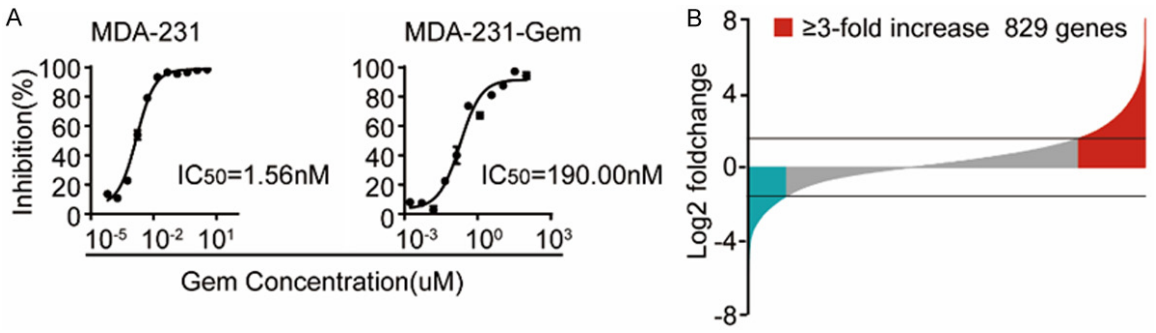
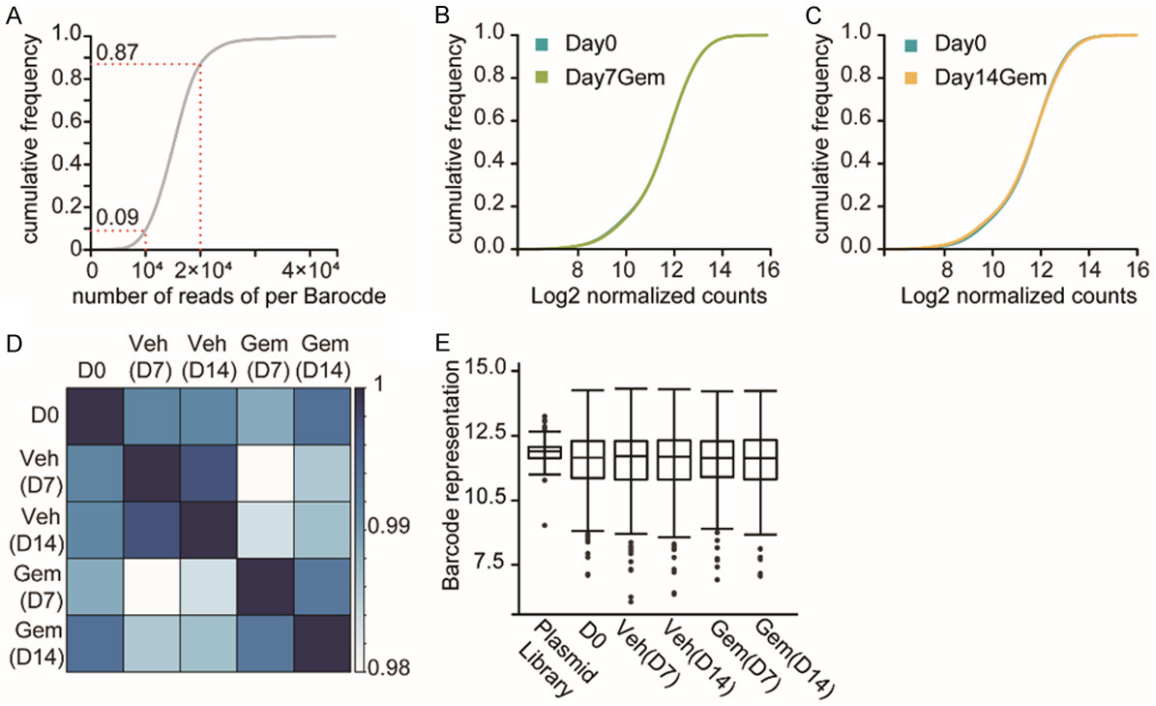
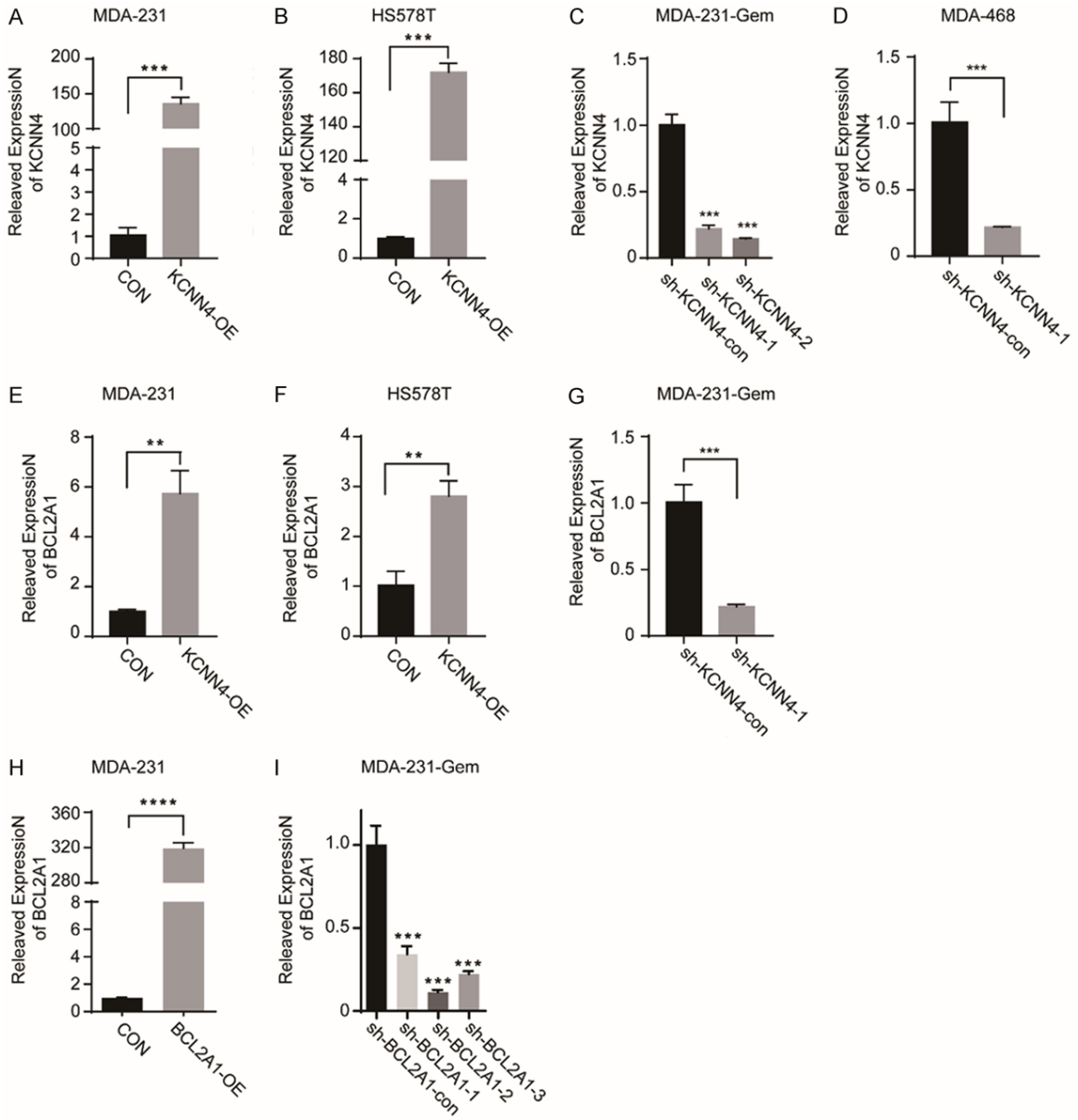


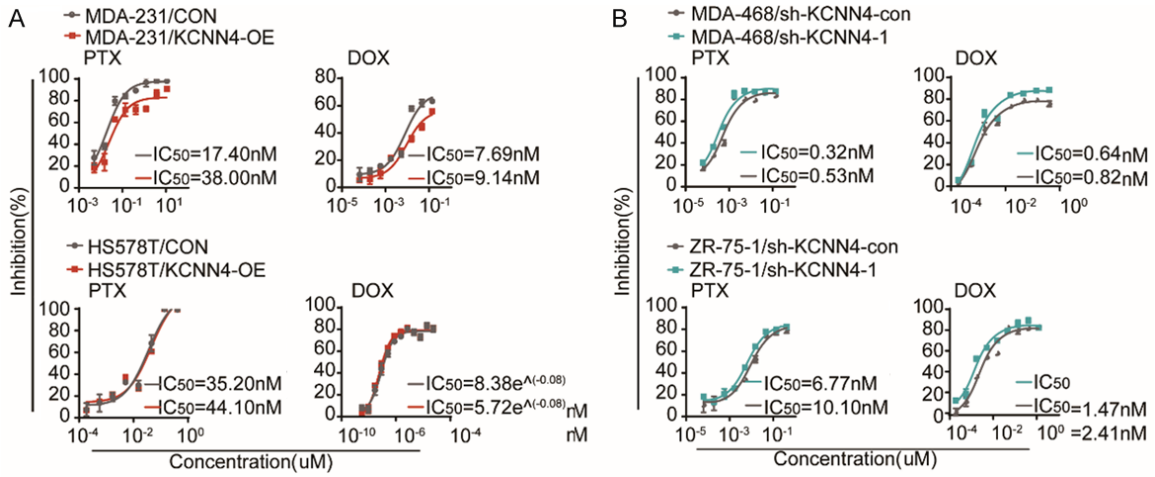
Supplementary Figure 1. Genes associated with gemcitabine resistance based on microarrays conducted in MDA-231-Gem and MDA-231 cells. A. The gemcitabine half-maximal inhibitory concentration (IC50) value for MDA-231-Gem cells compared with parental cells. B. The analysis of expression profile chip showed that there were 829 resistance-related genes. Experiments were done in experimental triplicate and representative results were shown.



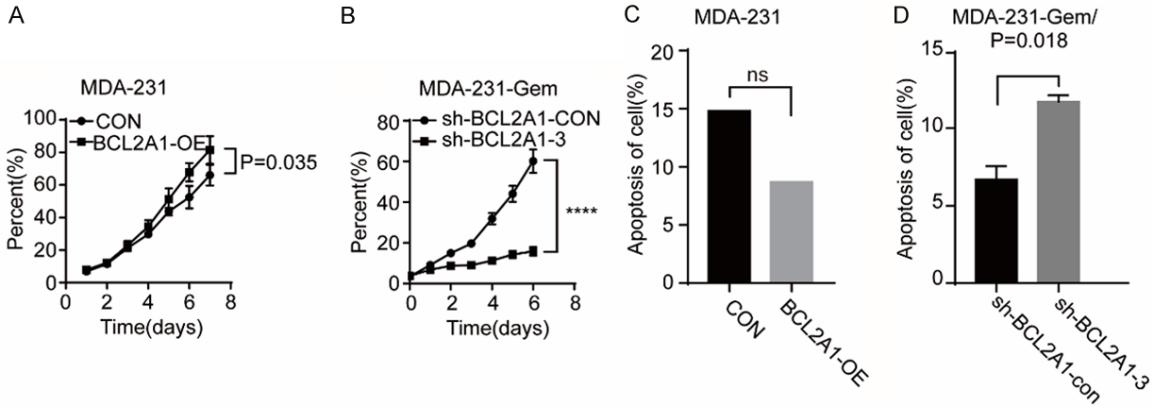
Supplementary Figure 2. Barcode frequency, distribution and correlation analyses of different treatment conditions. A. Cumulative distribution of the number of reads per barcode in GRGB library. 78% of the barcodes detected with 10000-20000 reads. B, C. Cumulative frequency of barcodes in the gemcitabine response assays on Day 0, Day 7 and Day 14 after transduction. D. Rank correlations of normalized read counts between biological replicates and treatment conditions in MDA-231 cells (Veh vehicle, Gem gemcitabine). E. Boxplot showing the distribution of barcode frequencies at different time points, with and without gemcitabine treatment. The box extends from the first to the third quartile with the whiskers denoting 1.5 times the interquartile range. Experiments were done in experimental triplicate and representative results were shown.



Supplementary Figure 3. mRNA levels of target genes were determined by qPCR in difference breast cancer cell lines. GAPDH was used as an internal control. A, B. After being infected with a KCNN4-expressing retrovirus or control retrovirus, the cells were subjected to qPCR. C, D. The mRNA level of KCNN4 in MDA-231-GEM and MDA-468 cell line after infected with sh-KCNN4-expression or -negative lentiviruses. E-G. The mRNA level of BCL2A1 in the above cell lines. H, I. Expression level of BCL2A1 was detected in related cell lines. (**, $P < 0.01$; ***, $P < 0.001$; ****, $P < 0.0001$). Experiments were done in experimental triplicate and representative results were shown.



Supplementary Figure 4. The impact of KCNN4 on sensitivity of breast cancer cells to taxanes. (A) MDA-231 (up) and HS578T (down) cell lines with KCNN4-OE were treated with paclitaxel (left) or docetaxel (right) in an increasing concentration for 4 days, the IC50 were listed. (B) MDA-468 (up) and ZR-75-1 (down) cell lines with KCNN4-knockdown were treated as mentioned in (A) and IC50 was presented.



Supplementary Figure 5. Elevated BCL2A1 expression promotes cell proliferation, inhibits apoptosis. A, B. As the downstream of KCNN4, overexpression of BCL2A1 could promote cell proliferation and knockdown the expression of BCL2Al shown the different effect. C, D. MDA-231/BCL2A1-OE or MDA-231-Gem/sh-BCL2A1-3 cells and the respective control group were treated with 200 nM gemcitabine and incubated for 4 days. The analysis was mentioned in Materials and Methods. (****, $P < 0.0001$). Experiments were done in experimental triplicate and representative results were shown.