Supplementary Materials

Fig S1

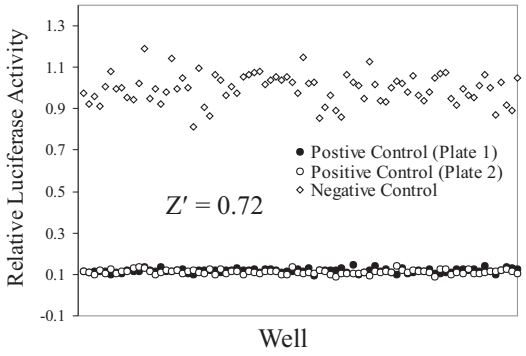

Fig S1. The reporter assay based on the integrated *MDMX* promoter is highly reproducible and suitable for high-throughput drug screening. Recombinant cells carrying the integrated *MDMX* promoter were plated into two 96-well plates, treated with 1 μM of actinomycin D (positive control, 2 plates) or DMSO (negative control, 1 plate) for 6 h, and lysed for luciferase activity assays. The assay results from the two positive-control plates were combined and used to calculate *Z′* as described previously (34).

Fig S2

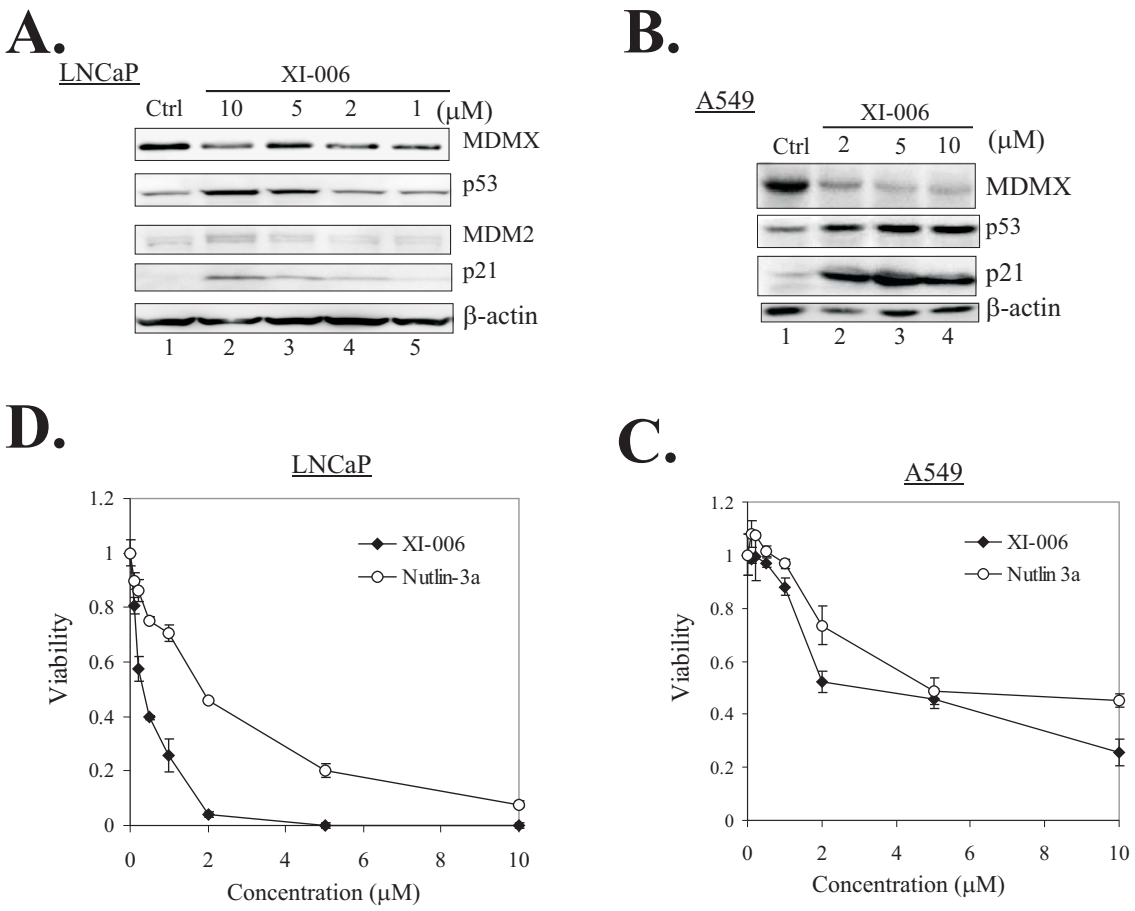

Fig S2. XI-006 activates p53 and induces death of LNCaP and A549. A & B, LNCaP (**A**) or A549 (**B**) cells were treated with XI-006 for 24 h as indicated, and subjected to immunoblotting. **C & D**, LNCaP (**C**) or A549 (**D**) cells were treated with XI-006 for 4 days and subjected to MTT assays to measure cell viability.

Fig S3

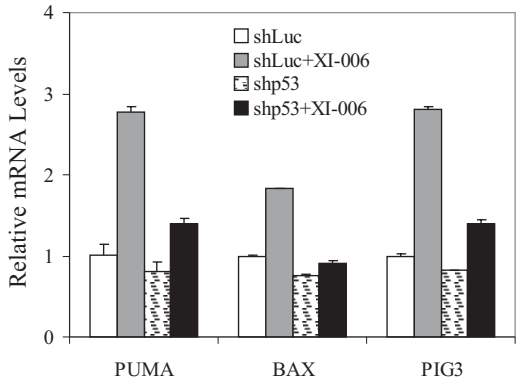

Fig S3. Knockdown of p53 expression impairs proapoptotic gene expression induced by XI-006 MCF-7 cells infected with Lentiviruses expressing a p53-specific shRNA (shp53) or shLuc were treated with 2 μM of XI-006 overnight and lysed for qRT-PCR assays to measure the mRNA levels of the indicated pro-apoptotic genes.

Fig S4

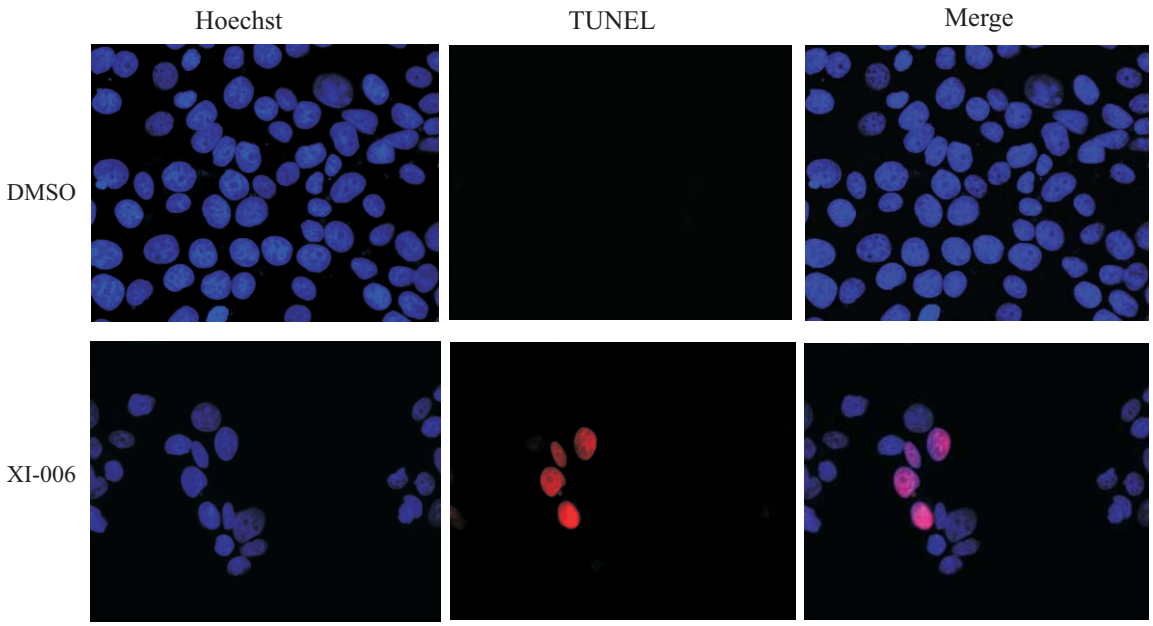

Fig S4. XI-006 induces apoptosis. MCF-7 cells treated with 10 μM of XI-006 or DMSO for 48 h were fixed in 4% paraformadelhyde, and then incubated with TMR Red-labeled dUTP in the presence of terminal deoxynucleotidyl transferase.

Fig S5

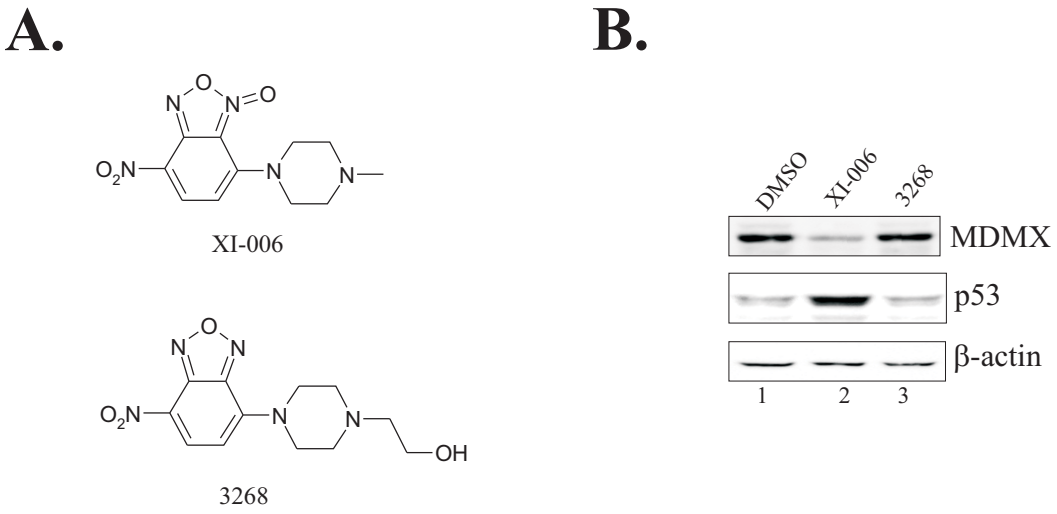

Fig S5. An XI-006 analog incapable of inhibiting *MDMX* expression is devoid of p53-activating activity. A, Structures of XI-006 and the analog. **B,** MCF-7 cells were treated with 5 μM of XI-006 or compound 3268 for 24 h, and subjected to immunoblotting assays.

Fig S6

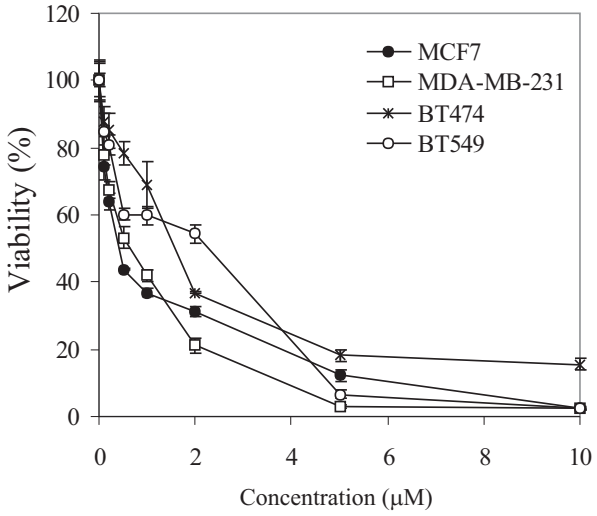

Fig S6. XI-006 decreases the viability of p53-mutated breast cancer cells. The indicated breast cancer cells were treated with XI-006 for 3 days followed by MTT assays to measure cell viability.

Fig S7

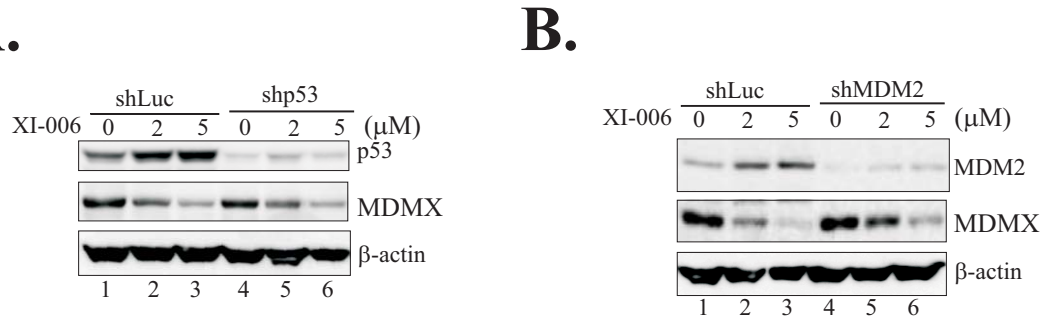

Fig S7. Inhibition of MDMX expression by XI-006 is not a consequence of p53 *trans*-activation or MDM2 induction. MCF-7 cells infected with shLuc, shp53 (**A**), or shMDM2 (**B**) were treated with the indicated amounts of XI-006 for 24 h, and lysed for immunoblotting assays.