Figure S1

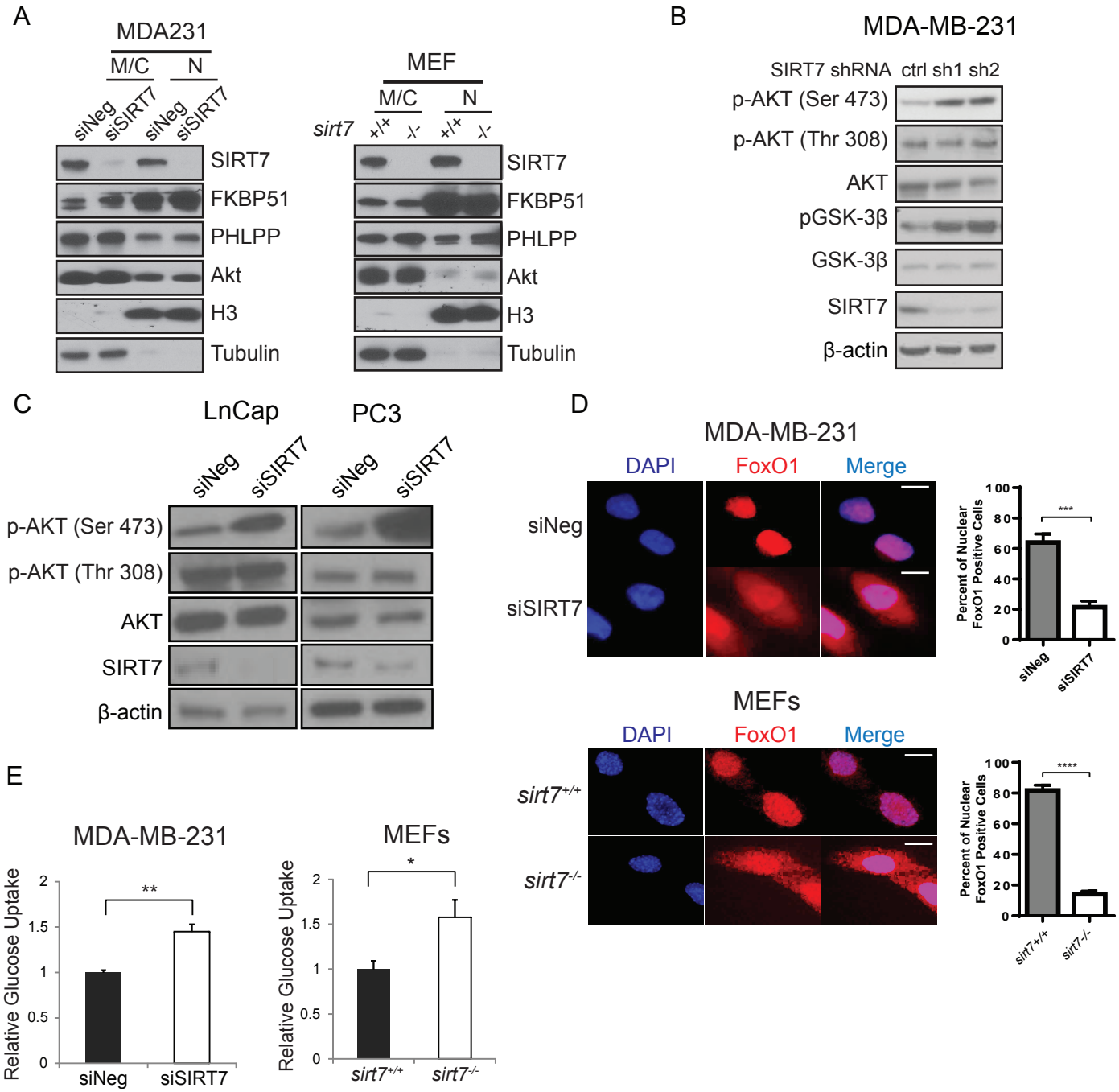

Figure S1 (Related to Fig 2). SIRT7 regulates the phosphorylation of the Akt at Ser473

(A) MDA-MB-231 cells were transfected with SIRT7 siRNAs (siSIRT7) or control siRNA (siNeg) before fractionation. Western blot was performed to analyze SIRT7 protein levels in nuclear and membrane/cytoplasmic fractions of MDA-MB-231 and SIRT7 MEFs. Validation of antibody specificity was done by testing in SIRT7 knock-down cell or SIRT7 knock-out MEF cells.

(B) MDA-MB-231 cells were infected with the indicated shRNA lentivirus and the phosphorylation levels of Akt and GSK-3β in cell lysates were detected by the indicated antibodies.

(C) The prostate cancer cell lines LnCap and PC3 were transfected with control siRNA or SIRT7 siRNA for 72 hours and phosphorylation of Akt in cell lysates was detected by the indicated antibodies.

(D) Immunofluorescence of localization of FoxO1 in MDA-MB-231 cells transfected with SIRT7 siRNA or a control siRNA, or in *sirt7*$^{+/+}$ or *sirt7*$^{-/-}$ MEF cells. Cells are counterstained with DAPI (blue). Scale bar 10 μm. Relative quantification of nuclear only FoxO1 positive cells was normalized to control cells and data represents means ± SE. Comparison was done by 2-tailed *t-test* (***P<0.001, ****P<0.0001)

(E) Glucose uptake in both MDA-MB-231 cells and SIRT7 MEF cells were measured. Relative glucose uptake was normalized to control cells and data represents means ± SE (in 3 replicates). Data were compared with an unpaired 2-tailed *t-test* (*P<0.05, **P<0.01).

Figure S2

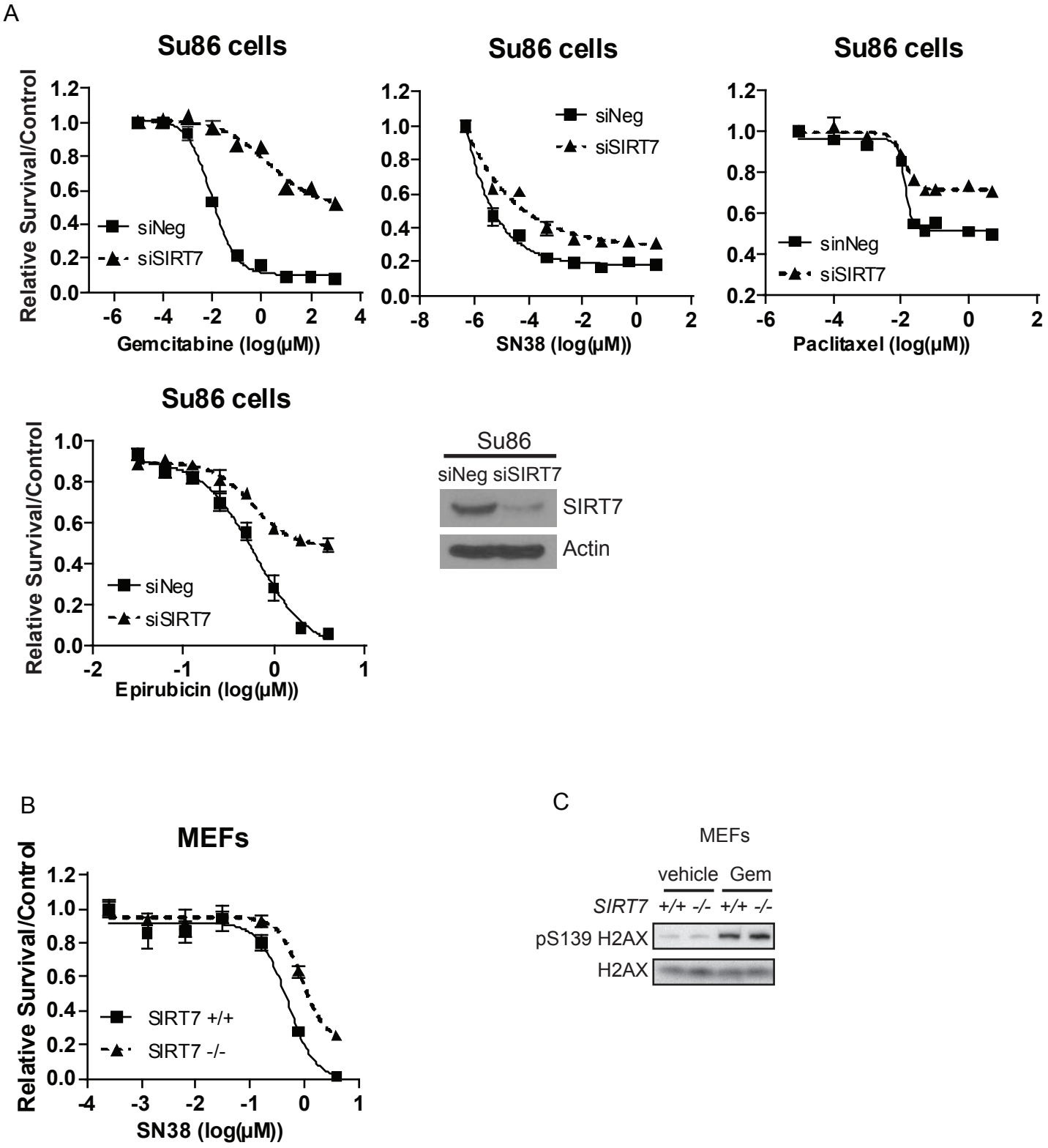

Figure S2 (Related to Fig 3). SIRT7 depletion sensitizes Su86 cells to different genotoxic agents
(A) Su86 cells were transfected with control siRNA or SIRT7 siRNA and were then treated with the indicated drugs for 72 hours. Cell survival was determined by MTS assay. Each point indicates the mean value for three independent experiments. Error bars represent standard error of the mean (n=3).
(B) *sirt7*$^{+/+}$ or *sirt7*$^{-/-}$ cells were treated with the indicated drugs. Cell survival was determined by MTS assay.
(C) Cells treated with vehicle or 1μM gemcitabine for 24 hours and cells were subsequently subjected to western blot.

Figure S3

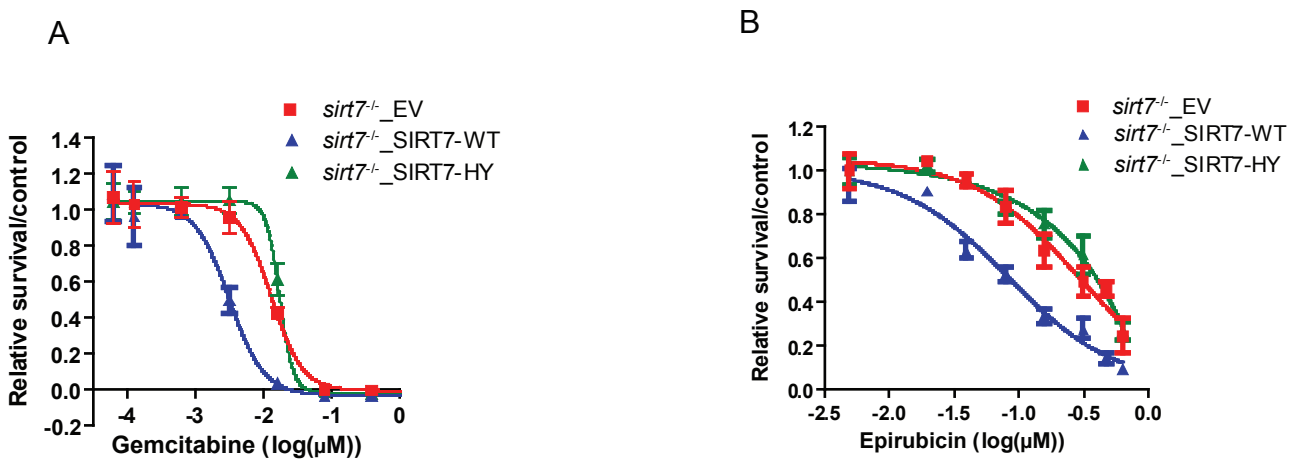

Figure S3 (Related to Fig 3). SIRT7 regulates cell sensitivity to different genotoxic agents
sirt7$^{-/-}$ MEF cells transfected with empty vector (EV), SIRT7 wild type (WT) and SIRT7 H187Y mutants were treated with gemcitabine (A) or epirubicin (B). Cell survival was determined by MTS assay.

Figure S4

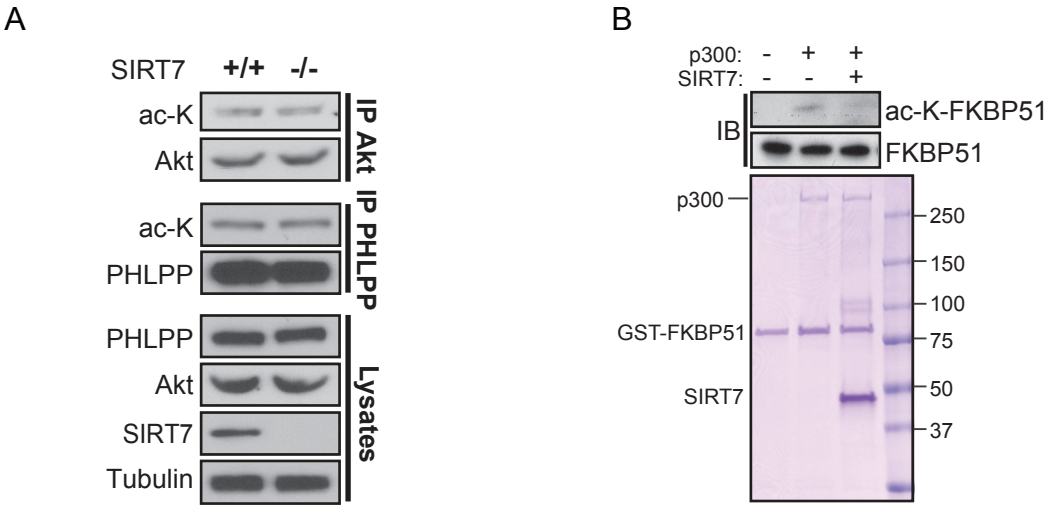

Figure S4 (Related to Fig 5). SIRT7 does not regulate acetylation of Akt or PHLPP
(A) *sirt7*$^{+/+}$ and *sirt7*$^{-/-}$ MEF cells were subjected to IP using anti-Akt or PHLPP antibodies followed by immunoblotting with anti-acetylation antibody.
(B) *In vitro* deacetylation assay demonstrating that p300 acetylates FKBP51 and SIRT7 deacetylates FKBP51.

Figure S5

A

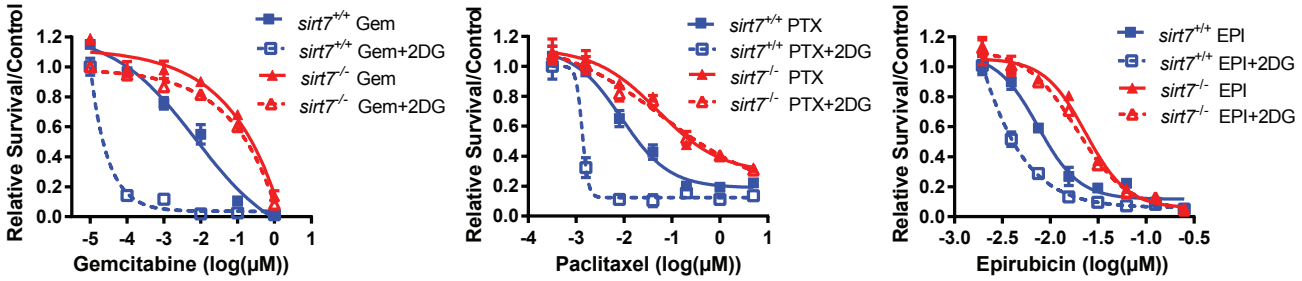

Figure S5 (Related to Fig 7). 2-DG sensitized MEF cells to genotoxic agents
(A) *sirt7*$^{+/+}$ and *sirt7*$^{-/-}$ MEF cells were treated with either the indicated drugs alone or combined with 2 mM 2DG for 72 hours. Cell survival was determined by MTS assays.