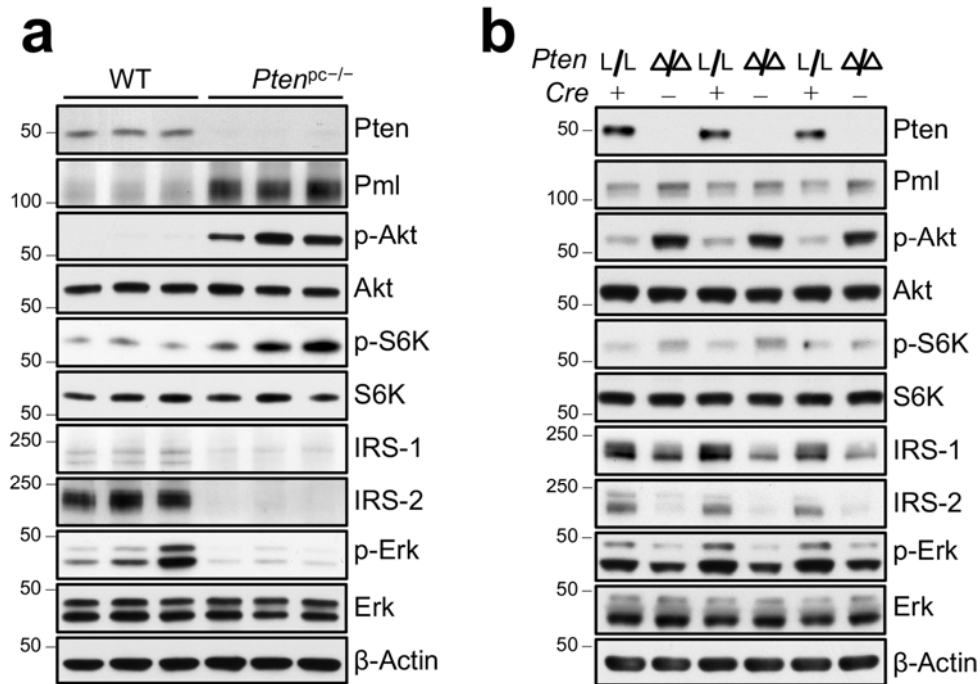
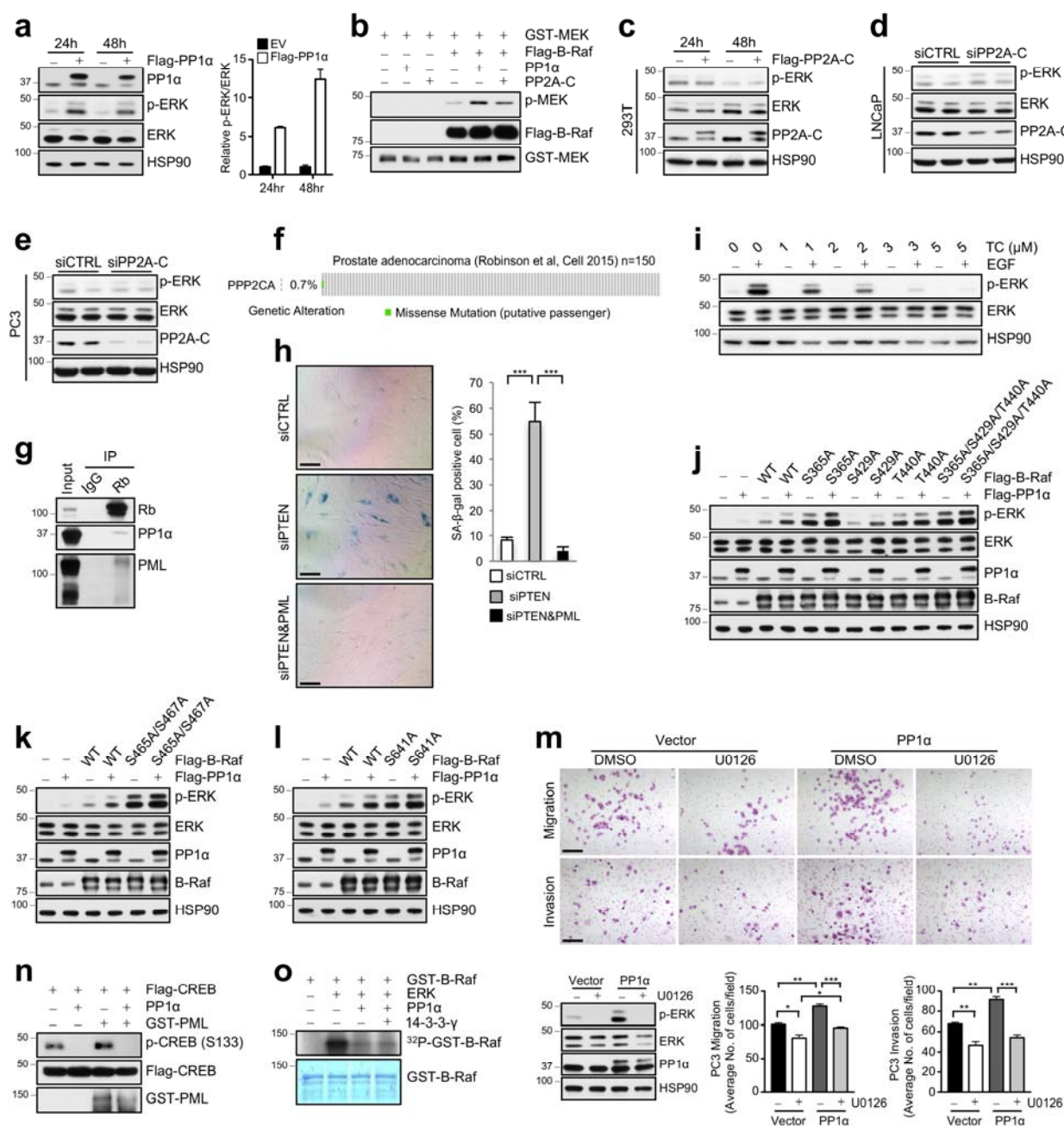




Supplementary Figure 1 *PTEN* loss leads to feedback inhibition of ERK-MAPK signaling.

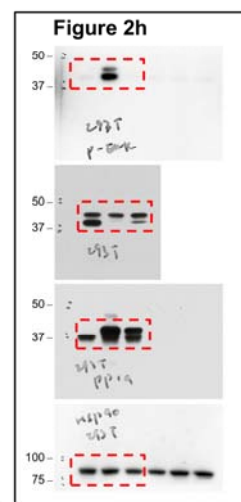
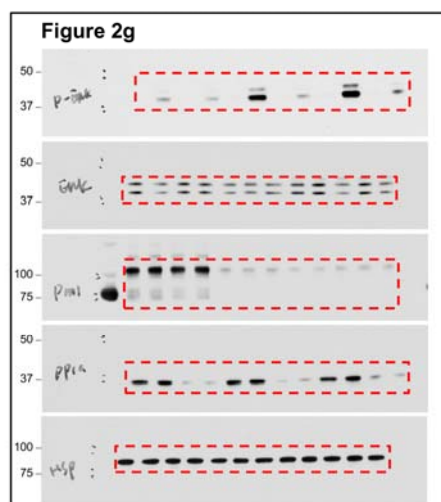
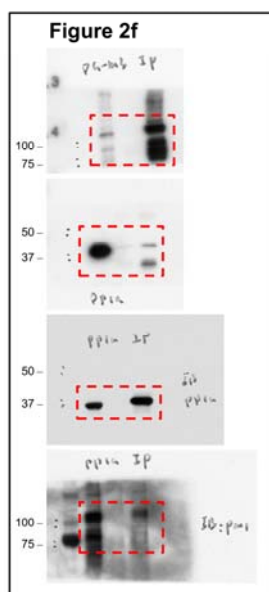
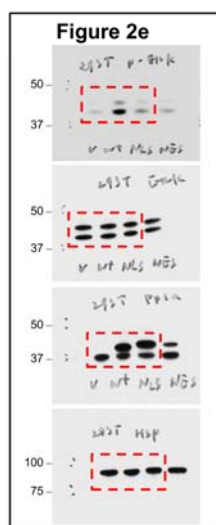
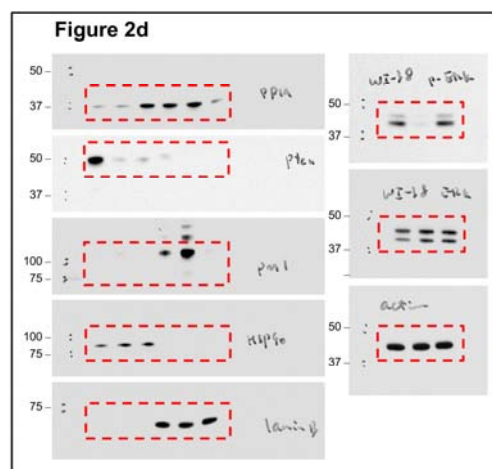
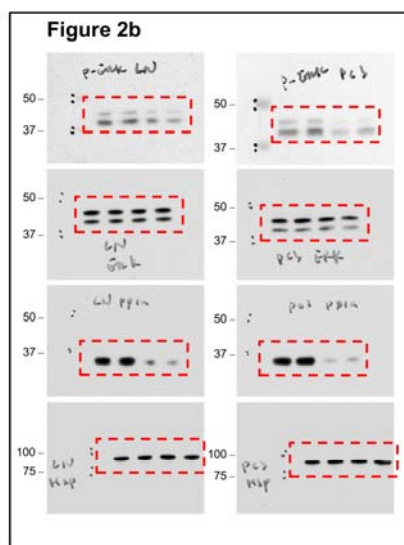
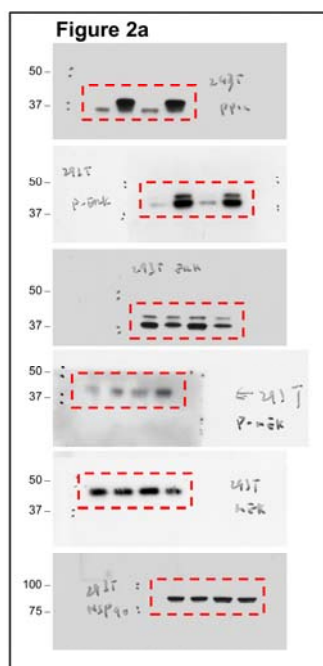
(a,b) IB analysis of dorsal-lateral prostate tissues from wild type and prostate epithelium-specific *Pten* inactivation (*Pten^{pc-/-}*) mice at 12 weeks of age (a), lysates from primary *Pten^{lox/lox}* MEFs transduced with control or *Cre* retrovirus at 72 hrs after selection (b).

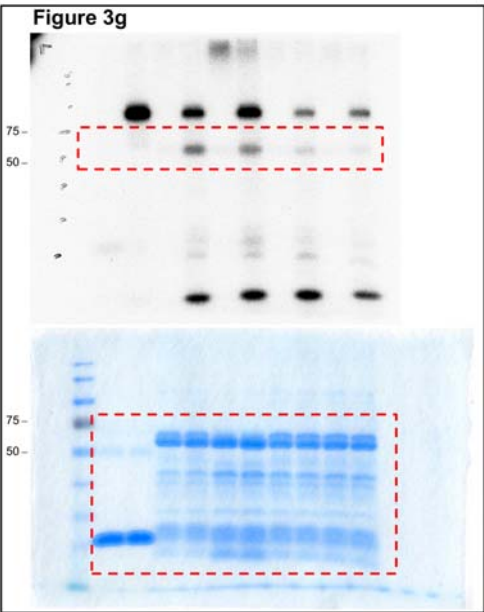
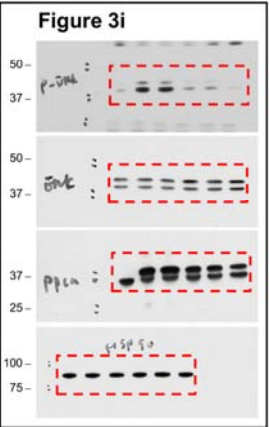
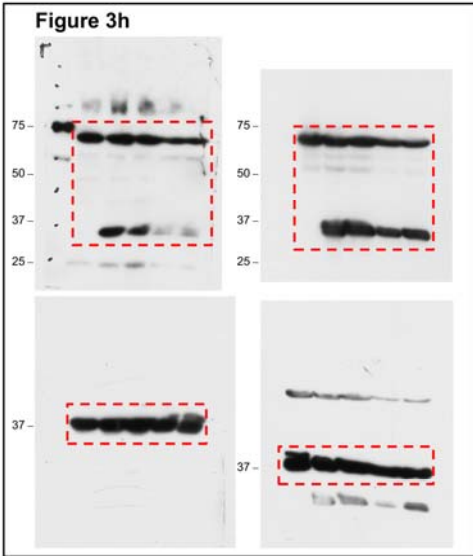
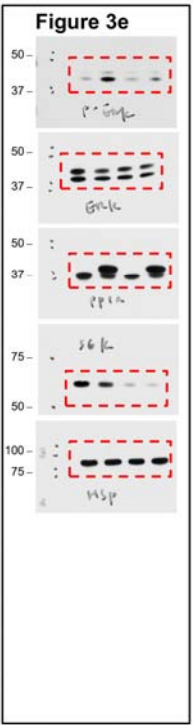
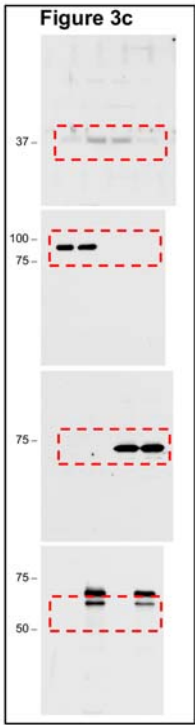
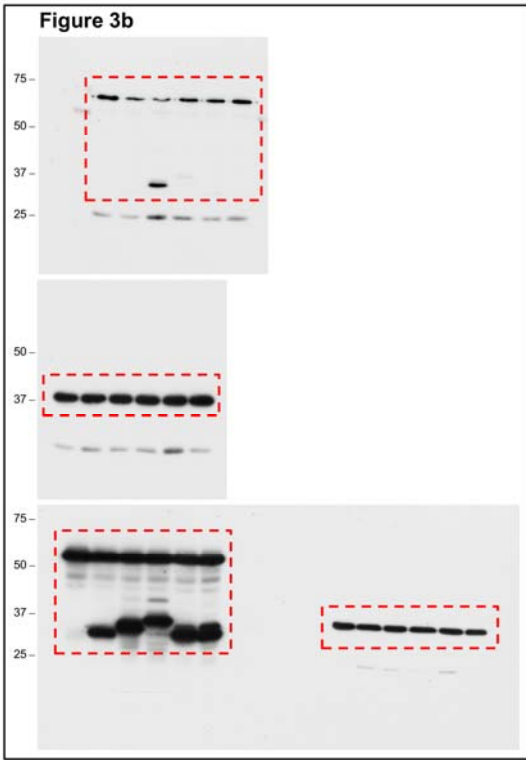
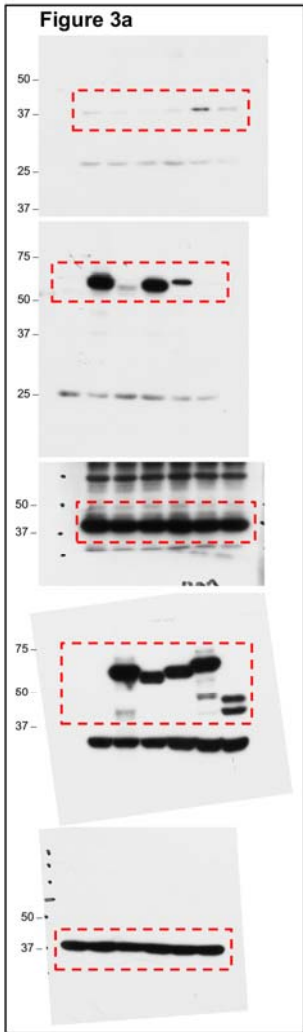


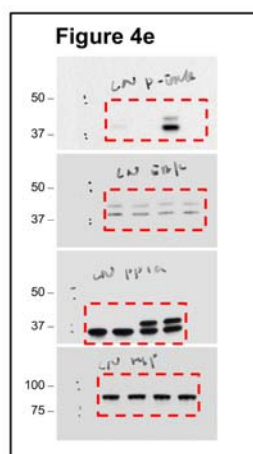
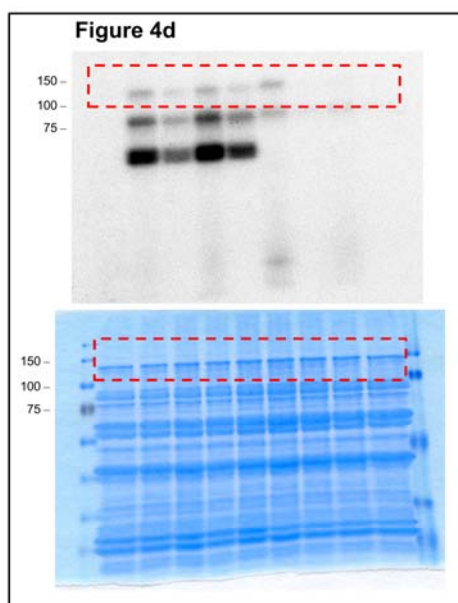
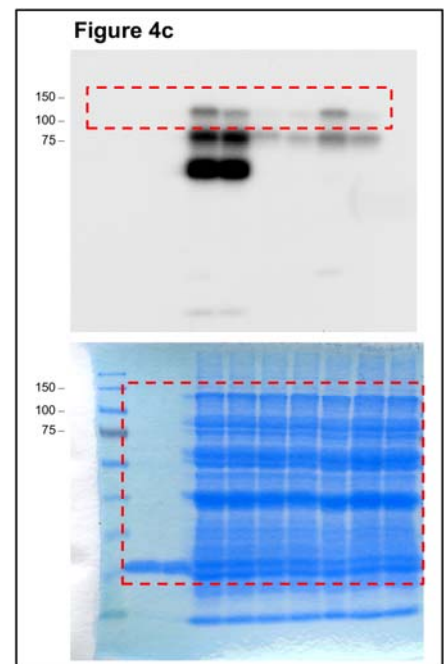
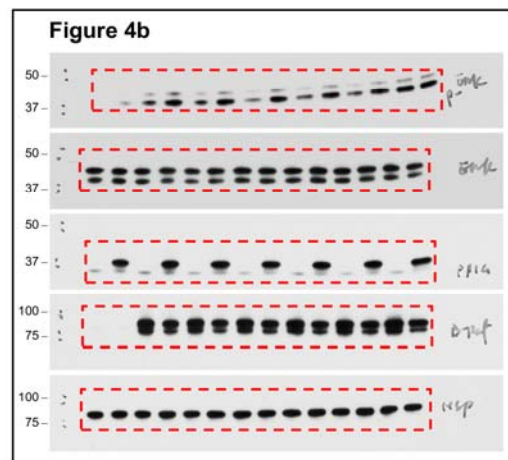
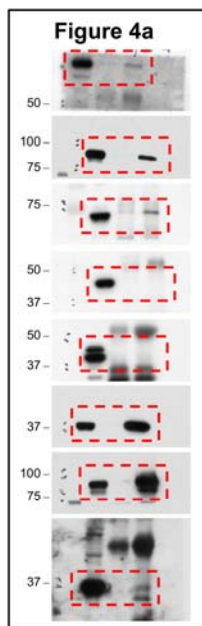
Supplementary Figure 2 PP1α mediates *PML*-loss induced MAPK activation and promotes CaP cell invasiveness through activation of MAPK signaling. (a) Immunoblot (IB) analysis of lysates from LNCaP cells transfected with EV or Flag-PP1α for the indicated time periods. Quantification of p-ERK/ERK levels was carried out with Image J software. Numbers indicate

the relative ratios to controls for phosphoprotein/total protein. Data shown are mean $\pm$ s.e.m. of three independent experiments. **(b)** *In vitro* kinase assays showing that both PP2A-C and PP1 α promoted B-Raf kinase activity towards phosphorylating GST-MEK1. **(c-e)** IB analysis of lysates from 293T cells transfected with empty vector or PP2A-C for the indicated times **(c)**, lysates from LNCaP **(d)** or PC3 cells **(e)** transfected with control or PP2A-C siRNA for 48 hrs. **(f)** Genetic alterations of *PPP2CA* in the Robinson *et al.* dataset⁹. The gene alteration percentages are shown. It should be noted that neither genomic amplification nor deletion was observed for *PPP2CA* in this dataset of 150 samples from mCRPC patients. **(g)** Endogenous co-immunoprecipitation of Rb with PP1 α and PML in PC3 cells. Input is 10% of total cell extracts used for immunoprecipitation. **(h)** Cytochemical staining and quantification of senescence-associated β -galactosidase (SA- β -gal) activity in WI-38 cells transfected with control, PTEN siRNA or PTEN plus PML siRNA at 5 days post-transfection. Data shown are mean $\pm$ s.d. of three independent experiments. *** P <0.001 by unpaired two-tailed *t*-test. Scale bar, 100 μ m. **(i)** IB analysis of lysates from serum-starved PC3 cells pretreated with tautomycin at the indicated concentration for 3 hrs, followed by stimulation with 10ng/ml EGF for 5 min. **(j-l)** IB analysis of lysates from 293T cells transfected with the indicated WT or mutant Flag-B-Raf constructs plus EV or Flag-PP1 α for 24 hrs. **(m)** Representative images and quantitation of migrated and invaded PC3 cells in the migration and invasion assay. PC3 stable cells were subjected to migration or invasion assay (24 hrs) (n=3 per group, 4 fields per insert) in the absence or presence of 20 μ M U0126. Western blotting confirmed the expression of phospho-ERK and PP1 α . Data shown are mean $\pm$ s.e.m. of three independent experiments. * P <0.05, ** P <0.01, *** P <0.001 by unpaired two-tailed *t*-test. Scale bar, 100 μ m. **(n)** *In vitro* phosphatase assays showing that PML did not affect PP1 α phosphatase activity towards dephosphorylating

Flag-CREB. (o) *In vitro* kinase and phosphatase assays showing that 14-3-3 γ did not affect PP1 α phosphatase activity towards dephosphorylating GST-B-Raf.







Supplementary Figure 3 Uncropped scans for Western blot data in main figures.

Supplementary Table 1. Sequences of siRNAs used in this study

Names	Sequences of siRNAs
h-PML-siRNA1	5'-GCAACCAGUCGGUGCGUGA-3'
h-PML-siRNA2	5'-CCGACUUCUGGUGCUUUGA-3'
h-PTEN-siRNA-SMARTpool	5'-GUGAAGAUCUUGACCAAUG-3'
	5'-GAUCAGCAUACACAAAUUA-3'
	5'-GGCGCUAUGUGUAUUAUUA-3'
	5'-GUAUAGAGCGUGCAGAUAA-3'
h-PPP1CA-siRNA-1	5'-CCGCAUCUAUGGUUUCUAC-3'
h-PPP1CA-siRNA-2	5'-CAUCUAUGGUUUCUACGAU-3'
h-PPP2CA-siRNA-1	5'-CUGGUUACACCUUUGGGCA-3'
h-PPP2CA-siRNA-2	5'-UAACCAAGCUGCAAUCAUG-3'
h-S6K1-siRNA-1	5'-GGAAUAUUUAUGGAAGACA-3'
h-S6K1-siRNA-2	5'-GAUAGUAAGAAUAGCUAAA-3'
siGENOME Non-Targeting siRNA #2	5'-UAAGGCUAUGAAGAGAUAC-3'