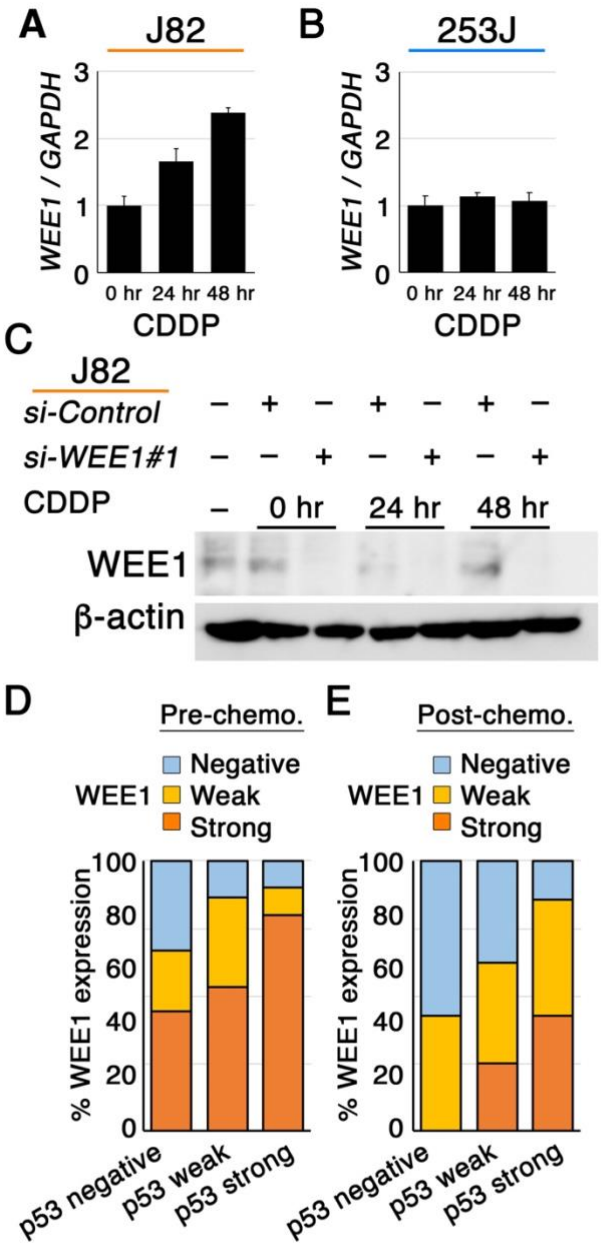
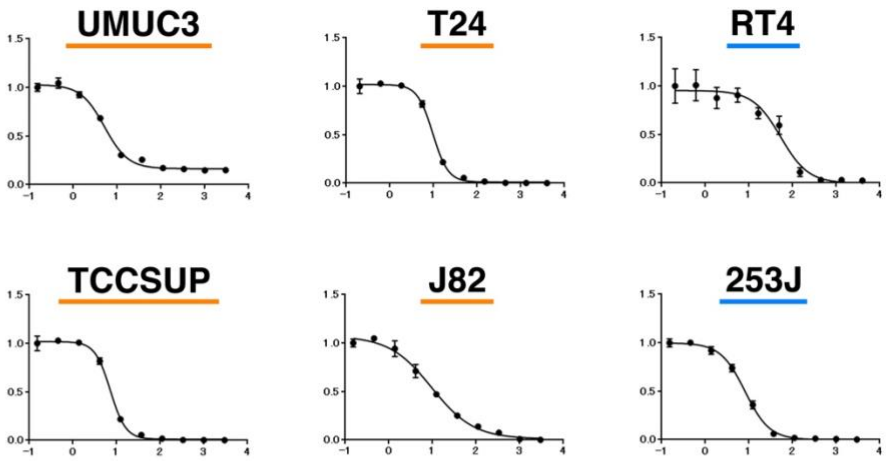
Supplementary Figure S1



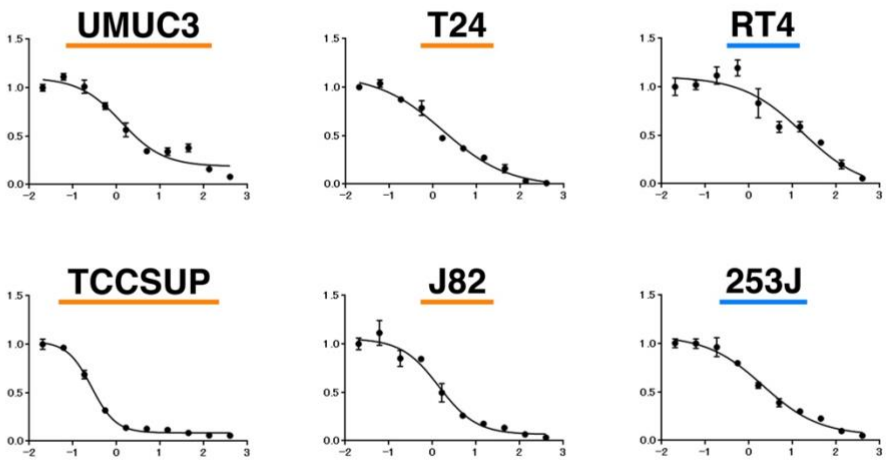
A–B. Expression levels of WEE1 mRNA were evaluated by quantitative RT-PCR in J82 (**A**) and 253J (**B**) cells. Cells were treated with 1 μM CDDP and mRNA was extracted at indicated time points (0, 24 and 48 hrs). Values were normalized to GAPDH mRNA levels. **C.** Western blotting of WEE1 expression in J82 cells. □-actin served as the loading control.
D–E. Distribution of WEE1 immunostaining in 34 preoperative (**D**) and 29 post-chemotherapy MIBC specimens (**E**), as shown in Figs. 1A and 1B and Supplementary Table S1, with regard to p53 immunostaining.

Supplementary Figure S2

CDDP

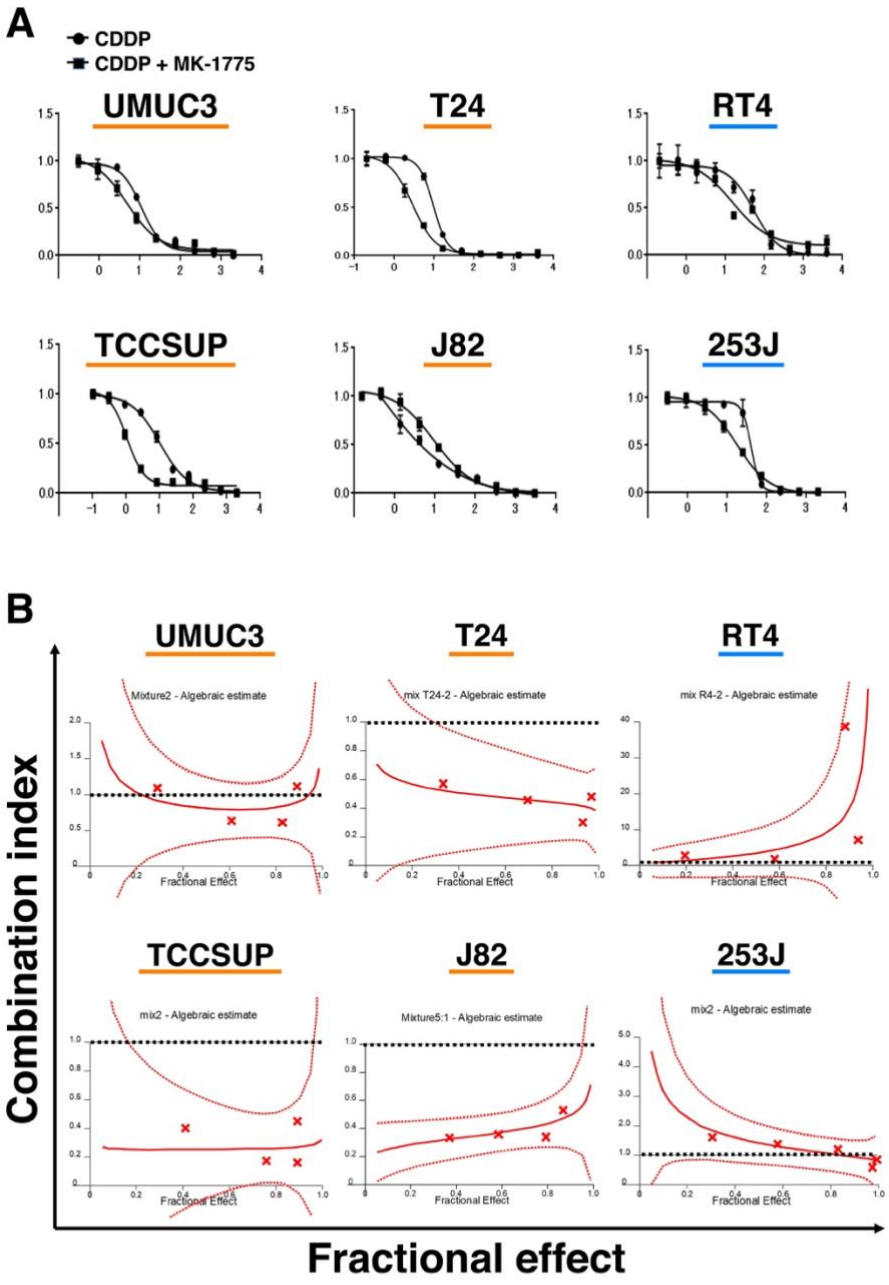


MK-1775



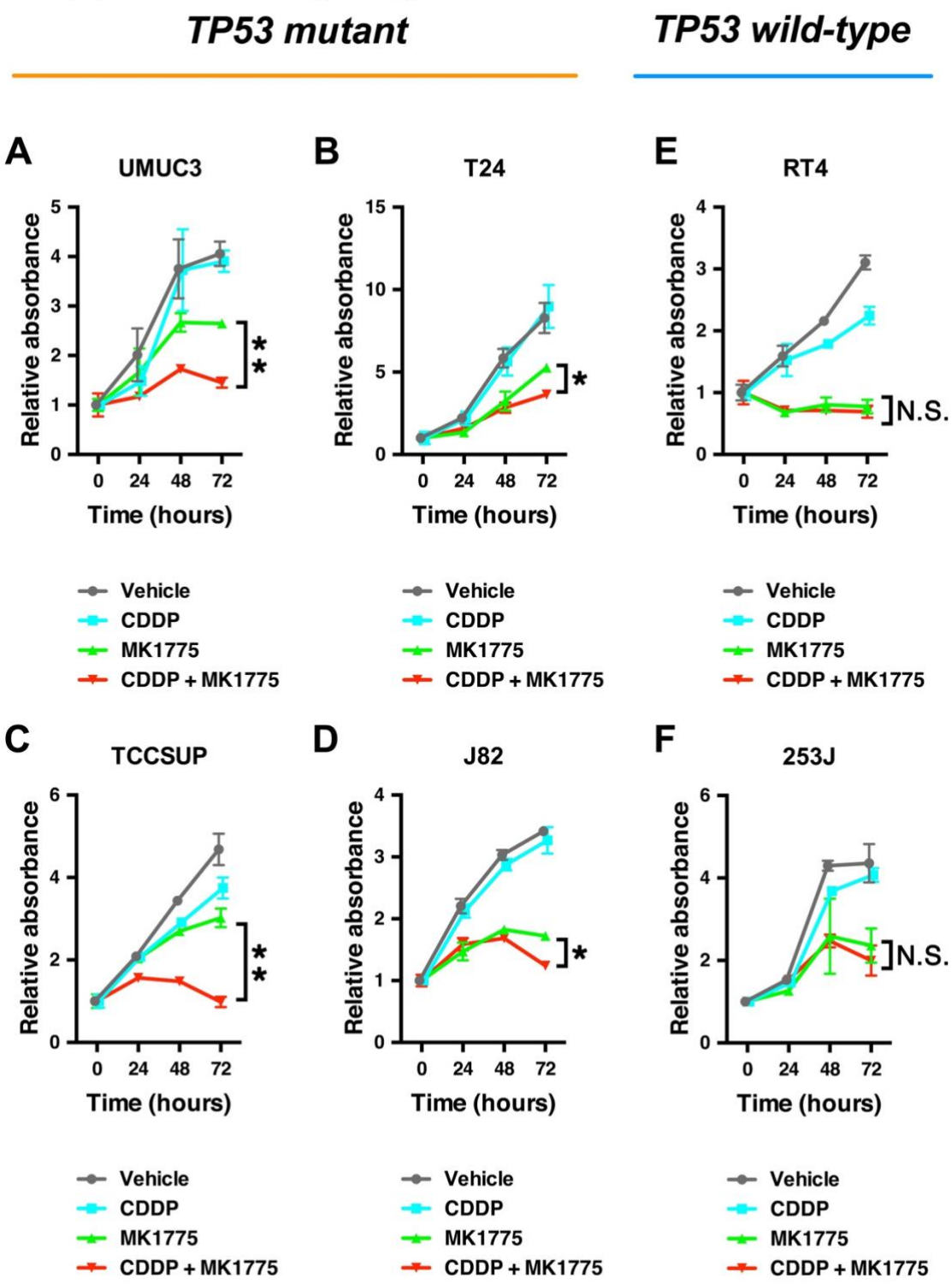
Dose-effect curves for CDDP (upper panels) and MK-1775 (lower panels) in the indicated UC cell lines. Estimated IC50 values from these analyses are shown in Figs. 1E and 1F. The vertical axes indicate the proliferation rate normalized by that of vehicle-treated cells, while the horizontal axes indicate the drug concentration in log scale.

Supplementary Figure S3



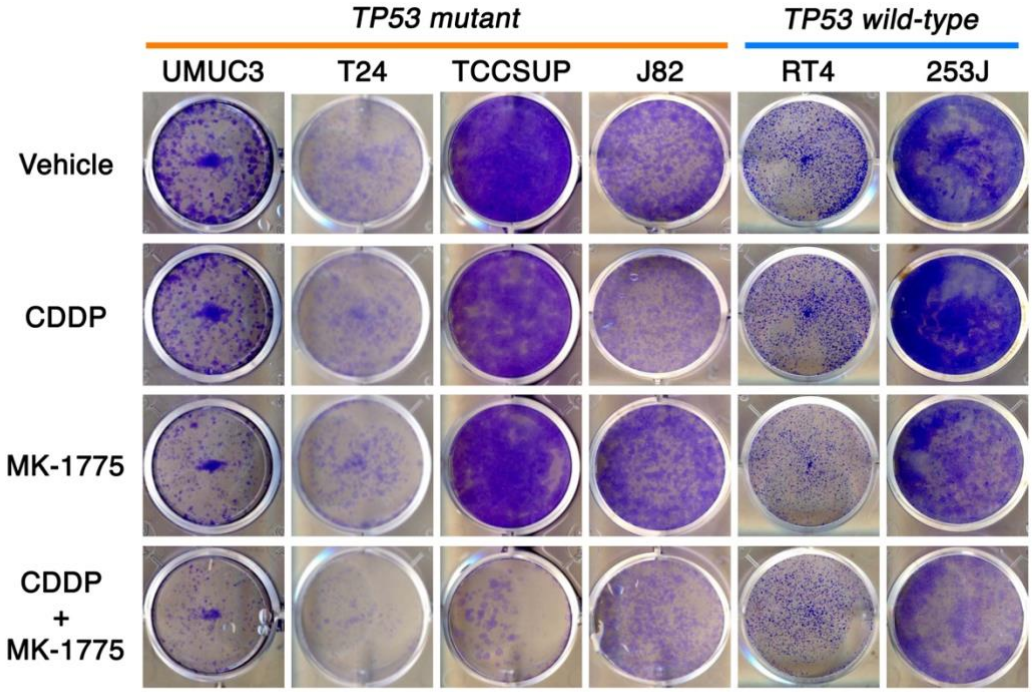
A. Dose-effect curves for CDDP in the presence (circle) and absence (square) of MK-1775 in the indicated UC cell lines. The vertical axes indicate the proliferation rate normalized by that of vehicle-treated cells, while the horizontal axes indicate the drug concentration in log scale. **B.** Combination indices for the combination treatment of CDDP plus MK-1775 in the indicated human UC cells were plotted (red crosses) using CalcuSyn software. A combination index <1 (dotted line) denotes a synergistic effect. MK-1775 with CDDP shows a synergistic effect in TP53-mutant cell lines (orange lines) but not in TP53-wild-type cells (blue lines). The results are summarized in Fig. 1G.

Supplementary Figure S4



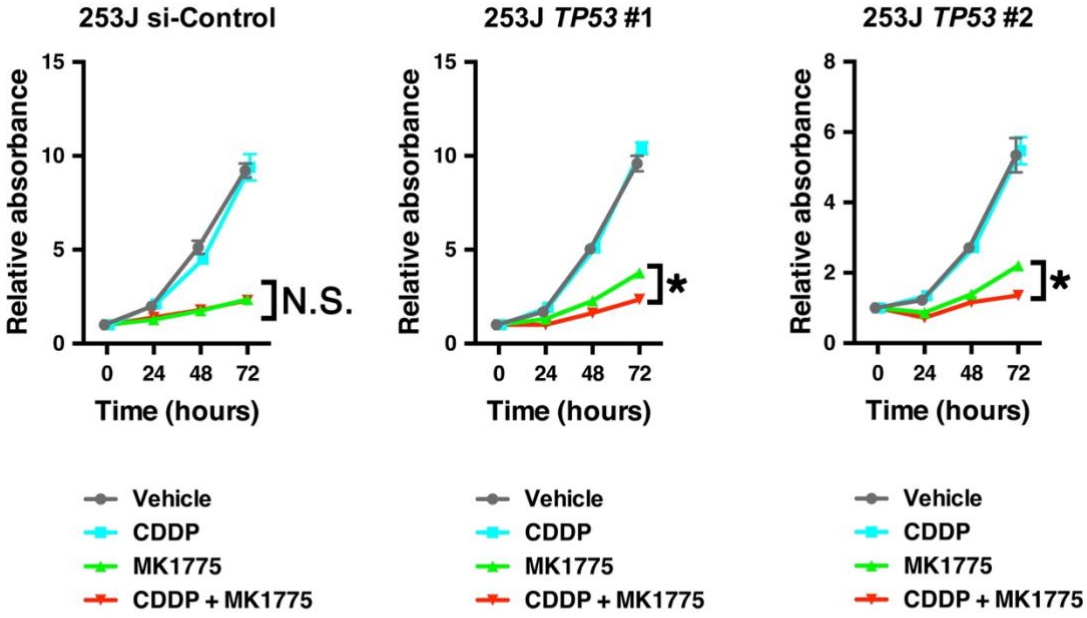
Proliferation curves of human UC cells treated with CDDP and MK-1775. Indicated cells were treated with vehicle (DMSO), CDDP, MK-1775, or CDDP plus MK-1775.
Cell proliferation rate was evaluated by WST-8 assays at the indicated time in triplicate.
*p<0.05, **p<0.01. The results are summarized in Fig. 2A.

Supplementary Figure S5



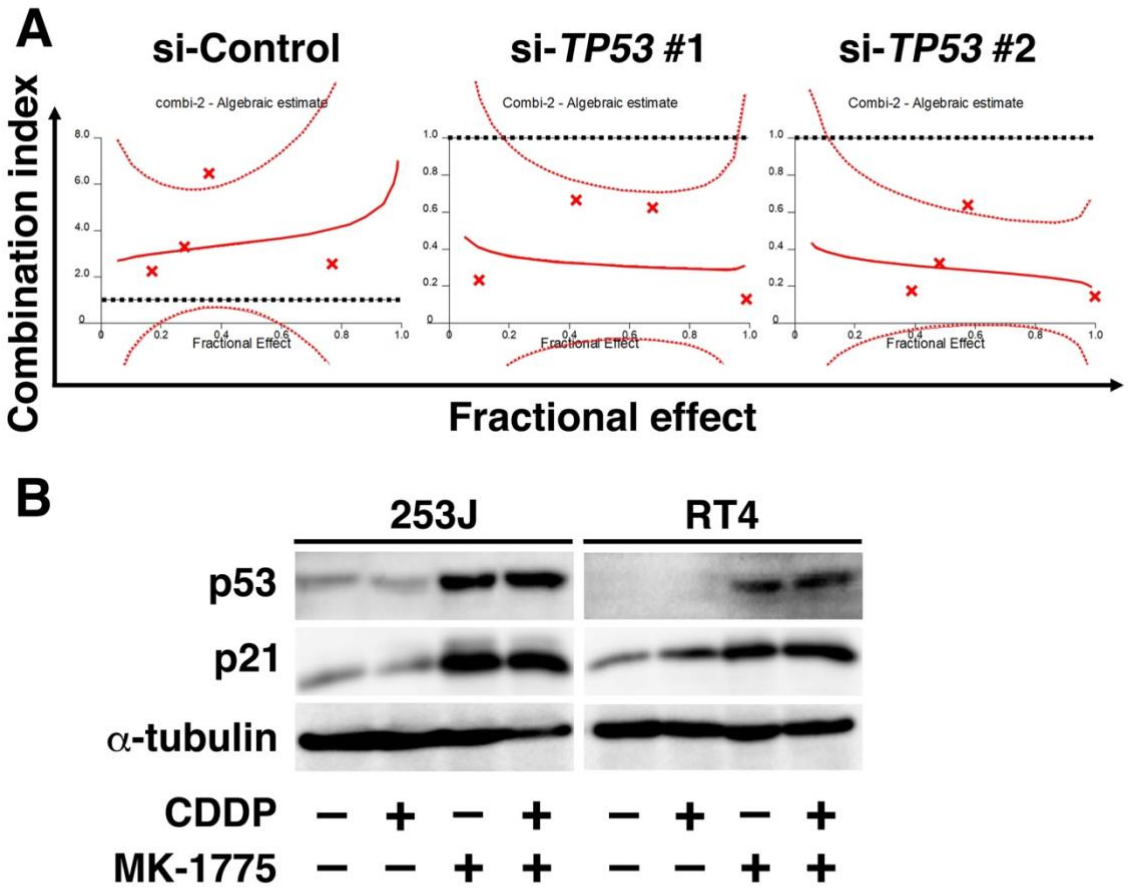
Proliferation ability of human UC cells treated with CDDP and/or MK-1775 was evaluated using colony-forming assays. Indicated cells were treated with vehicle (DMSO), CDDP, MK-1775, or CDDP plus MK-1775. Cells were fixed and stained with crystal violet after 72 h of treatment in triplicate. The results are quantitated and summarized in Fig. 2B.

Supplementary Figure S6



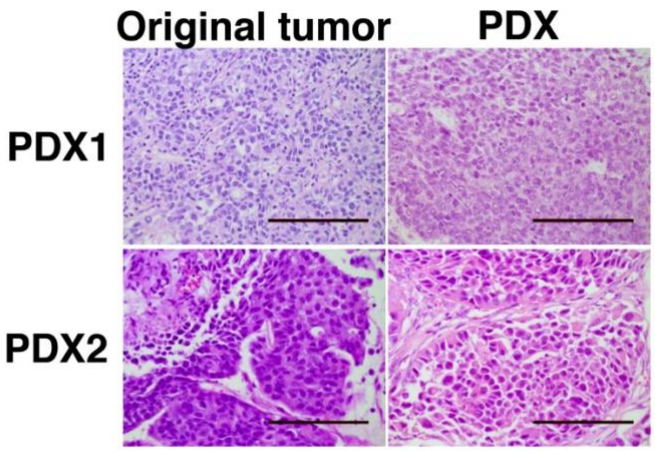
Proliferation curves of 253J cells treated with the indicated siRNA in the absence or presence of CDDP and MK-1775 alone or in combination. Cell proliferation rate was evaluated by WST-8 assays at the indicated time in triplicate *p<0.05. The results are summarized in Fig. 2F.

Supplementary Figure S7



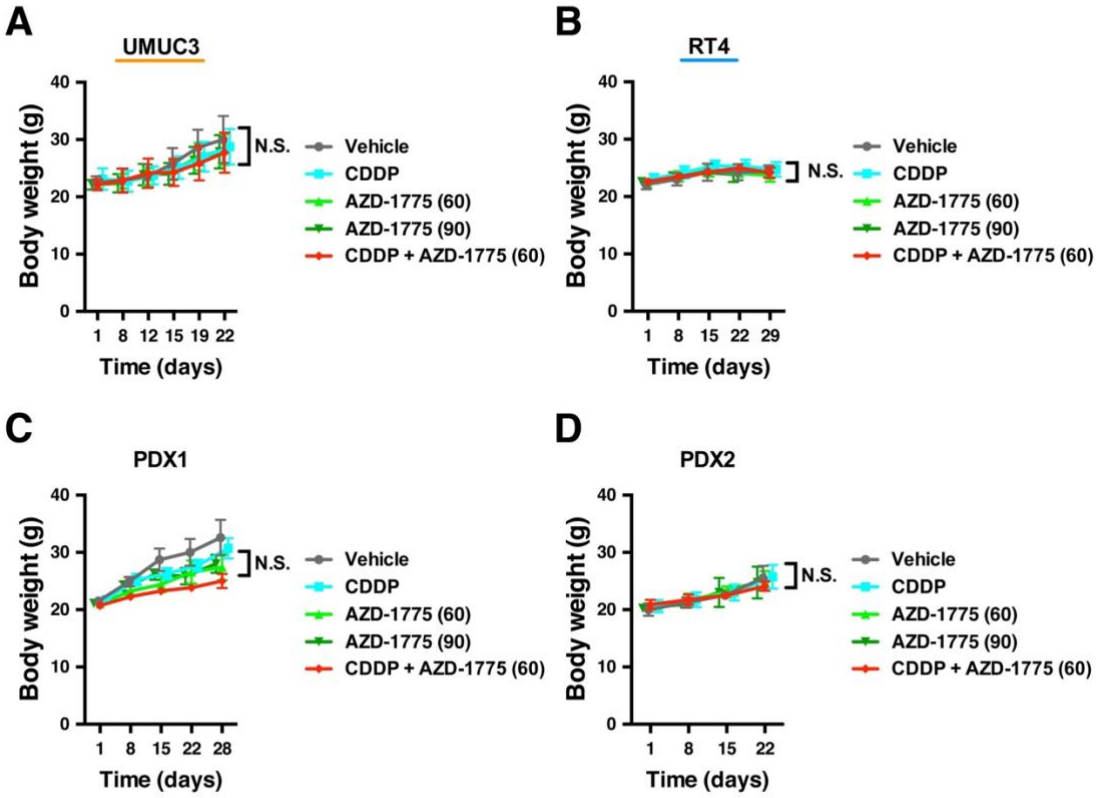
A. Combination indices for the combination treatment of CDDP plus MK-1775 in 253J cells treated with the indicated siRNA were plotted (red crosses) using CalcuSyn software. A combination index <1 (dotted line) denotes a synergistic effect. MK-1775 combined with CDDP showed a synergistic effect in cells transfected with siRNAs for TP53 but not in cells transfected with control siRNA. The results are summarized in Fig. 2G. **B.** 253J and RT4 cells were treated as indicated and p53 and p21 expressions were analyzed by western blotting. α-tubulin acts as loading control.

Supplementary Figure S8



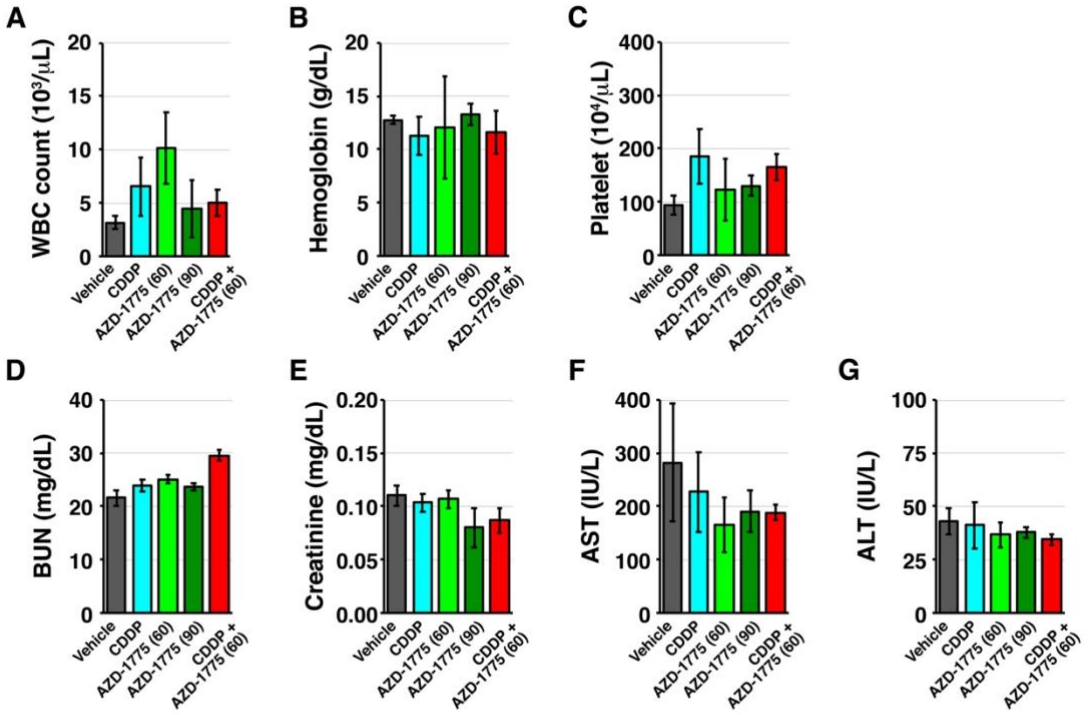
Representative images of H&E staining of original tumors and xenograft tumors for PDX1 and PDX2. Bars indicate 100 μm.

Supplementary Figure S9



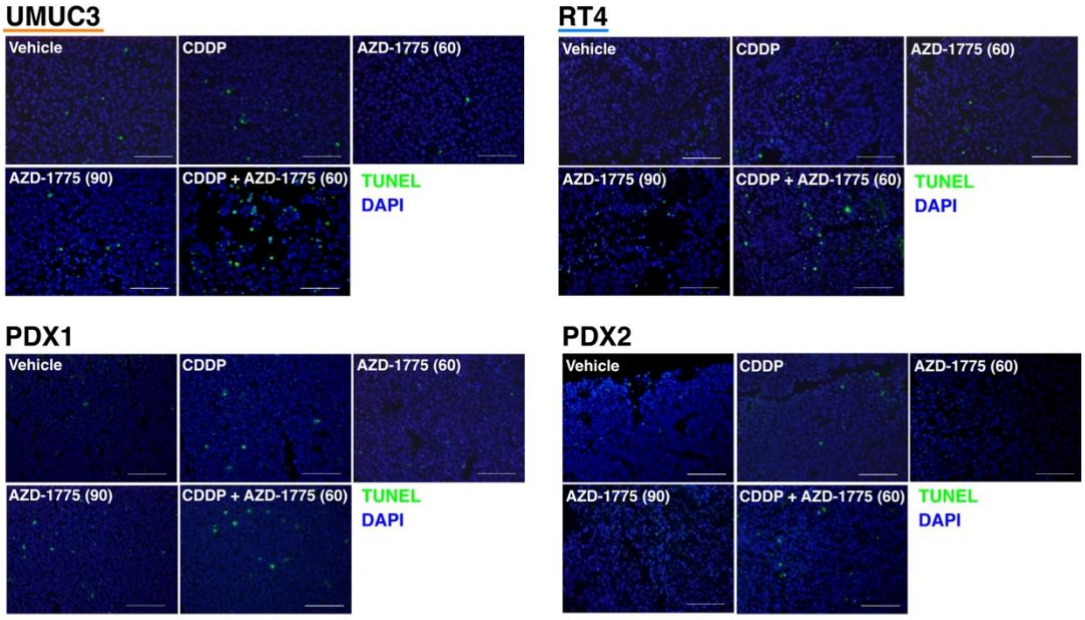
Charts for body weight changes in mice implanted with the UMUC3 cell–based xenograft (**A**), RT4 cell–based xenograft (**B**), PDX1 (**C**), and PDX2 (**D**) during the indicated treatment.

Supplementary Figure S10



Charts for blood tests in mice administered with CDDP and AZD-1775 alone or in combination. Mice were treated as in Fig. 4A, and blood samples were collected at the end of the treatment. WBC, white blood cell; BUN, blood urea nitrogen; AST, aspartate aminotransferase; ALT, alanine aminotransferase.

Supplementary Figure S11



A–D. Representative fluorescent images of TUNEL assays in tumors after the 3-week treatment. CDX UMUC3 (**A**), CDX RT4 (**B**), PDX1 (**C**) and PDX2 (**D**) were treated as shown in Fig. 4A. Quantified results are summarized in Figs. 4B–E (right).