Supplementary Materials
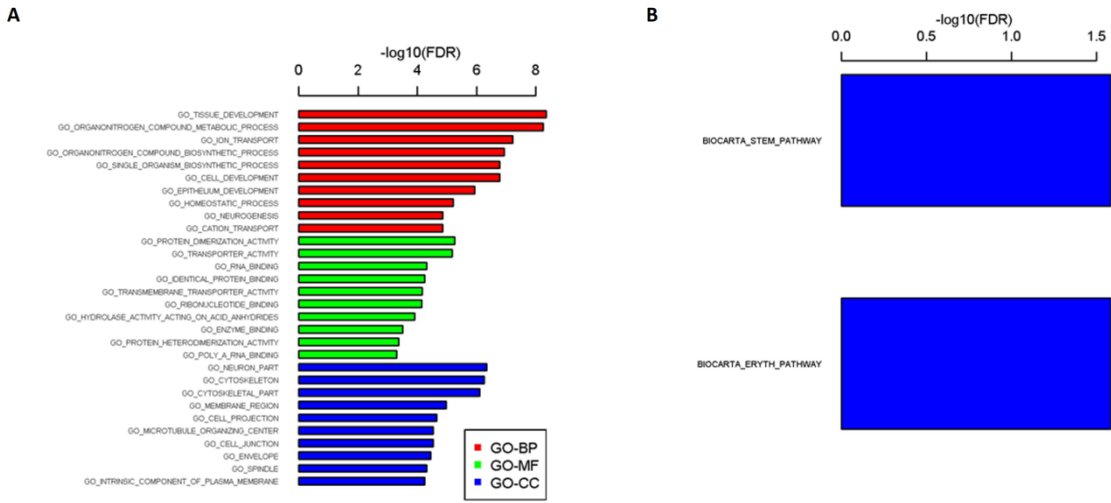

Supplementary Figure 1. Pathways related to the CRISPR-Cas9 screen investigating mediators of cisplatin response in T24 cells. (A) Top GO analysis and (B) pathway analysis of the 327 regulated genes in T24 cells after CRISPR-cas9 genome editing.

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Gene Ontology (Biological Process)

Up-regulated genes

Down-regulated genes
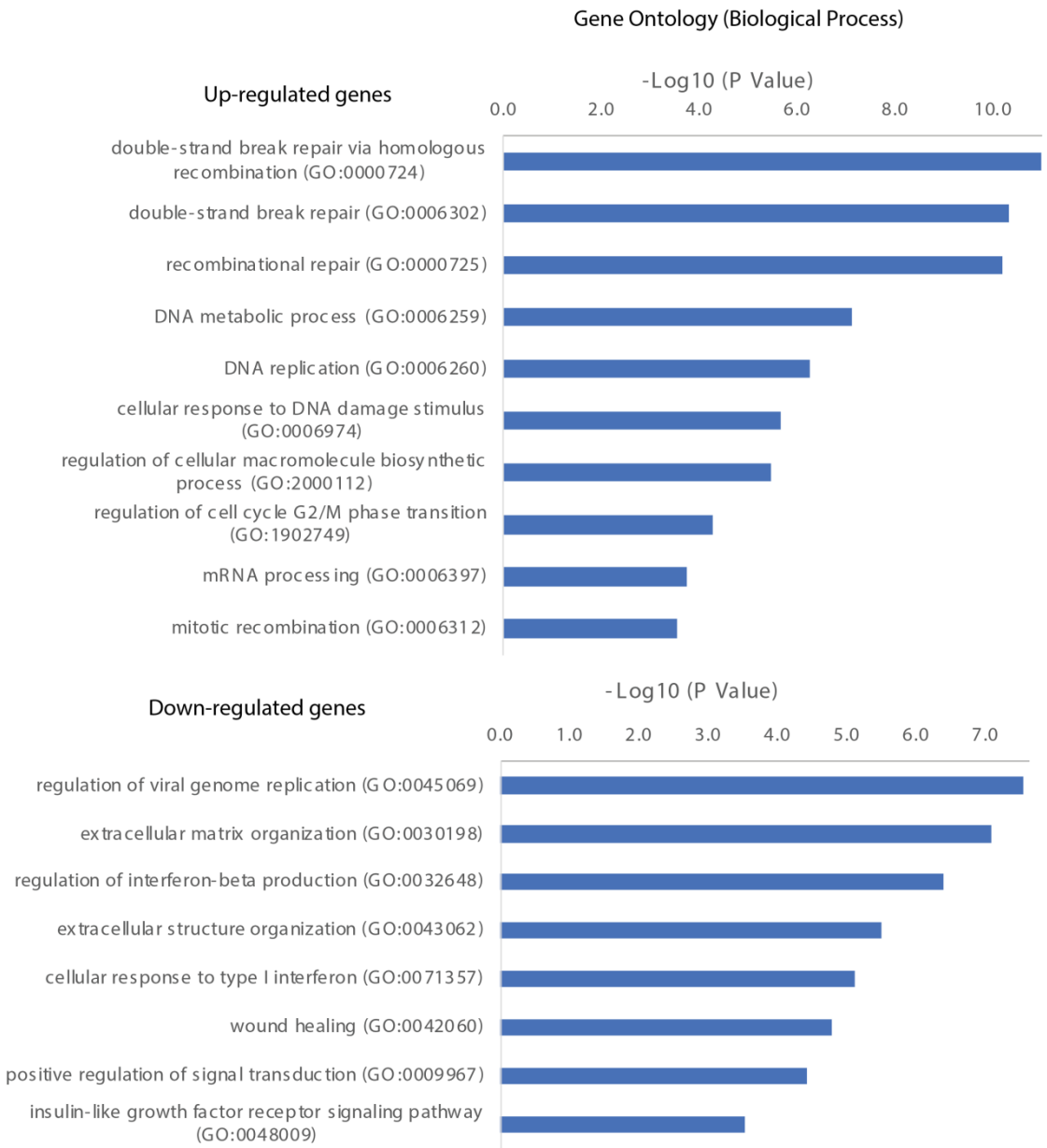
76 **Supplementary Figure 2**. Gene ontology pathway enrichment of the microarray data. Enrichment of

77 both upregulated and downregulated DEG (differentially expressed genes) is shown.

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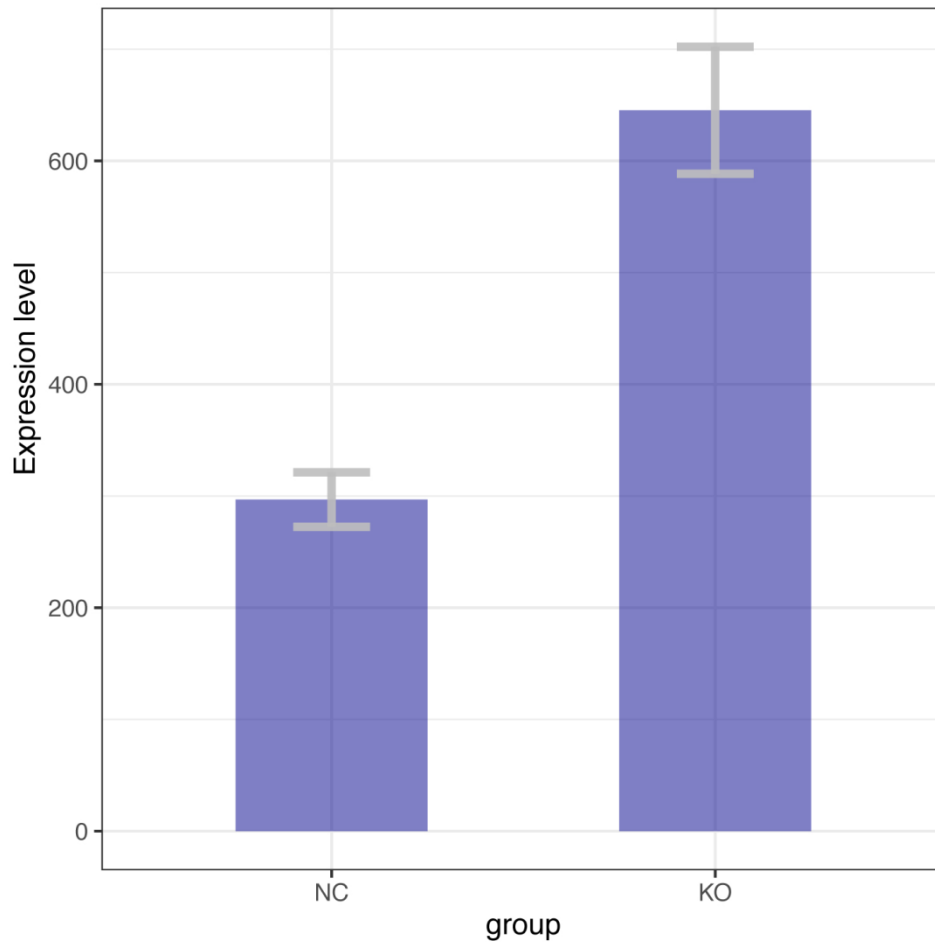
Supplementary Figure 3. AHCTF1 expression profile from HNRNPU-KO microarray dataset.
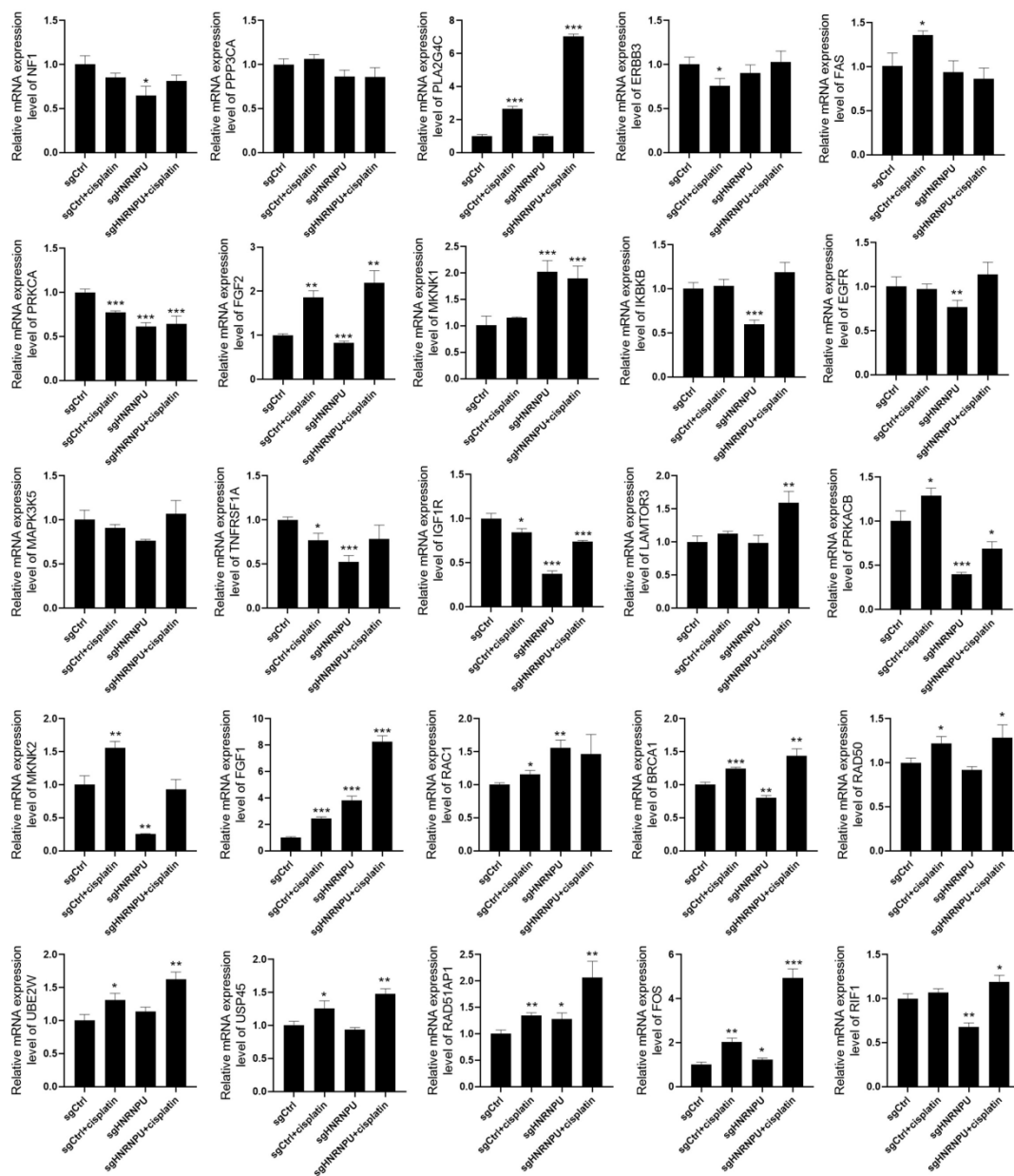
Supplementary Figure 4. Validation of the MAPK pathway and DNA double-strand break repair gene expressed in the HNRNPU-depleted cells after cisplatin treatment. T24 cells were transfected with sgHNRNPU and then treated with cisplatin for 5 days. The qRT-PCR assay was used to detect the mRNA expression of genes. The data indicate mean ± SD from three independent experiments. The data indicate mean ± SD from three independent experiments. *p<0.05, **p<0.01, ***p<0.001 vs. the sgCtrl group.
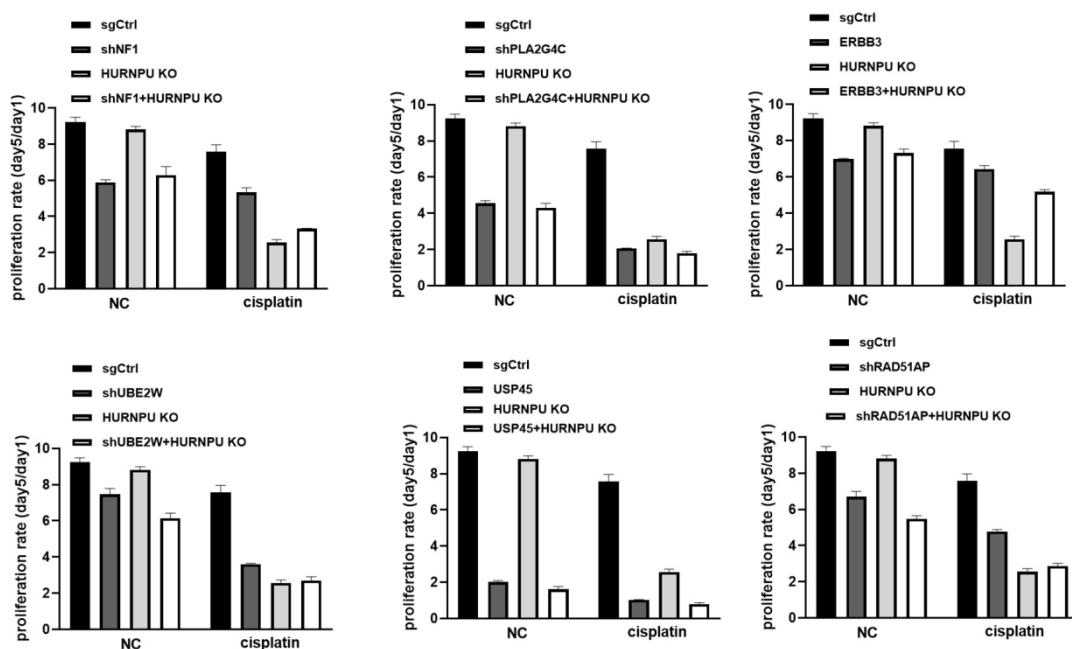
Supplementary Figure 5. Screening of HNRNPU downstream genes. T24 cells were transfected with sgHNRNPU, with or without the downstream gene knockdown or overexpression, and then treated with or without cisplatin for 5 days. The CCK-8 assay was used to detect the cell proliferation in the indicated group.

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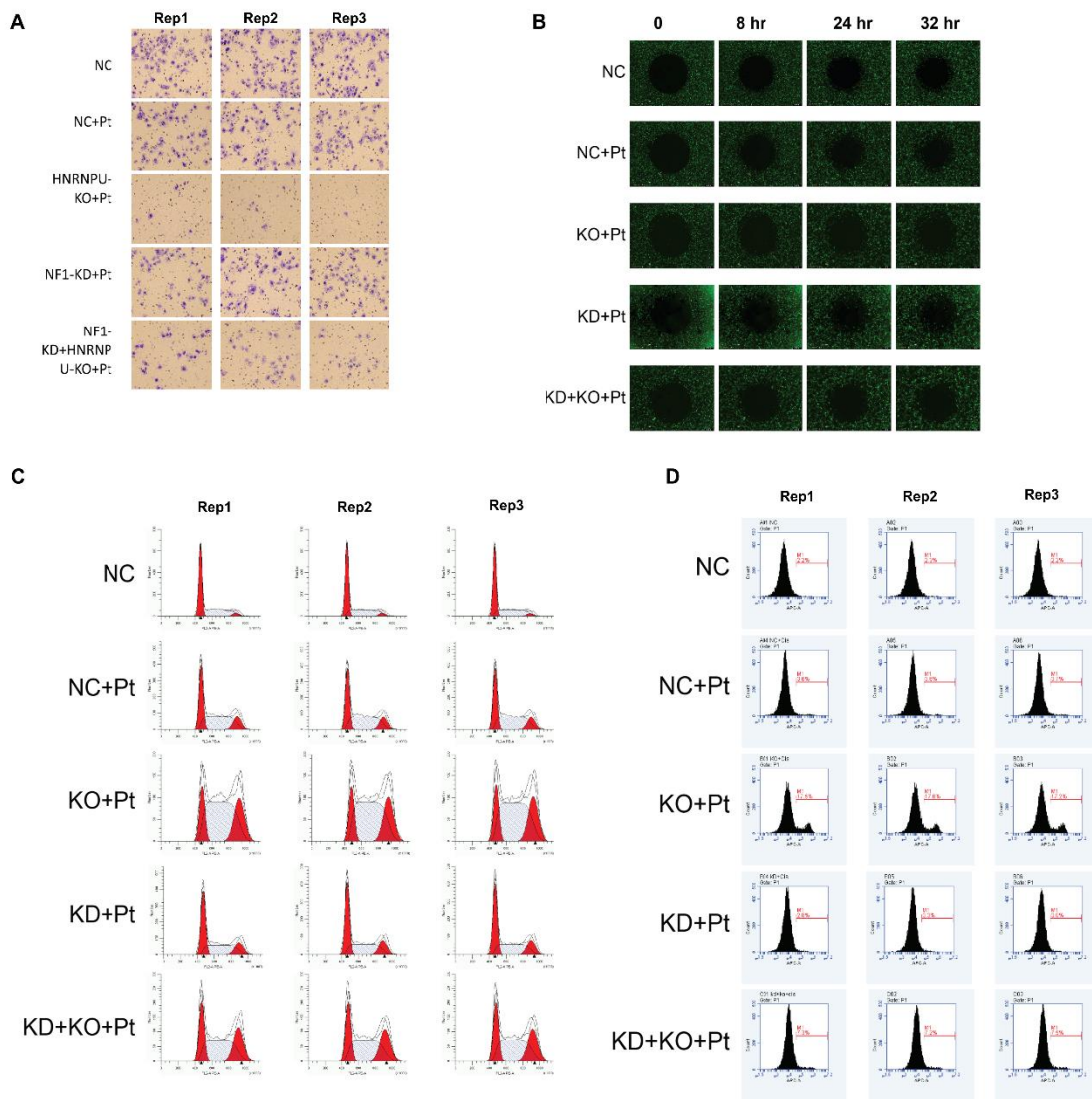
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217 **Supplementary Figure 6.** A. Cell invasion assay results under different NF1, HNRNPU KO or

218 combination treatments. Rep = replication. **B.** Cell migration assay results under different NF1,

219 HNRNPU KO or combination treatments. Hr= hour. **C.** Cell cycle arrest results under different NF1,

220 HNRNPU KO or combination treatments. Rep = replication. **D.** Cell apoptosis results under different

221 NF1, HNRNPU KO or combination treatments. Rep = replication.
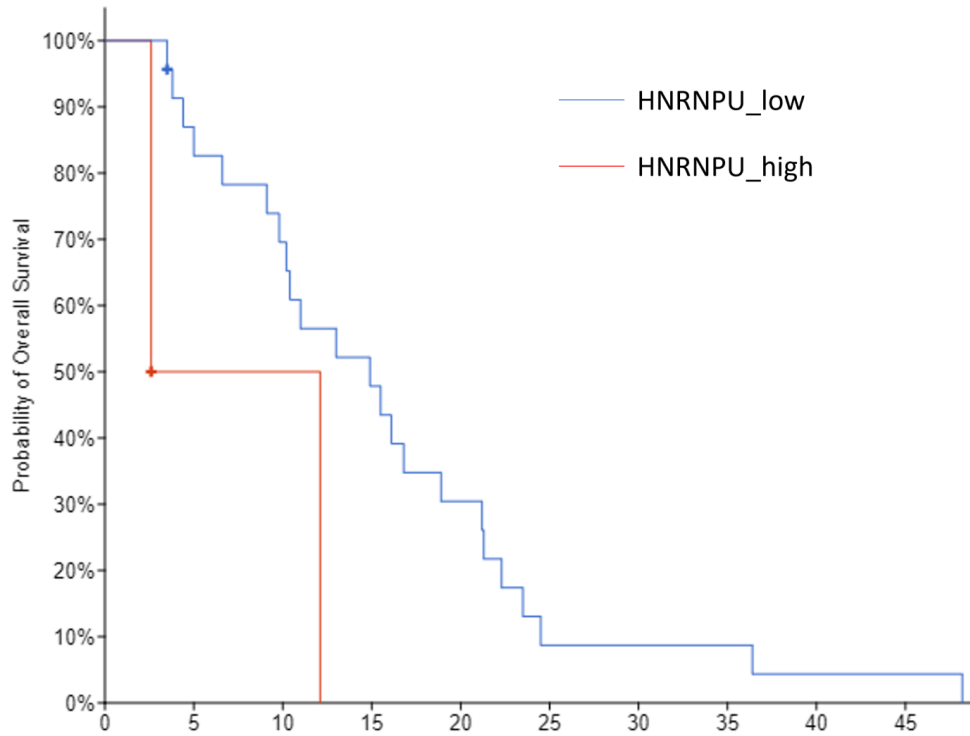
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Supplementary Figure 7. Survival outcome of patients with low HNRNPU (blue line) and high HNRNPU expression (red line). Data was from Iyer et al., 2013, total case number = 59.

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Supplementary Table S1. Primers of genes for RT-PCR.

Gene	Sequences
NF1	F 5'-TCCATCCCCTTTATCCCAGCC-3'
	R 5'-CCAGTTAGGAGGGTCACGGA-3'
PPP3CA	F 5'-GCCGCGGACCTTCTAGGATA-3'
	R 5'-TGACGCCCCCGTCAATAAAA-3'
PLA2G4C	F 5'-CACGTGATCCCACGGATGAA-3'
	R 5'-TGCACCCAATCCCTGGTACT-3'
ERBB3	F 5'-CTTGCCTCGATGTCCTAGCC-3'
	R 5'- CTGAGACCGTGCCCATACC-3'
FAS	F 5'-CAAGAATTGCCAGGCGAACAA-3'
	R 5'-TTGCATCCCAAACAGAGCCA-3'
PRKCA	F 5'-AAGAACGTGCACGAGGTGAA-3'
	R 5'-CCCGCCGGTTCCAAGTTATC-3'
FGF2	F 5'-TCCATTTCGTGGGTTCTCGC-3'
	R 5'-AAATTGGCACACCCCAAAGC-3'
FOS	F 5'-GCGGTAGGTACTCTGTGGGT-3'
	R 5'-AGGTTGGCAATCTCGGTCTG-3'
MKNK1	F 5'-GTTCTCGGAGGAGCGATCTG-3'
	R 5'-GAAAAGCGTCCCCTTAGGCT-3'
IKBKB	F 5'-GGTCACCTTCCCTGACAACG-3'
	R 5'-GTCCCAAGATGACCAAAGCCA-3'
EGFR	F 5'-CCAGTATTGATCGGGAGAGCC-3'
	R 5'-CGCAGCTGATCTCAAGGAAA-3'
MAPK3K5	F 5'-CTTTGGAGAAACCACCGTGC-3'
	R 5'-TAAATGCTTCCCGCCCAGAA-3'
TNFRSF1A	F 5'-CTATGCCCGAGTCTCAACCC-3'
	R 5'-CCCTTTGTCCCTGGTCTCAC-3'
IGF1R	F 5'-GTTTTTGGAGGGGGGAGCGAA-3'
	R 5'-GCCCCTCGGAGGAAAAGTT-3'
LAMTOR3	F 5'-GGCTTGAGGAGGAACCTGTC-3'
	R 5'-GGCCTCAAAACCAGGCAAAG-3'
PRKACB	F 5'-TTGTCCCAGACTGTGGAGTG-3'
	R 5'-GCCTTCAACTCACCGCTCTC-3'
MKNK2	F 5'-TTCCACCGTTCGTTCAAGGT-3'
	R 5'-GAGCCGATCTTAGGGGCG-3'
FGF1	F 5'-CTGCAGCTGTCCTGGTAGAA-3'
	R 5'-GCCAAGCAGAAAGTCTGTAGC-3'
RAC1	F 5'-AGCAAGCGCTCTTGGAGATT-3'
	R 5'-TATGATCGACTTGACCGCCG-3'
BRCA1	F 5'-TCCCATCTGGTAAGTCAGCAC-3'
	R 5'-CCGGACCACAGGATTTGTGT-3'
RIF1	F 3'-AGTTTTGCCAGTTGACTCAAAAGC-3'
	R 5'-TGCCCCTAGGCAACTTTAGG-3'
RAD50	F 5'-ACGATCCCAAGGTAATGGTGC-3'
	R 5'-GTGCTAAAACTGTGTGGGGC-3'
UBE2W	F 5'-TGTCAGTGCGTCTCAACCAT-3'
	R 5'-GTAGAGCGTCCCCAGCATTT-3'
USP45	F 5'-GGGCTTTTTGCATAGCCTGTT-3'
	R 5'-CCATTTGAGGCAAAAGGGCA-3'
RAD51AP1	F 5'-AACTTGGGCAGAGTCATAGGTC-3'
	R 5'-GTGCTGGGTCCTGTCAAAAC-3'

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Supplementary Table S2. Student's t-test results of Figure 4G with indicated comparison.

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T-TEST_tumor weight	P VALUE
NC VS NC+Cisplatin	0.496145642
NC VS KO	0.87067181
NC VS KO+Cisplatin	0.00069077
NC+Cisplatin VS KO	0.426861325
NC+Cisplatin VS KO+Cisplatin	0.010703857
KO VS KO+Cisplatin	0.000833118

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243 **Supplementary Table S3.** Drug sensitivity of bladder cancer cell lines to chemotherapeutic drugs.

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	IC_{50} values $\pm$ SD [a] (μM)		
Treatment	Cisplatin	Doxorubicin	Paclitaxel
T24	7.637±0.980	0.341±0.043	0.066±0.013
RT4	7.426±0.840	0.193±0.002	0.337±0.110
HT1197	4.493±0.777	0.266±0.010	0.301±0.051
SW780	3.856±0.279	0.135±0.009	0.029±0.002
RT112	3.966±0.445	0.094±0.007	<1 nM
HT1376	3.181±0.034	0.300±0.115	0.258±0.086

245 [a] IC_{50} values are represented as the mean $\pm$ SD of at least three independent experiments.