Supporting Information

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HeLa pSuper	No Treatment	Cisplatin	Aclarubicin	UV
G1	36.4 +/- 1.8	49.9 +/- 0.6	30.9 +/- 2.8	19.1 +/- 0.6
S	26.4 +/- 2.6	13.6 +/- 1.0	14.0 +/- 1.6	28.1 +/- 1.2
G2	21.9 +/- 1.3	9.3 +/- 1.0	9.2 +/- 1.2	26.2 +/- 2.1
Sub-G1	7.9 +/- 0.8	22.7 +/- 0.5	42.1 +/- 1.3	21.8 +/- 2,8
Poly	7.1 +/-0.5	4.2 +/- 1.8	3.6 +/- 0.4	4.5 +/- 1.0
HeLa shDDB2	No Treatment	Cisplatin	Aclarubicin	UV
G1	65.7 +/- 0.8	35.9 +/- 1.8	44.1 +/- 3.6	24.5 +/- 1.3
S	11.9 +/- 0.4	46.3 +/- 1,1	22.6 +/- 2.5	44.2 +/- 2.5
G2	13.7 +/- 0.2	11.9 +/- 0.9	11.4 +/- 0.9	17.2 +/- 1.1
Sub-G1	5.0 +/- 0.9	4.3 +/- 0.9	16.3 +/- 2.3	8.3 +/- 1.6
Poly	3.5 +/- 0.3	6.5 +/- 2.0	5.3 +/- 0.2	5.4 +/-0.5

Fig. S1. Flow-cytometric analyses of HeLa cells expressing DDB2-shRNA after treatments with different DNA-damaging agents. The average distribution from three samples is shown.

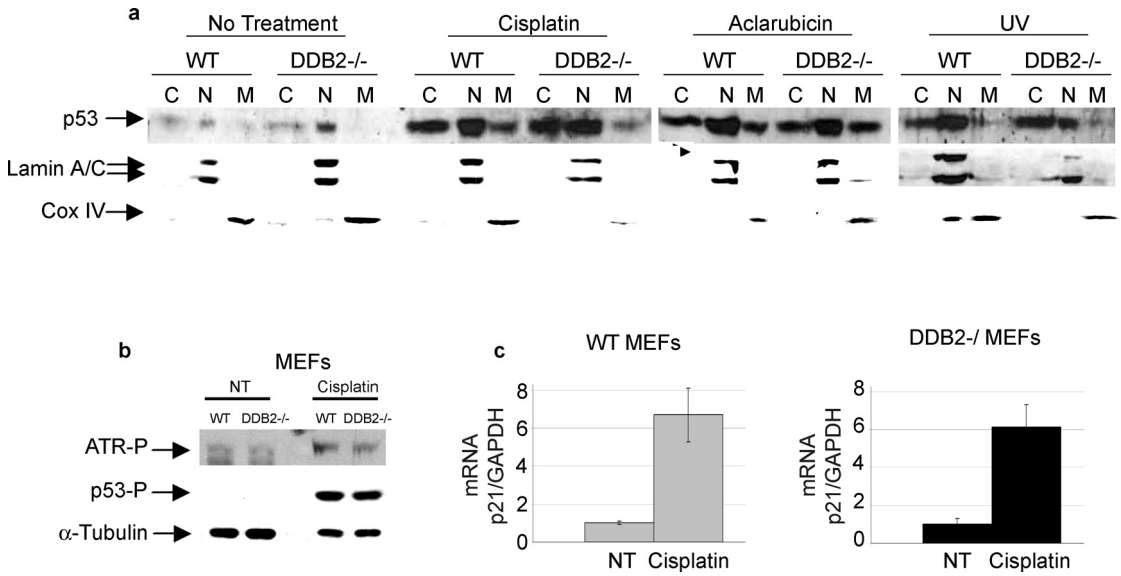


Fig. S2. (*a*) Wild-type or DDB2$^{-/-}$ MEFs were either not treated or treated with cisplatin (30 μm) or aclarubicin (0.5 μM) or UV-C (50 J/m^2). Eighteen hours after treatment, cells were harvested and subjected to fractionation. C, cytoplasmic; N, nuclear; M, mitochondrial. Western blots were performed to detect fractionation of p53. Lamin A/C was assayed as a marker for the nuclear fraction, and Cox IV was used as a marker for the mitochondrial fraction. (*b*) Wild-type or DDB2$^{-/-}$ MEFs were treated with cisplatin. Four hours after treatment, cells were harvested and the extracts were analyzed for ATR-P and phospho(Ser-18)-p53. (*c*) Total RNA from cisplatin treated or untreated cells was subjected to real time RT-PCR assay for p21-mRNA following a procedure described in Reference (11) in main text).

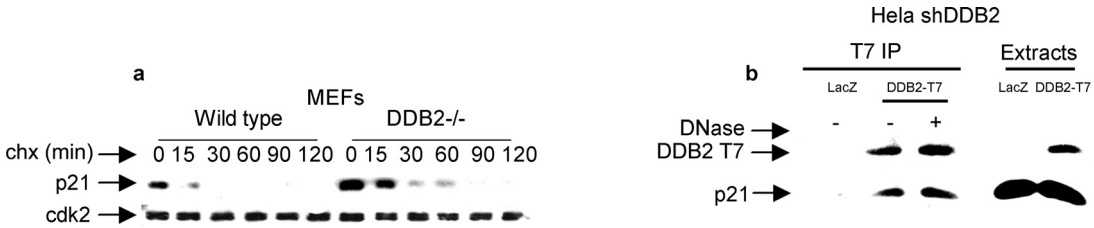


Fig. S3. (*a*) Wild-type MEFs or DDB2$^{-/-}$ MEFs were treated with cycloheximide for the indicated time periods. Cells were harvested and the extracts were subjected to Western blot analysis for the levels of p21. (*b*) HeLa cells expressing shRNA against DDB2 were infected with adenovirus expressing T7-tagged DDB2 or Lac Z. Extracts of the infected cells were treated with or without DNase (5 units) in the presence of 10 mM MgCl2 for 20 minutes at RT. The extracts were then subjected to immunoprecipitation with T7-antibody followed by Western blot for p21.

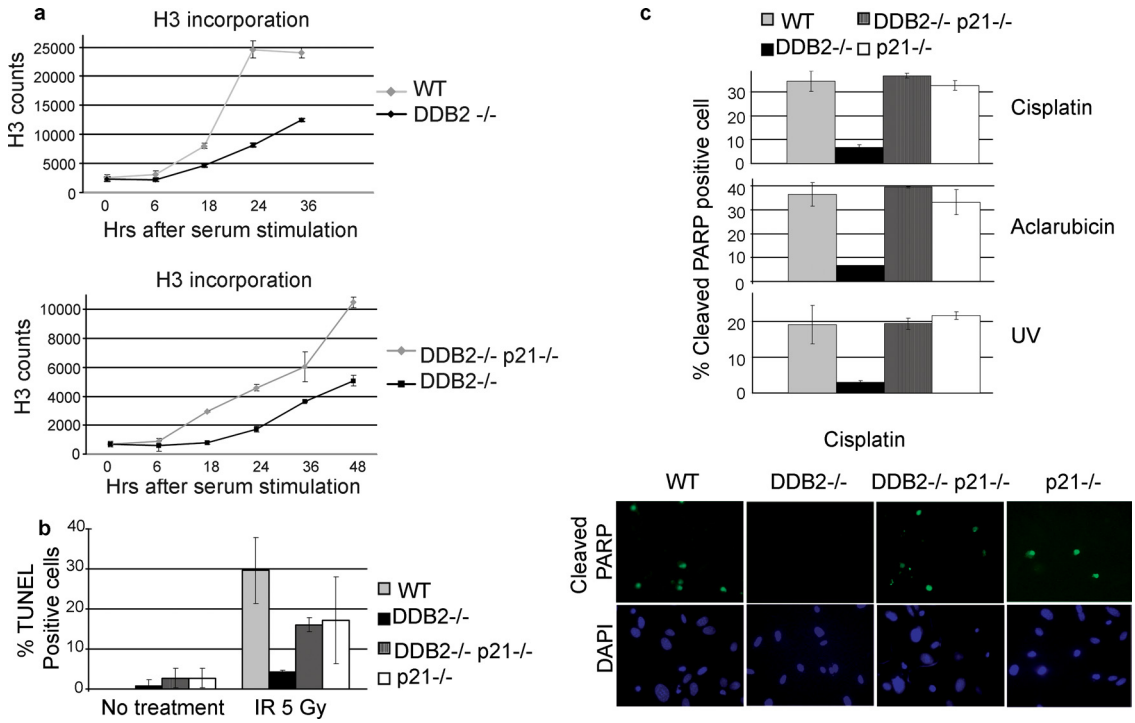


Fig. S4. (*a*) MEFs of the indicated genotype were synchronized by serum starvation and then stimulated by serum addition. At the indicated time points, 3H-thymidine was added for 30 minutes, and the incorporation was measured by determining the TCA-insoluble counts. (*b*) The MEFs were treated with 5 Gy of ionizing radiation. Eighteen hours after treatment, the cells were subjected to TUNEL assay. (*c*) The cells were treated as in Fig. 4*A* and then subjected to caspase activation by assaying for cleaved PARP. Cleaved PARP was measured by immunostaining. A representative field of cleaved PARP is shown in the *lower panel*, and quantification is shown in the *upper panel*.

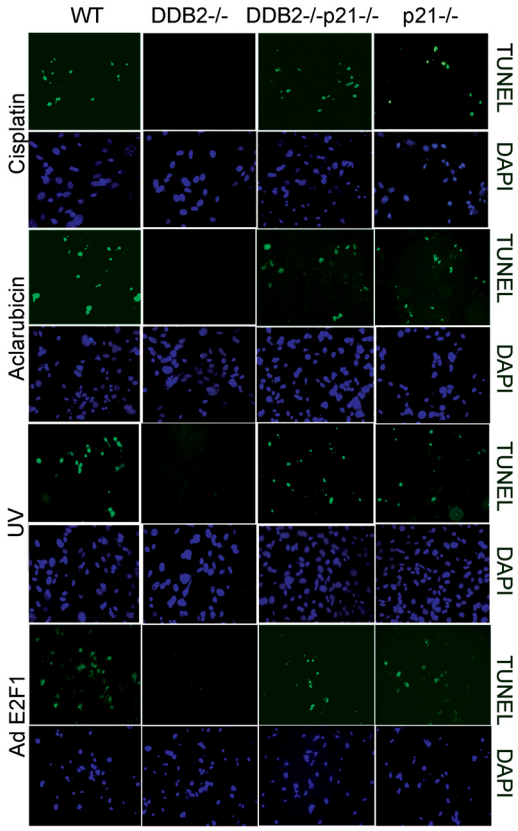


Fig. S5. WT, DDB2$^{-/-}$, DDB2$^{-/-}$p21$^{-/-}$ or p21$^{-/-}$ MEFs were treated with cisplatin, aclarubicin, UV or infected with adenovirus expressing E2F1. Twenty-four hours after treatment or infection cells were subjected to TUNEL assay to measure apoptosis.

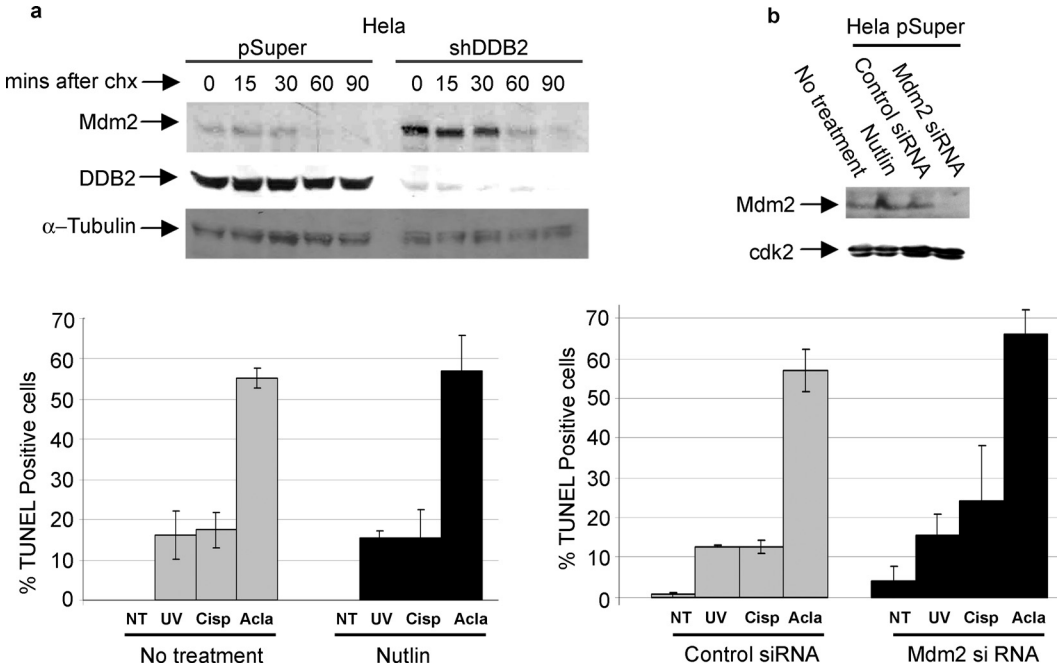
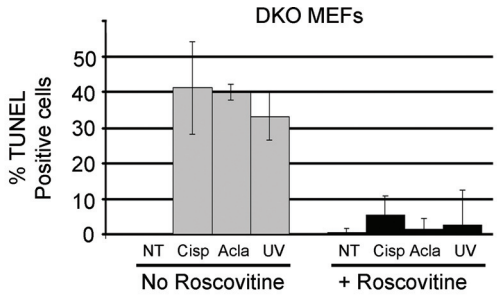


Fig. S6. (*a*) Decay rates of Mdm2 in control HeLa cells or HeLa cells expressing DDB2-shRNA. (*b*) Control HeLa cells (pSuper) transfected with Mdm2-siRNA or treated with nutlin were further treated with UV, cisplatin, or aclarubicin. The cells were then subjected to TUNEL assay.

a



b

DKO	No treatment	Cisplatin	Aclarubicin	UV
G1	44.06 +/- 2.7	38.6 +/- 1.0	34.7 +/- 6	37.2 +/- 1.3
S	15.5 +/- 2.8	18.3 +/- 1.1	18.5 +/-0.6	17.9 +/- 0.7
G2	18.4 +/- 2.5	19.6 +/- 0.5	14.8 +/- 1.2	17.9 +/- 1.3
Sub G1	7.5 +/- 0.4	16.7 +/- 0.1	20.5 +/-0.4	19.8 +/- 2.1
Poly	11.9 +/- 1.9	7.7 +/-0.2	11.7 +/- 3.9	7.7 +/- 0.6
DKO Roscovitine				
G1	37.1 +/- 6.3	44.7 +/- 0.6	53.2 +/- 1.5	43.1 +/- 1.6
S	13.4 +/- 1.3	17.5 +/- 0.7	16.4 +/- 0.3	17.6 +/- 1.0
G2	23.6 +/- 3.7	23.4 +/- 1.1	13.2 +/- 0.6	21.14 +/- 0.8
Sub G1	7.7 +/- 3.1	6.6 +/- 0.8	11.1 +/- 0.54	5.58 +/- 1.2
Poly	17.1 +/- 7.0	7.5 +/- 0.6	5.5 +/- 0.7	10.1 +/- 0.5

Fig. S7. DDB2$^{-/-}$ or DDB2$^{-/-}$p21$^{-/-}$ MEFs were treated with cisplatin, acalrubicn, or UV followed by further treatment with roscovitine (20 nM). The cells were then subjected to TUNEL assay (*a*) and flow-cytometric analyses (*b*).