Table. S1. Nucleolin contributes to ATR-dependent phosphorylation following replication stress.

A

	Negative (-)	Negative 1hr	Negative 4hr	Negative 8hr	NCLsi (-)	NCLsi 1hr	NCLsi 4hr	NCLsi 8hr
NCL	1	1	0.87	1	0.47	0.59	0.44	0.48
pKAP1	1	4.3	9.3	13.1	0.71	1.4	3.4	7.5
pChk1	1	3.2	3.9	2.8	0.94	1.5	1	0.92
pRad17	1	2	1.6	2.1	0.95	0.95	0.9	0.9
pRPA32	1	2.5	3.2	2.7	0.32	0.45	0.82	1.2

B

	Negative (-)	Negative 1hr	Negative 4hr	NCLsi (-)	NCLsi 1hr	NCLsi 4hr
NCL	1	1	0.97	0.65	0.74	0.78
pRad17	1	1.7	1.7	0.55	0.89	1.4
pChk1	1	5.6	4.6	1.4	3.4	3
pKAP1	1	2.8	2.4	1.3	2.1	2.1
pRPA32	1	3.5	4.5	1.5	0.89	1.6

*Quantification about Fig. 2A and 2B was carried out by ImageJ software and the ratios to unirradiated samples of negative knockdown were calculated.

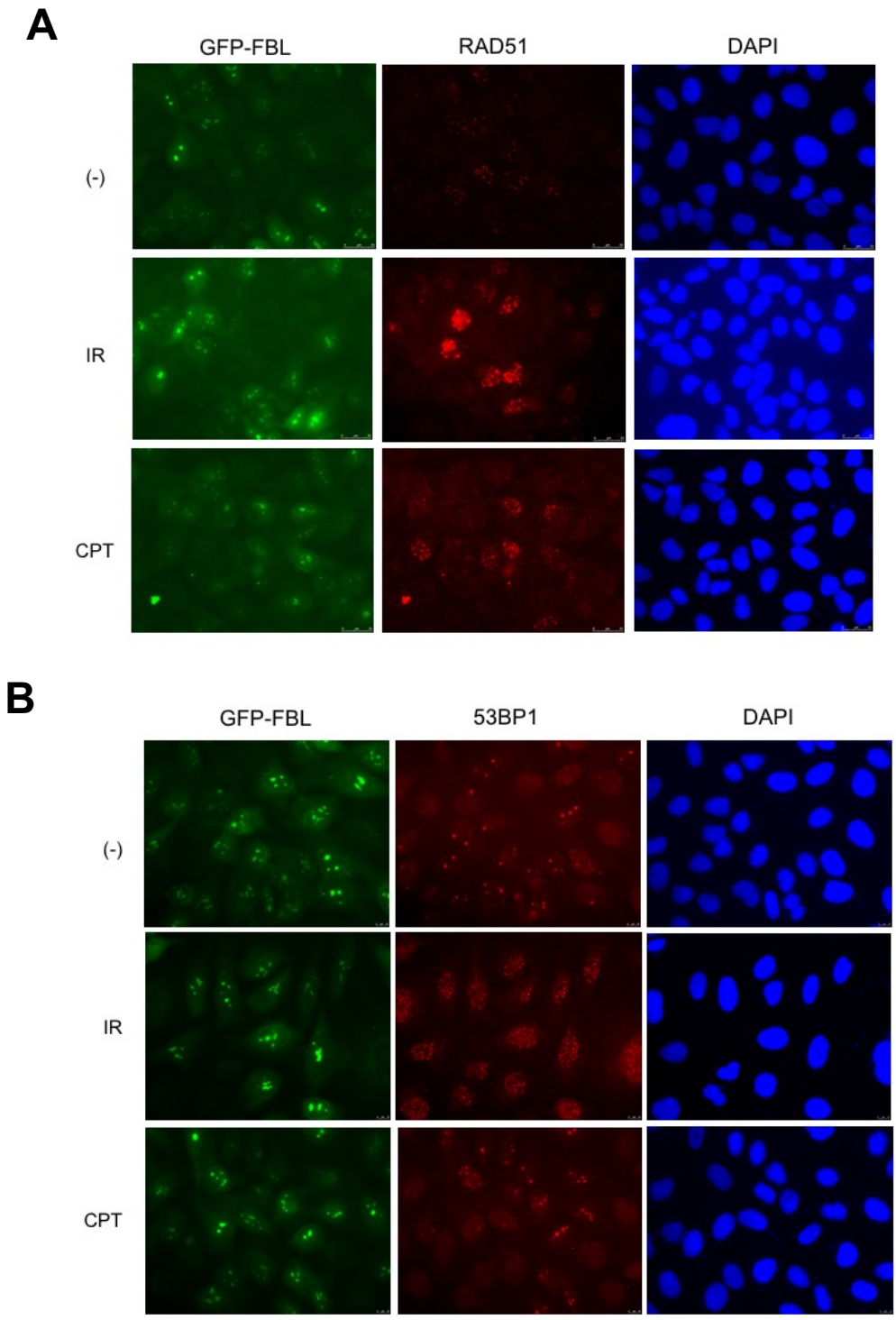


Fig. S1. DDR proteins cannot form foci in nucleolus.

GFP-FBL-expressing U2OS cells were treated with γ-ray or CPT. Then, immunofluorescence staing was performed for these cells. Above pictures are original pictures in Fig 1A.

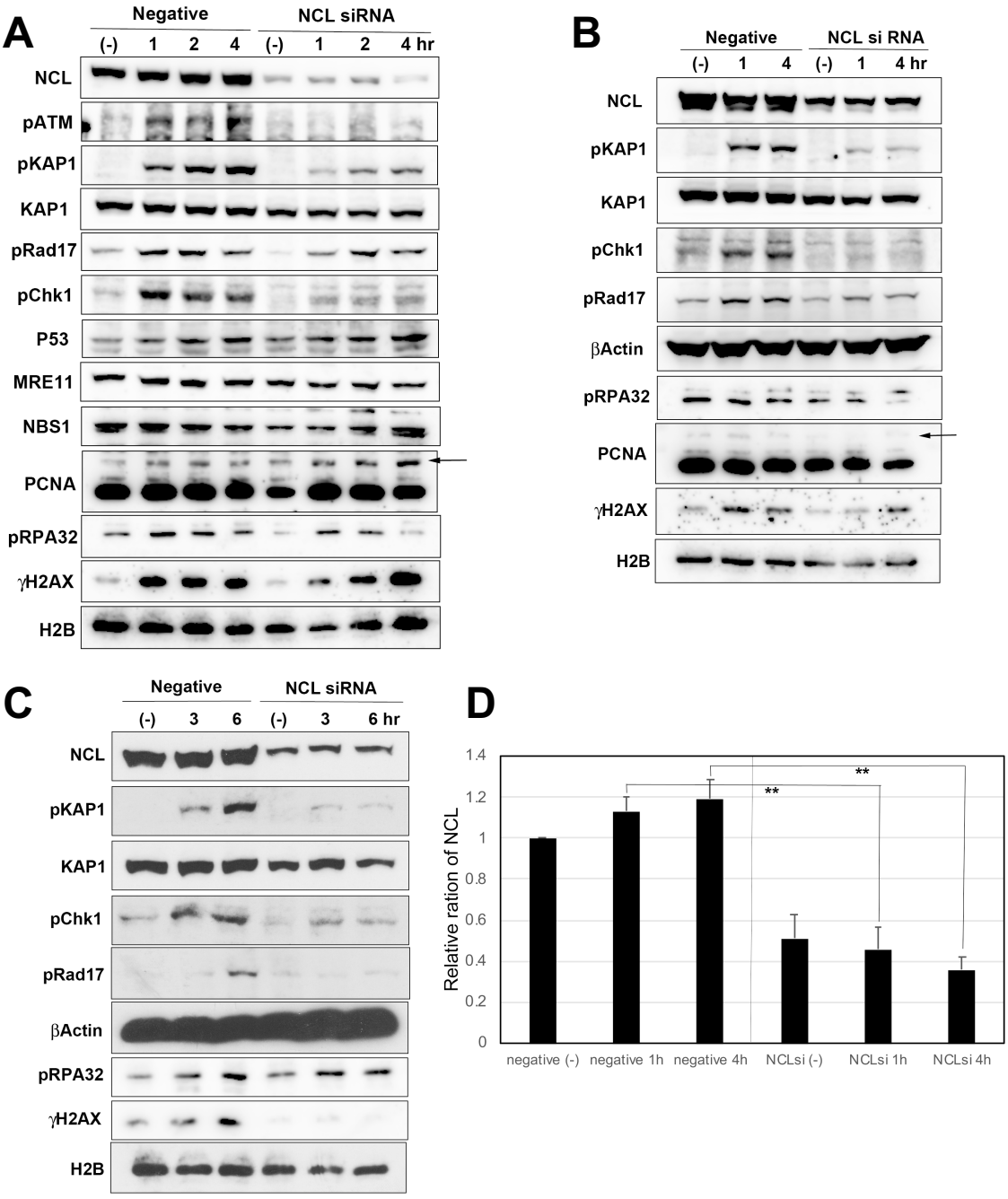
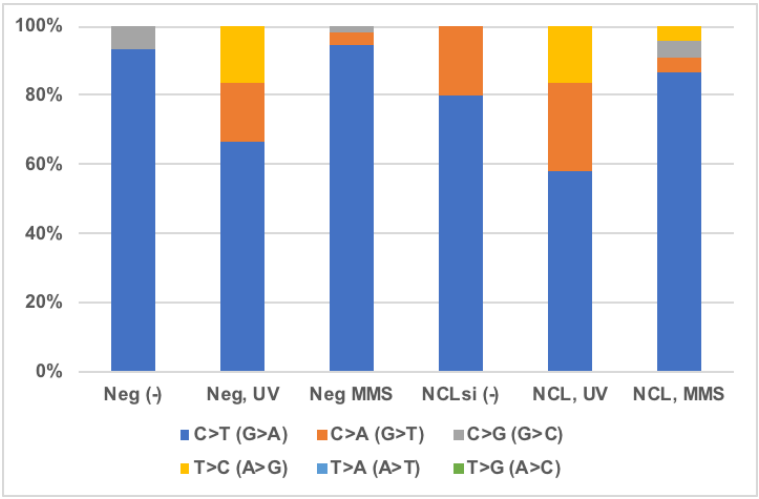


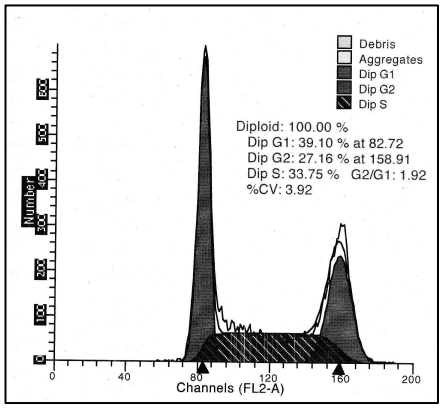
Fig. S2. Nucleolin contributes to ATR-dependent phosphorylation following replication stress. 48BR cells were transfected by nucelolin siRNA. After 2 days, these cells were irradiated by 10J of UV (A) or treated with 2 μM of CPT (B) or 10 mM of hydroxyurea (C). Then, their cells were harvested at indicated times and analyzed by Western blot using indicated antibodies. Arrows indicate the bands of mono-ubiquitinated PCNA in (A) and (B). (D) The efficiency of NCL knockdown. Quantification of Fig. 2C and other two experiments were carried out by ImageJ software (**$p<0.01$).

A



B

Negative siRNA



NCL siRNA

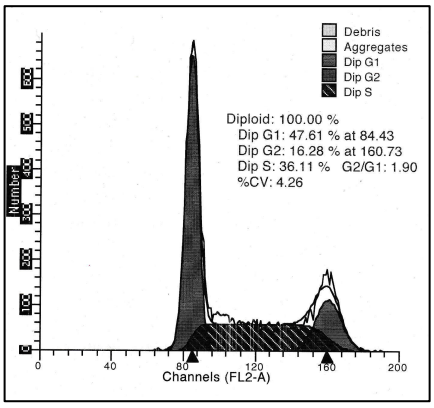


Fig. S3.

(A) *sup*F mutant frequency in nucleolin-depleted cells. UV-irradiated, MMS-treated or un-irradiated pSP189 was transfected into NCL siRNA or negative control RNA-introduced cells. After 48 hours, replicated pSP189 was recovered from cells, and *sup*F mutation in the plasmids was determined. (B) Nucleolin-knockdown dose not disturb the cell cycle distribution. U2OS cells were transfected by nucleolin siRNA. After 2 days, these cells were fixed at indicated times by ethanol. After staining them by propidium iodide, the distribution of cell cycle was analyzed by flowcytometer.

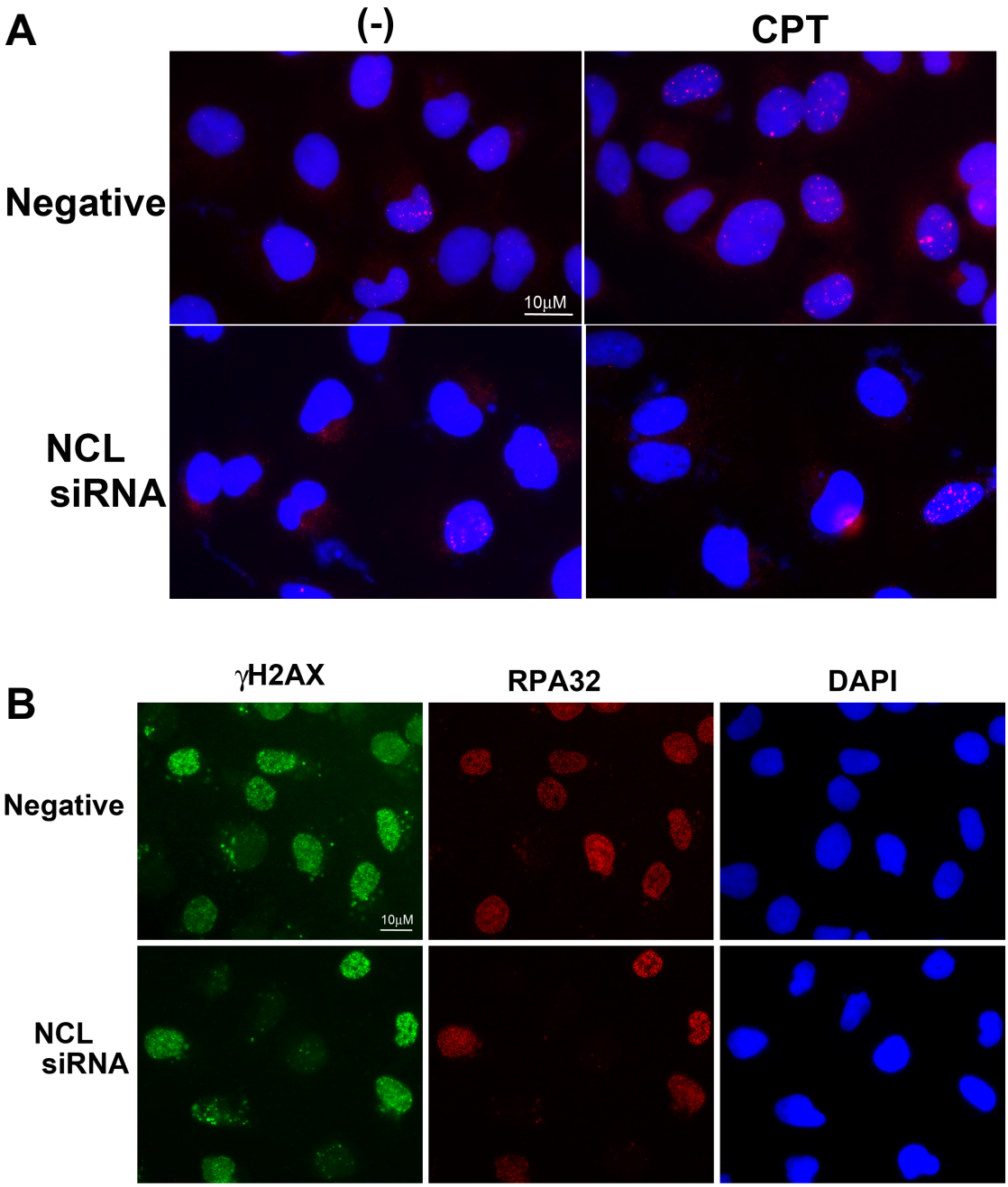


Fig. S4. Nucleolin participates in HR pathway following replication stress.

(A and B) U2OS cells were transfected by nucleolin siRNA or negative control siRNA, and after 2 days these cells were treated by 2 μM of CPT. After 4 hours, their cells were fixed and immuno-staining was performed using anti-RAD51 antibody (A) or anti-RPA32 antibody (B). The percentage of focus positive cells was shown in Fig. 3AB.

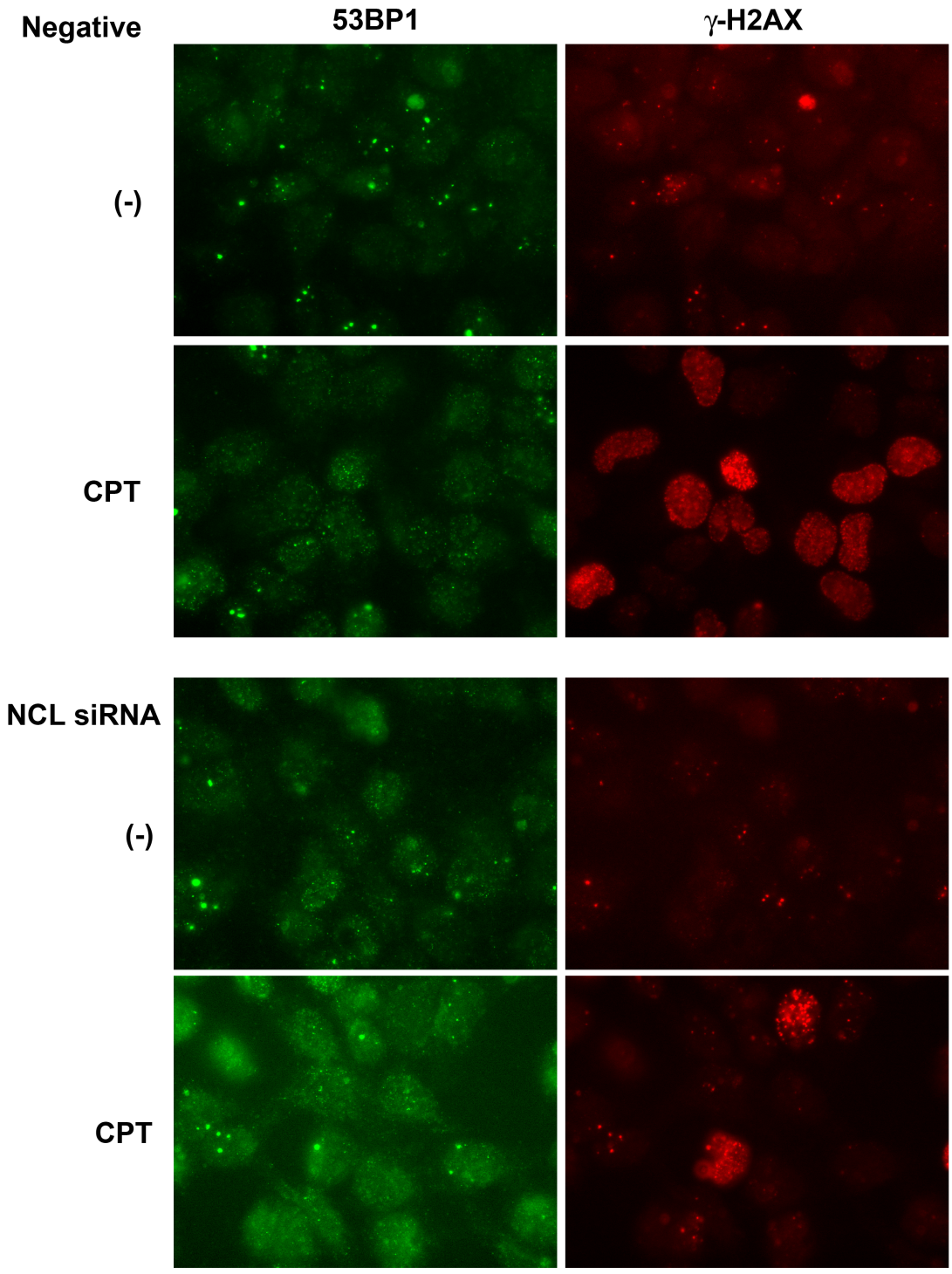


Fig. S5. Focus formation of 53BP1 in nucleolin-depleted cells.

U2OS cells were transfected by nucleolin siRNA or negative control siRNA, and after 2 days these cells were treated by 2 μM of CPT. After 4 hours, their cells were fixed and immuno-staining was performed using anti-53BP1 and γH2AX antibodies.

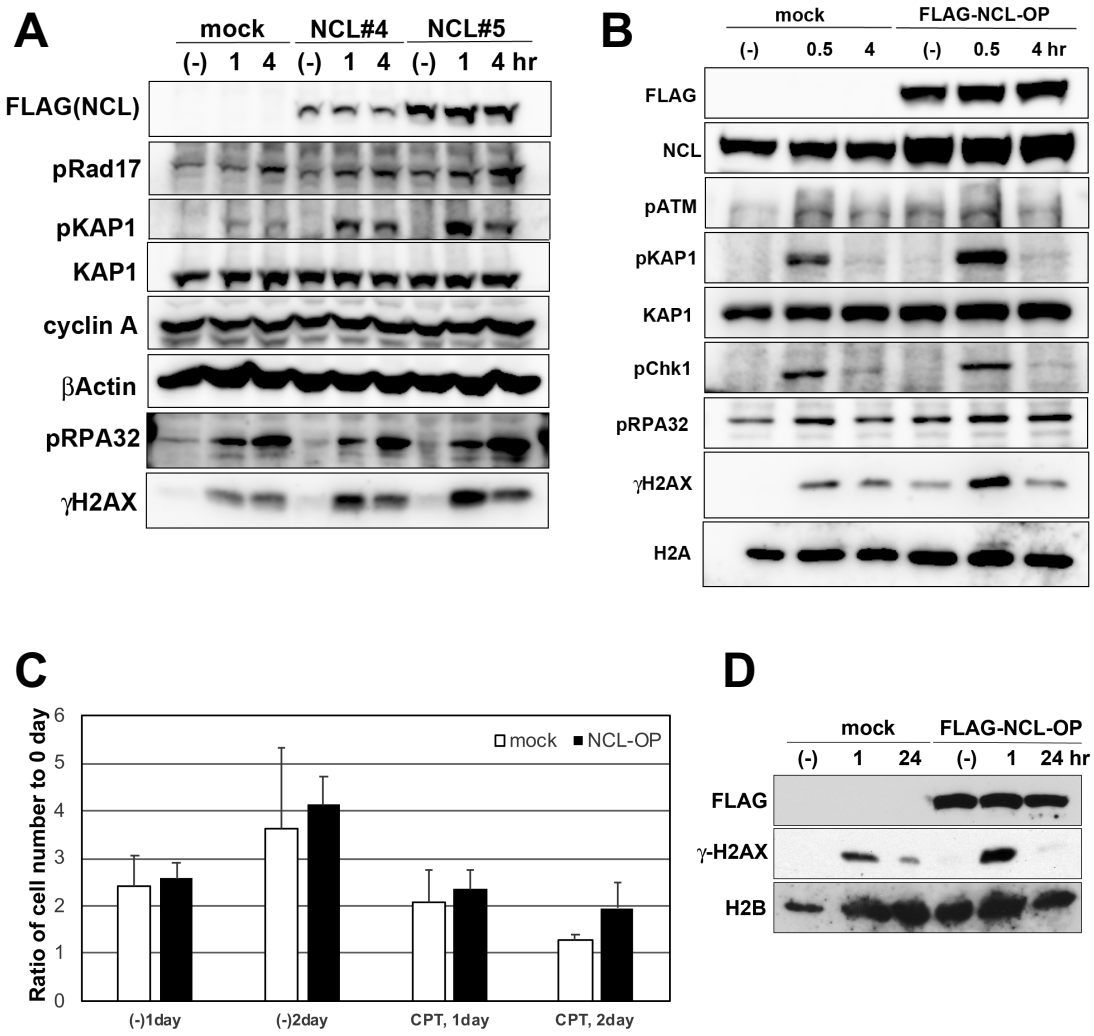


Fig. S6. Overexpression of nucleolin amplified DNA damage responses.

Nucleolin-overexpressing (B and D:NCL#5) or mock cells were treated by 2 μM of CPT for indicated times (A), 1μM of CPT for 1 hour (D) or irradiated with 5 Gy of γ-ray (B). After indicated times, their cells were harvested at indicated times and analyzed by Western blot using indicated antibodies. (C) Nucleolin-overexpressing (B:NCL#5) or mock cells were treated by 1μM of CPT for 1 hour, and then the cell numbers were counted with cell counter (BIO-RAD). The experiments were repeated three times and the standard deviation were calculated.

Supplementary method

SupF mutation assays

Western blotting analysis of whole cell extracts and chromatin fraction isolation were performed as described previously [14, 15]. As briefly explained, The pSP189 plasmid DNA (50 μg) dissolved in 1 ml of TE buffer (10 mM Tris [pH 7.5], 1 mM EDTA) was irradiated with 200 J/m2 UV or treated with MMS (methylmethanesulfonate; 0.1, 30 min) in a sterile plastic 60 mm tissue culture dish. The plasmid DNA was then precipitated with ice-cold ethanol, redissolved in TE buffer, and transfected into the indicated cells using Lipofectamine 2000 (Invitrogen). After 48 hr, the plasmid DNA was isolated, and mutation frequency and mutation sites in the plasmids were determined.