

Figure S1. Representative images of colony formation assays in DT40 and TK6 cells. (A) DT40 cells treated with APG. (B) TK6 cells treated with APG. The representative images were taken with a camera. APG, apigenin; WT, wild-type; TDP1, tyrosyl-DNA phosphodiesterase 1.

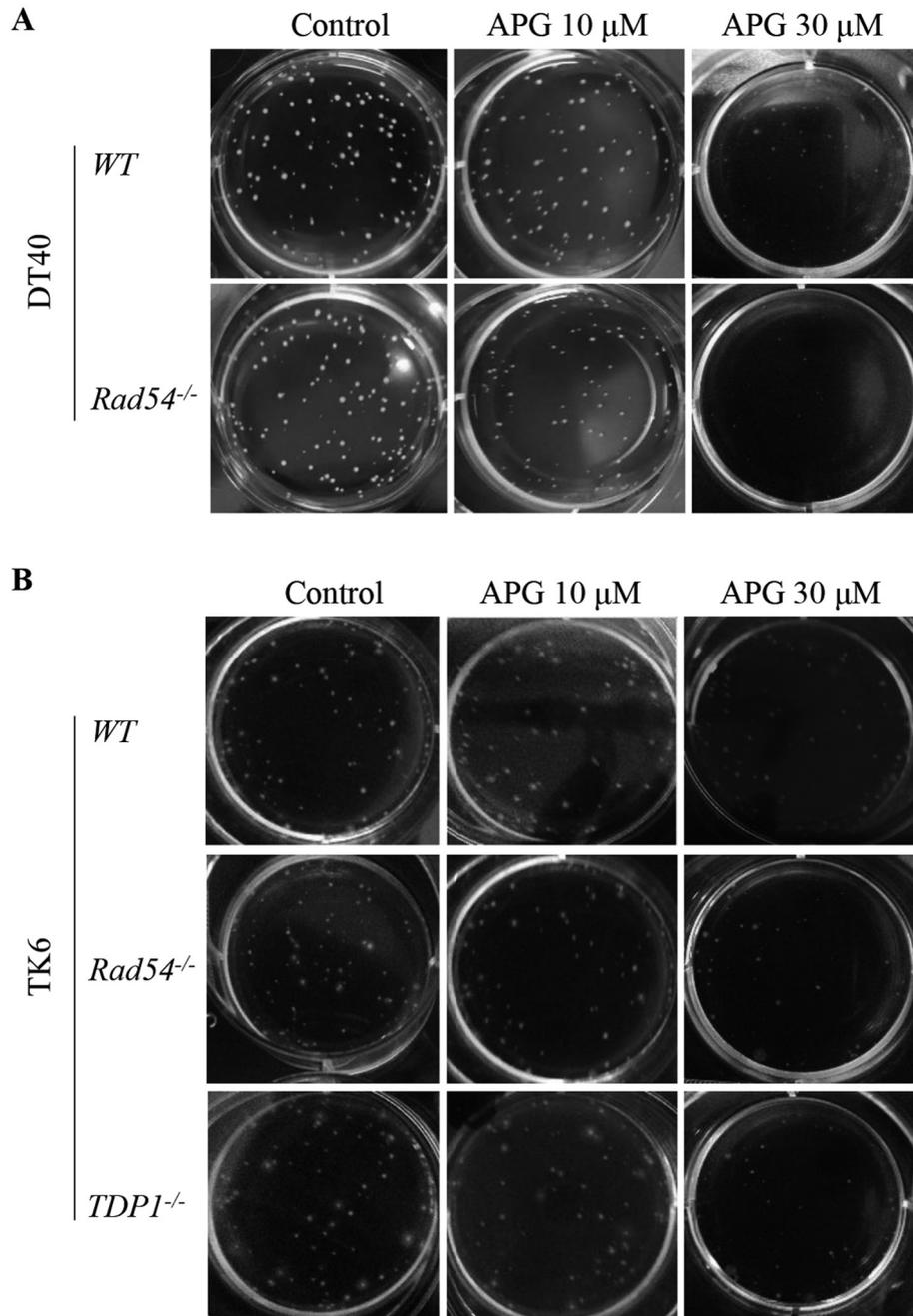


Figure S2. Representative images of immunostaining in DT40 and TK6 cells. (A) Immunostaining of *WT* and *Rad54*^{-/-} DT40 cells using an anti- γ -H2AX antibody and DAPI. Cells were treated with 30 μ M APG or 100 nM CPT for 6 h (scale bar, 10 μ M; magnification, x1,000). (B) Immunostaining of *WT*, *Rad54*^{-/-} and *TDPI*^{-/-} TK6 cells using an anti- γ -H2AX antibody and DAPI. Cells were treated with 80 μ M APG or 20 nM CPT for 6 h (scale bar, 10 μ M; magnification, x1,000). TDPI, tyrosyl-DNA phosphodiesterase 1; *WT*, wild-type; γ -H2AX, γ -phosphorylated H2A.X variant histone; APG, apigenin; CPT, camptothecin.

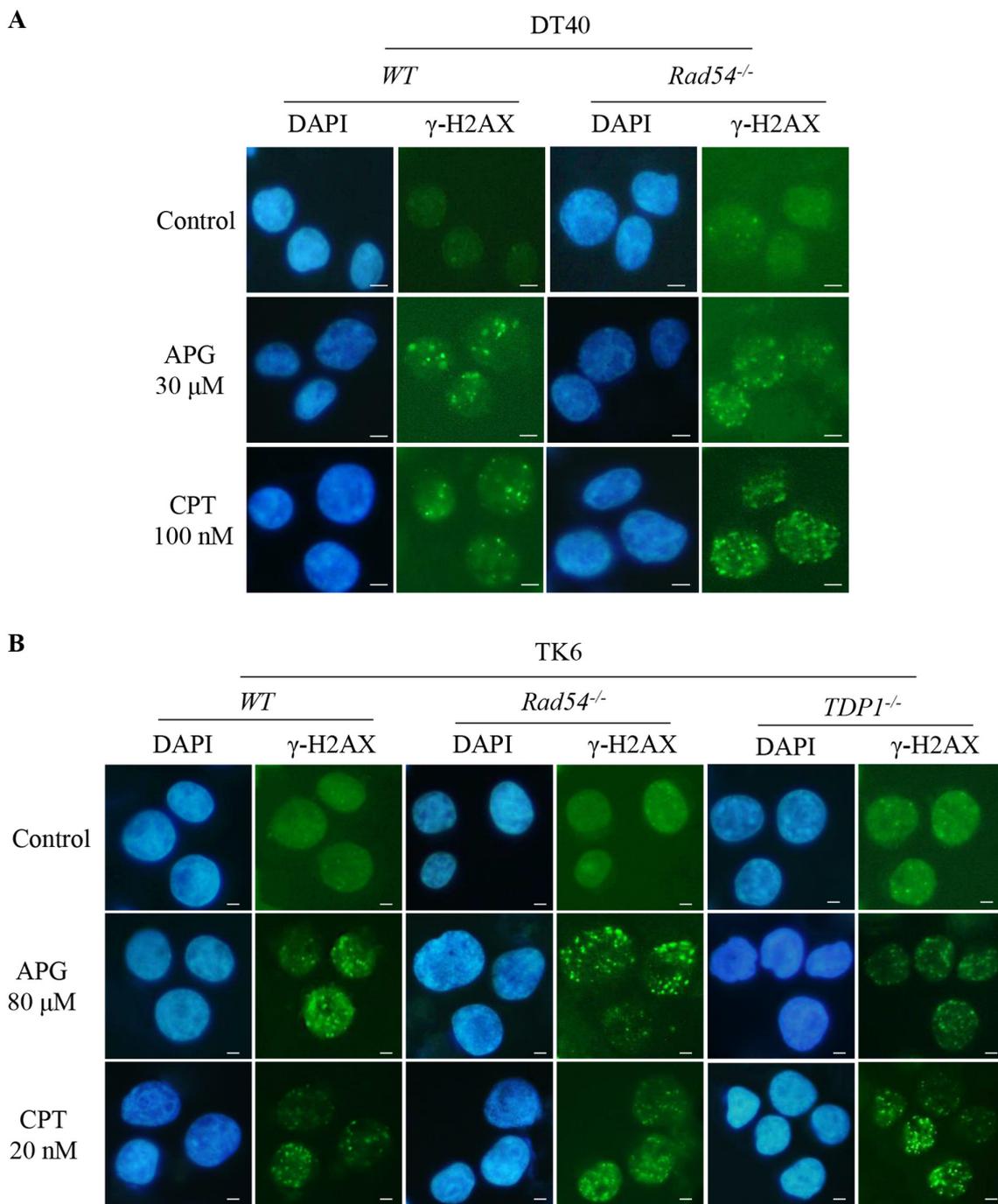


Figure S3. Effects of APG on proliferative ability and DNA damage in *TDPI*^{-/-} TK6 cells. Proliferative ability of (A) APG- and (B) CPT-treated TK6 cells determined by colony formation assays. The x-axis represents the concentration of drugs and the y-axis represents the fractions of surviving colonies on a logarithmic scale. Survival data were log-transformed to approximate normality. Two-way analysis of variance was used to test for differences in the linear dose-response curves between *WT* and *TDPI*^{-/-} cells after 72 h. **P*<0.05 (C) Quantification of γ -H2AX foci in *WT* and *TDPI*^{-/-} cells after treatment with 80 μ M APG. (D) Quantification of γ -H2AX foci in *WT* and *TDPI*^{-/-} cells after treatment with 20 nM CPT. TK6 cells were treated for 0, 3, 6 and 9 h; 100 cells were analyzed for each data-point. (E) APG induced formation of Top1cc in TK6 cells. TK6 cells were treated with 100 μ M APG and 2 μ M CPT for 2 h to detect Top1cc. Values are expressed as the mean \pm standard deviation. The experiments were performed three times independently. **P*<0.05, compared with *WT* after treatment for 3 h; [‡]*P*<0.05, compared with *WT* after treatment for 6 h; [#]*P*<0.05, compared with *WT* after treatment for 9 h. APG, apigenin; CPT, camptothecin; *WT*, wild-type; Top1cc, topoisomerase I covalent protein DNA complex; TDPI1, tyrosyl-DNA phosphodiesterase 1; γ -H2AX, γ -phosphorylated H2A.X variant histone.

