Information on Supplementary figures

Figure S1. Repair of TopII-poison-induced DSBs. TopII-cleavage complex induced by etoposide is subject to proteasome-mediated protein degradation, leaving short polypeptides associated with DSBs through covalent bonding between a tyrosine and the 5' end of the DNA strand. Elimination of the short-polypeptides is carried out either by nucleolytic processing (the left branch) or the Tdp enzymes (the right branch). DSBs are subsequently repaired by homologous recombination (HR) or nonhomologous end-joining (NHEJ).

Figure S2. DNA-damage response of *RAP80*-deficient cells. Colony formation of asynchronous populations of cells exposed to γ-ray (A) and cisplatin (B). The cells were grown in the medium containing methylcellulose for 7-10 days. The dose for each genotoxic agent is displayed on the x-axis on a linear scale. The relative percentage of surviving colonies is displayed on the y-axis on a logarithmic scale. Error bars show standard error of the mean for at least three independent experiments.

Figure S3. Plating efficiency of gene-disrupted DT40 clones. Cells of indicated genotypes were plated in a semi-solid methylcellulose medium and were cultured for 1 week. Plating efficiency was calculated by dividing the number of colonies formed by the number of the cells inoculated in the medium and multiplying by 100.

Figure S4. Enrichment of cells at G_1 phase by elutriation. Cells were separated by

centrifugal elutriation, fixed with 70% ethanol, and stained with propidium iodide. The DNA content was analyzed using FACS.

Figure S5. *BRCA1* gene disruption in *RAP80*$^{-/-}$ cells. (A) Disruption of the *BRCA1* gene in *RAP80*$^{-/-}$ cells was verified by Southern blot. (B) RT-PCR of the indicated genotype for *BRCA1* (*β-actin* was used as control). (C) The relative growth rates plotted for the indicated genotypes. Each value represents the mean and S.E. of the results from three independent experiments.

Figure S6. Generation and epistasis analysis of *RAP80*$^{-/-}$*TDP2*$^{-/-/-}$ clones. (A) Southern blot analysis of each clone. Three alleles of chicken *TDP2* genes were disrupted by insertion of *puro*, *bsr* and *hisD* selection marker cassettes (ZZ and KC; manuscript in preparation). *RAP80* alleles were then replaced with *neo* and *hyg* selection marker cassette to create the *RAP80*$^{-/-}$*TDP2*$^{-/-/-}$ cells. The genomic DNA was digested with *Eco*RV and *Bam*HI, and the *RAP80* locus was visualized by the probe shown in Fig. 1A. The upper and lower band represent the wild-type and targeted allele of *RAP80*, respectively. (B) RT-PCR of each clone. β-actin was used as a control. (C) Cellular sensitivity of each clone to topoisomerase inhibitor. Cell survival was assessed by measuring the number of live cells after 48-h exposure to etoposide. The relative percentage of live cells is displayed on the y-axis on a logarithmic scale. Note that the x-axis is not on a linear scale to show the cellular sensitivity at the low concentration. Error bars show the standard error of the mean for at least three independent

experiments.