## Supplemental material

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Figure S1. Ablation of *Blm* rescues genomic instability in *Brca1*<sup>411/411</sup> cells. (A) Quantification of genomic instability in metaphase spreads from primary mouse B lymphocytes after overnight treatment with 250 nM mitomycin C (A) or 5  $\mu$ M cisplatin (B). Graphs represent mean  $\pm$  SD of three independent experiments.



Figure S2. Analysis of SCEs in *Brca1*<sup> $\Delta$ 11/ $\Delta$ 11;*Blm*<sup> $\Delta$ / $\Delta$ </sup> cells and BLM overexpression and Rad51 foci in U2OS cells. (A) SCEs in B lymphocytes after overnight treatment with 2 µM olaparib. (B) Quantification of data from B. (C) Quantification of RAD51 IRIF in U2OS cells after the indicated knockdowns. (D) Western blot of BLM overexpression in U2OS cells. Graphs show mean ± SD of three independent experiments. Bars, 10 µm. EV, empty vector.</sup>



Figure S3. Ablation of *Blm* increases CSR in *Brca*  $1^{\pm 11/411}$  cells but has no effect on RPA intensity. (A) Flow cytometry analysis of CSR in B cells from mice of indicated genotypes. Numbers indicate the percentage of IgG1<sup>+</sup> cells. (B) Quantification of IgG1<sup>+</sup> B cells. (C) Flow cytometry analysis of RPA32 intensity versus DNA content (propidium iodide [PI]) in B cells from mice of indicated genotypes. (D) Histogram of RPA32 intensity from C. Labeled peak shows maximal intensity of RPA staining after IR treatment was equivalent in each genotype. Graphs show mean ± SD of three independent experiments.



Figure S4. Knockdown of PALB2, BRCA2, and XRCC2 in U2OS cells. (A) Western blot showing knockdown of PALB2. (B) Western blot showing knockdown of BRCA2. (C) Western blot showing knockdown of XRCC2.



Figure S5. Knockdown of *RECQ5*, *FBH1*, and *WRN* anti-recombination factors in U2OS cells. (A) Western blot showing knockdown of *RECQ5*. (B) Western blot showing knockdown of *FBH1*. (C) Western blot showing knockdown of *WRN*.

## Table S1. siRNA: Dharmacon siGENOME/ON-TARGETplus Human SMARTpool

Target protein (catalog number)	Target sequences (5' to 3')
siBRCA1 (M003461)	CAGCUACCCUUCCAUCAUA, GGGAUACCAUGCAACAUAA, GAAGGAGCUUUCAUCAUUC, CUAGAAAUCUGUUGCUAUG
siBLM (M007287)	GAGCACAUCUGUAAAUUAA, GAGAAACUCACUUCAAUAA, CAGGAUGGCUGUCAGGUUA, CUAAAUCUGUGGAGGGUUA
siXRCC2 (M004361)	UAGAGAAGCUUGUAAAUGA, GGAAGUAGAAGUCUUAUUU, GAAAUGCUUUAUCACCUAA, CUGGAUAGACCGCGUCAAU
siTOP3A (M005279)	GAAACUAUCUGGAUGUGUA, CCACAAAGAUGGUAUCGUA, CCAGAAAUCUUCCACAGAA, GAACAAGUCUGACCAAGCU
siBRCA2 (M003462)	GAAACGGACUUGCUAUUUA, GUAAAGAAAUGCAGAAUUC, GGUAUCAGAUGCUUCAUUA, GAAGAAUGCAGGUUUAAUA
siFBXO18 (L017404)	CCUCAACGCUGGUCAAGUA, AGGGAAGGGUGGAUUCAUA, GUGCCUAUUUGGUGUAAGA, AAACAAAACCUCGUCAUUA
siWRN (L010378)	GAUCCAUUGUGUAUAGUUA, GCACCAAAGAGCAUUGUUA, AUACGUAACUCCAGAAUAC, GAGGGUUUCUAUCUUACUA
siRECQL5 (M019338)	GAACGCUGGUGCAGAACGA, GGAUAAAGCCAAUGUCAGG, UAAGACGCCUUUACAGGAG, ACCCUAAAGGUACGAGUAA
siPALB2 (M012928)	GAAGCAACCUCUCUCUUU, GAUAAUGACUUGUCUAGGA, GCAGUGAACUUACUACUCA, GAAGUCACCUCACAAAAU

Table S2. siRNA custom synthesis: 3'-UTR targeting

Target protein	Sequences (5' to 3')
siBRCA1	Sense: GCAAGAUGCUGAUUCAUUAUU; antisense: UAAUGAAUCAGCAUCUUGCUU
siBLM	Sense: GAAUCUCAAUGUACAUAGAUU; antisense: UCUAUGUACAUUGAGAUUCUU