Supplementary Figure Legend:

Supplementary Fig. 1 Proteomic analysis of ATR-interacting proteins. ATR, ARID1A and ATRIP protein peptides identified from our mass spectrum analysis were shown.

Supplementary Fig. 2 ARID1A interacts with ATR in MDA-MB-231 Cells.

Interaction between ARID1A and ATR was further confirmed in MDA-MB-231 cells by endogenous reciprocal IP. Briefly, MDA-MB-231 cells were cultured to reach a confluence of 90% and subjected to nuclear fractionation. For each sample, 2 mg of the nuclear lysate was used for the subsequent IP analysis. 2 % of the total lysate was served as an input.

Supplementary Fig. 3 ARID1A recruitment to I-*Sce*I-induced DSBs analyzed by ChIP assay.

(A) The raw Ct values for Fig. 1D were listed.

(B) (Left) Schematic diagram of the primers used for ChIP assay based on the publication *(Rabih, Murr, et al., 2006, NCB).*Three primer sets were used for the following qPCR analysis. Primer 1: 0.5 Kb upstream DSB site; Primer 2: 2.0 Kb upstream DSB site; Primer 3: 9 Kb downstream DSB site. (Right) Recruitment of ARID1A to DSB site as detected by three pairs of primers. Briefly, DRGFP-U2OS cells with a confluence of 80% were transfected with I-*Sce*I plasmid. ChIP assay was conducted 8 h after I-*Sce*I transfection, and qPCR analyses were used to detect the enrichment of ARID1A relative to the IgG control using indicated primers. Data was shown as fold change to IgG Mock (mean ± SEM; n=3).

(C) Additional primer sets were used to verify the recruitment of ARID1A to DSB site by ChIP assay as described in (B). (Left, Primer 4: 0.6Kb upstream of I-SceI site; Right, Primer 5: 0.75Kb upstream of I-SceI site)

Supplementary Fig. 4 Schematic diagram of KillerRed system in U2OS TRE cells.

KillerRed (KR) is a light-stimulated ROS inducer fused to a tet-repressor (tetR-KR), which binds to a TRE cassette (~ 90 kb) integrated at a defined genomic locus in U2OS cells (U2OS TRE cell line). Targeting the expression of KR to one specific genome site allows visualization of the recruitment of proteins at DNA-damaged genetic loci.

Supplementary Fig. 5 Expression of ARID1A mutants.

Expression of ARID1A Wide-type (FL) and mutants in DR-GFP cells for Fig. 1L was examined by Western Blots. Briefly, DR-GFP cells were transiently transfected with indicated ARID1A constructs for 48 h, then cell lysates were prepared. A total of 30 μg of protein per sample was loaded to the SDS PAGE gel and the expression levels were determined by probing with anti-V5 antibody.

Supplementary Fig. 6 Knockdown BRG1, BRM, or ARID1A in U2OS cells.

U2OS cells were infected with shRNA lentivirus targeting BRG1, BRM, or ARID1A for 72 h. After puromycin (1 μg/ml) selection, the knockdown efficiency was evaluated by Western Blots. Luciferase knockdown served as a control (Sh-Ctrl).

Supplementary Fig. 7 ARID1A depletion did not affect the number of ATM foci after exposure to IR.

Control (+/+) and ARID1A-depleted (-/-) HCT116 cells were exposed to IR and immunostained with p-ATM (S1981). (Top) Representative images. Scale bar, 2 μm. (Bottom) Quantitative results represent the mean ± SD of three independent experiments.*p<0.01. untreat, untreated.

Supplementary Fig. 8 (A) **ARID1A depletion did not affect the presence of DSBs after exposure to IR.** Control (+/+) and ARID1A-depleted (-/-) HCT116 cells were exposed to IR, and DSBs were detected by comet assay. (Left) Representative images. Scale bar, 10 μm. (Right) Data from three independent experiments. (Student *t*-test did not indicate statistical significance.) untreat, untreated.

(B) Representative images containing multiple cells of p-RPA (S4/S8) staining for Fig. 4C.

Supplementary Fig. 9 ARID1A depletion did not affect the expression of DSB end resection factors. (Left) Schematic diagrams of HR repair assay and SSA repair assay. In these assays, DSB is induced by transfection with I-*Sce*I restriction enzyme and repaired via HR or SSA, which generates GFP-positive cells. (Right) Control (+/+) and ARID1A-depleted (-/-) HCT116 cells were exposed to IR, and Western blot analyses were performed to determine the expression levels of DSB end resection factors with the indicated antibodies.

Supplementary Fig. 10 ARID1A depletion did not affect the expression of ATM and MRN complex. Control (+/+) and ARID1A-depleted (-/-) HCT116 cells were exposed to IR, and Western blot analyses were performed with indicated antibodies. untreat, untreated. Densitometry analyses of indicated protein values (phosphorylated protein normalized against

total protein for each lane) were shown at the bottom of Western Blots. The control lane was set as 1. Each value represents the mean ± SD of three independent experiments (* $P \leq 0.05$).

Supplementary Fig. 11 (A) **ARID1A depletion sensitize MDA-MB-231 cells to PARP inhibitor.**

Colony formation assay was performed in MDA-MB-231 cells with PARP inhibitors treatments. (Left) Representative image of colony formation assay upon PAPR inhibitors treatments. (Right) Results presented were mean ± SD of three independent experiments. *$p<0.01$

(B) The growth effect of ARID1A depletion on HCT116 cells. Wide-type (+/+) and ARID1A deficient (-/-) HCT116 cells were cultured at an initial number of $2X10^6$ cells, and split every three days. The total cell number was calculated by trypan-blue cell counting. Quantitative results represent the mean ± SD of three independent experiments. *$p<0.01$

Supplementary Fig. 12 ARID1A knockdown sensitizes ovarian cancer cell line HOC8 to PARP inhibitor.

(Left) Wide-type and ARID1A-knockdown HOC8 cells were treatment by various doses of BMN673 and the apoptosis was determined by annexin V staining. (Right) Statistical results shown were mean ± SD of three independent apoptotic experiments by annexin V staining. *$p<0.01$. Knockdown efficiency was shown in Western Blots.

Supplementary Fig. 13 Ovarian cancer cells with lower expression levels of ARID1A are more sensitive to PARP inhibitor treatment than cells with higher ARID1A expression levels.

(A) Heatmap of ARID1A expression levels in indicated ovarian cancer cells based on Reverse Phase Protein Array data.

(B) Validation of ARID1A expression in selected cell lines by Western Blots, which is consistent with RPPA results.

(C) The distribution of BMN673 GI50 values in selected ovarian cancer cell lines.

(D) GI50 (50% growth inhibition) values of BMN673 in ovarian cancer cell lines with low or high ARID1A expression. Student t-test, *$p<0.01$

Supplementary Fig. 14 Rescuing experiments were conducted with ARID1A wild-type and mutant constructs (deletion mutants/patient-derived mutants).

(A) (Left) Indicated ARID1A constructs were transfected in ARID1A knockout HCT116 cells using a Tet-ON system. (Right) The next day after transfection, cells were treated with indicated concentrations of BMN673 for 48 hrs. Apoptosis was determined by annexin V staining. Statistical results shown were mean ± SD of three independent experiments. *$p<0.01$

(B) (Left) Indicated ARID1A constructs were transfected in ARID1A knockdown U2OS cells. (Right) The next day after transfection, cells were treated with indicated concentrations of BMN673 for 48 hrs. Apoptosis was determined by annexin V staining. Statistical results shown were mean ± SD of three independent experiments. *$p<0.01$

(C) Expression of ARID1A Wide-type (FL) and deletion mutants in HCT116 ARID1A-knockout cells was examined by Western Blots for Fig. 5G.

(D) Rescuing experiment was conducted using ARID1A constructs containing patient-derived mutations. (Left) Indicated ARID1A constructs were transfected in ARID1A knockout HCT116 cells. (Right) The next day after transfection, cells were treated with indicated concentrations of

BMN673 for 48 h. Apoptosis was determined by annexin V staining. Statistical results shown were mean ± SD of three independent experiments. *$p<0.01$

Supplementary Fig. 15 ATR inhibitor sensitizes cells to PAPR Inhibitor treatment.

Wild-type (+/+) and ARID1A deficient (-/-) HCT116 cells pre-incubated with DMSO, ATR inhibitor (ATRi, VE-821) for 30 min were treated with BMN673 at indicated concentrations for an additional 72 h. The apoptosis was determined by annexin V staining. Results presented were mean ± SD of three independent experiments.

Supplementary Fig. 16 Proposed model for ARID1A function in DSB End Resection and repair

ARID1A interacts with ATR, is recruited to sites of DNA damage in an ATR-dependent manner, and facilitates and/or accelerates effective DSB end resection. ARID1A-mediated chromatin remodeling, by promoting efficient DSB end resection, is required for sustaining ATR-dependent signaling.