Supplementary Figures

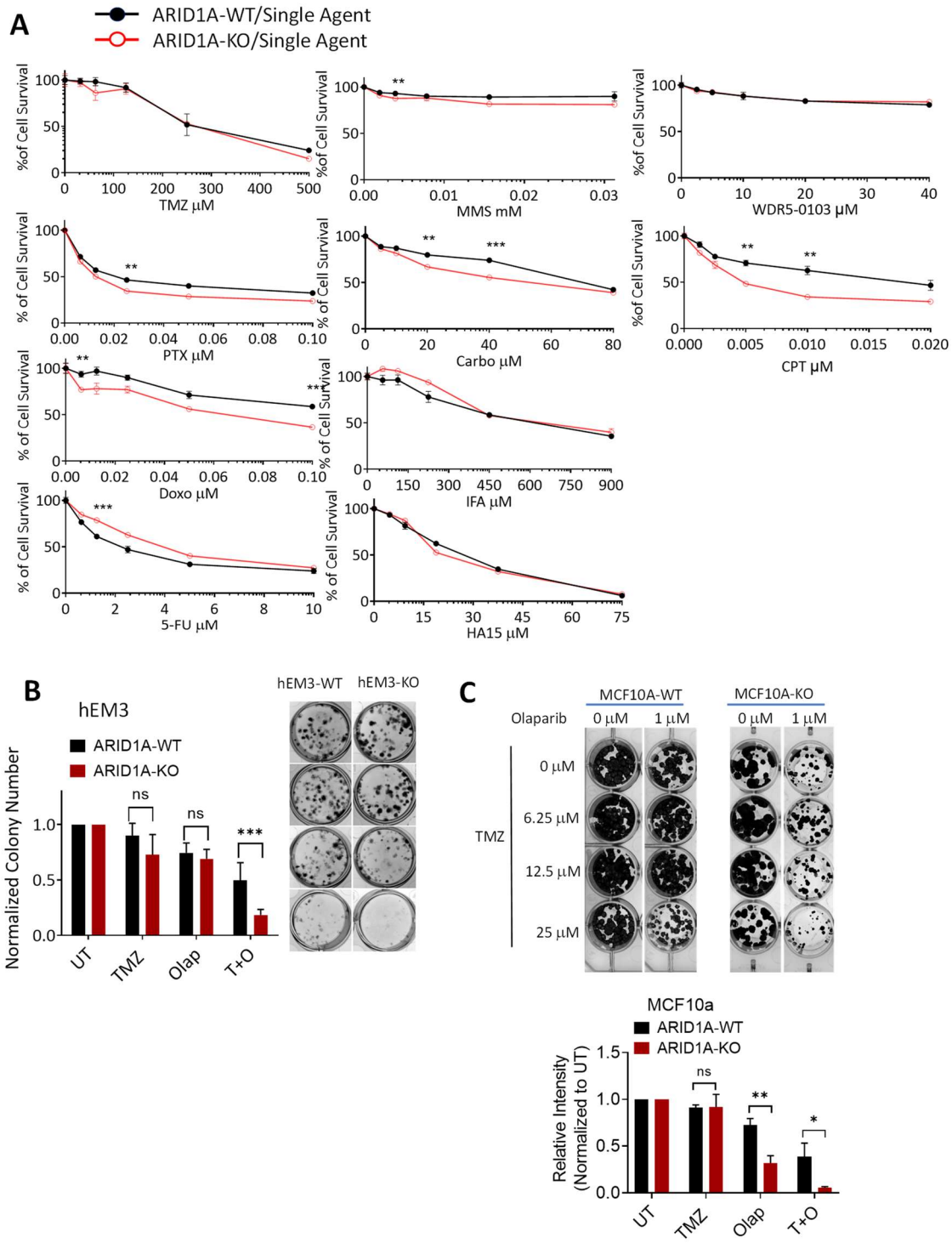


Figure S1. Single drug treatment versus TMZ/Olap combination treatment in ARID1A-WT and ARID1A-KO cells. (A) Percent cell survival of hEM3 ARID1A-WT and ARID1A-KO cells under single treatment of indicated cancer drugs. Temozolomide (TMZ), Methyl methanesulfonate (MMS), WDR5-0103, Paclitaxel (PTX), Carboplatin (Carbo), Camptothecin-11 (CPT), Doxorubicin (Doxo), incomplete Freund's adjuvant (IFA), Fluorouracil (5-FU), and HA15. **P < 0.01, ***P < 0.001, Student's *t*-test. (B) Clonogenic assay performed on an isogenic pair of hEM3 cells treated with TMZ alone or with TMZ/Olap combination. Left: Quantification of colony numbers on three replicated wells in different treatment conditions. ***P < 0.001, Student's *t*-test. (C) Clonogenic assay performed on an isogenic pair of MCF10a cells treated with TMZ alone or with TMZ/Olap combination. Bottom: Quantification of colony numbers on three replicated wells in different treatment conditions. *P<0.05, **P < 0.01, Student's *t*-test.

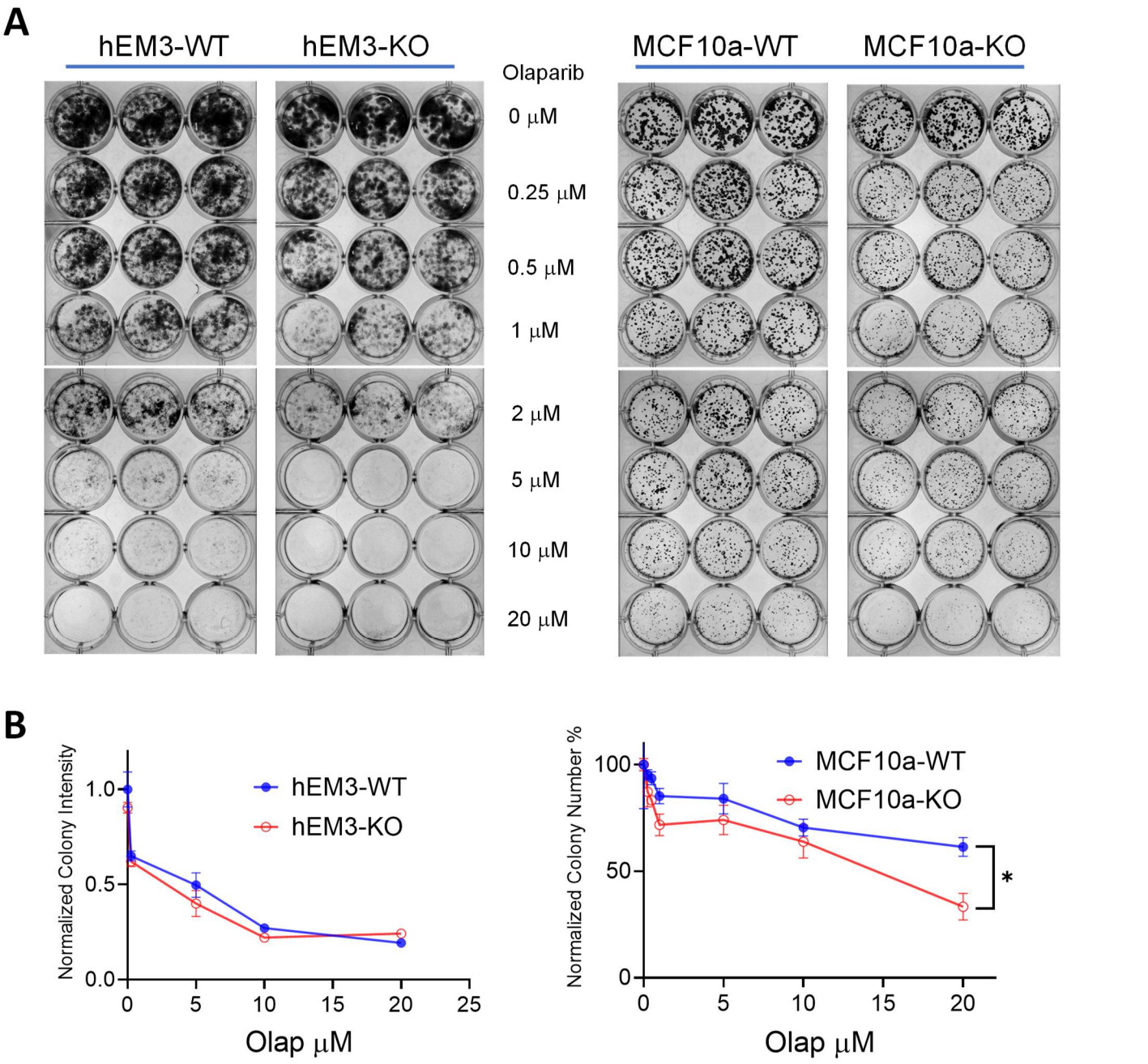


Figure S2. (A) Clonogenic assay performed on two isogenic pairs of cells (hEM3 and MCF10a) treated with various concentrations of Olaparib. (B) Quantification of colony numbers on three replicated wells in different treatment conditions. Student's *t*-test was performed, marginal difference was only identified in MCF10a cells when treated with 20 μM Olaparib (*P < 0.05).

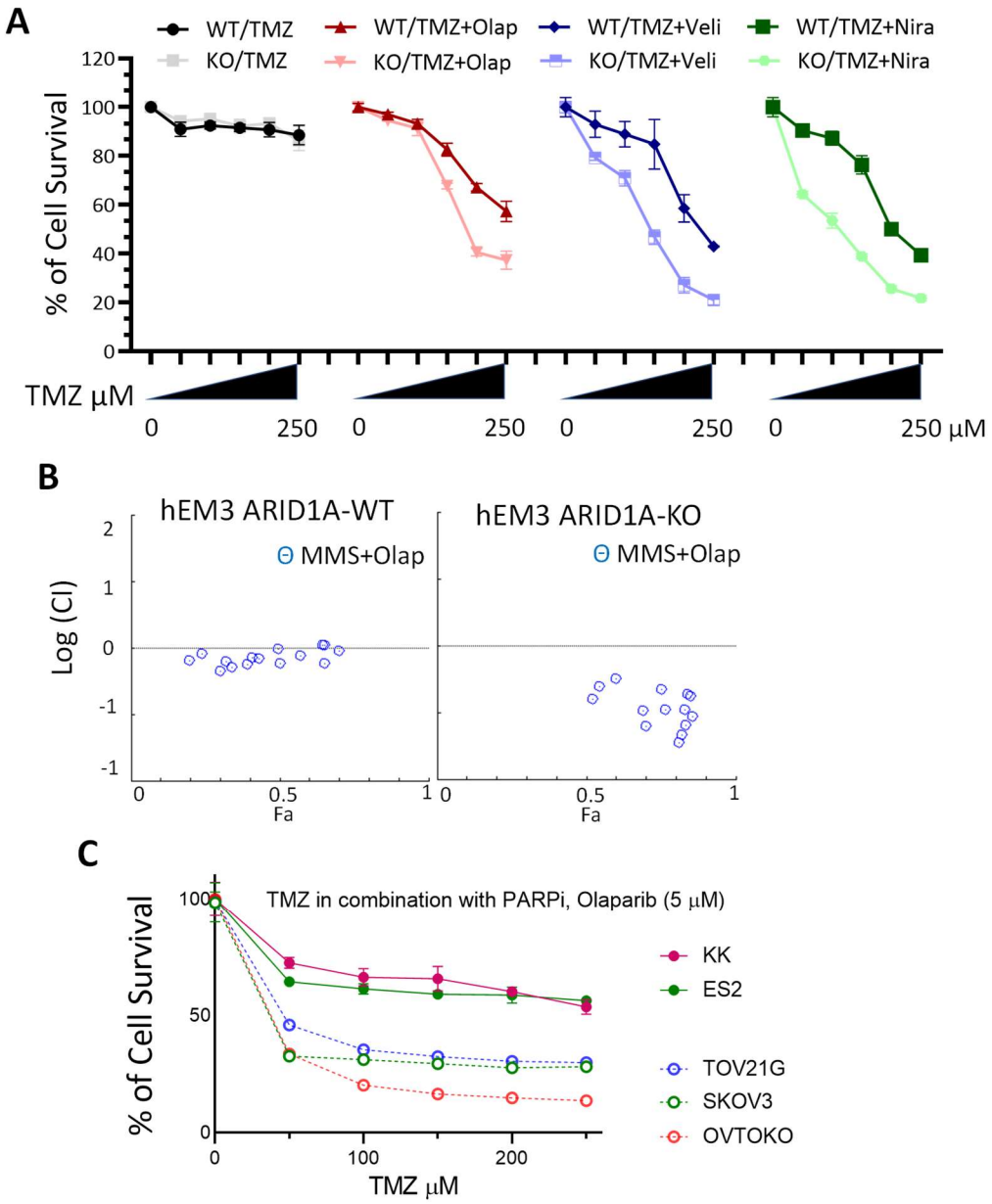
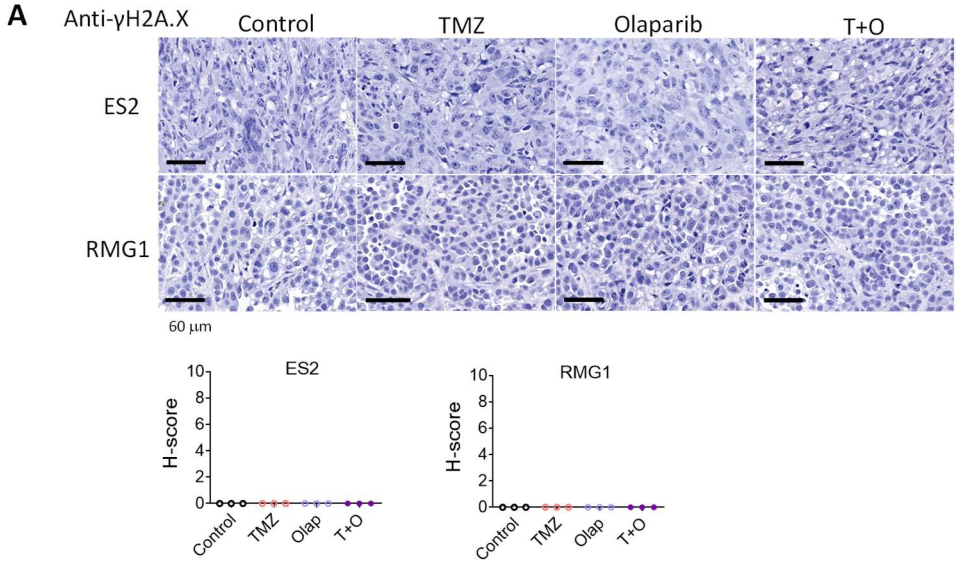
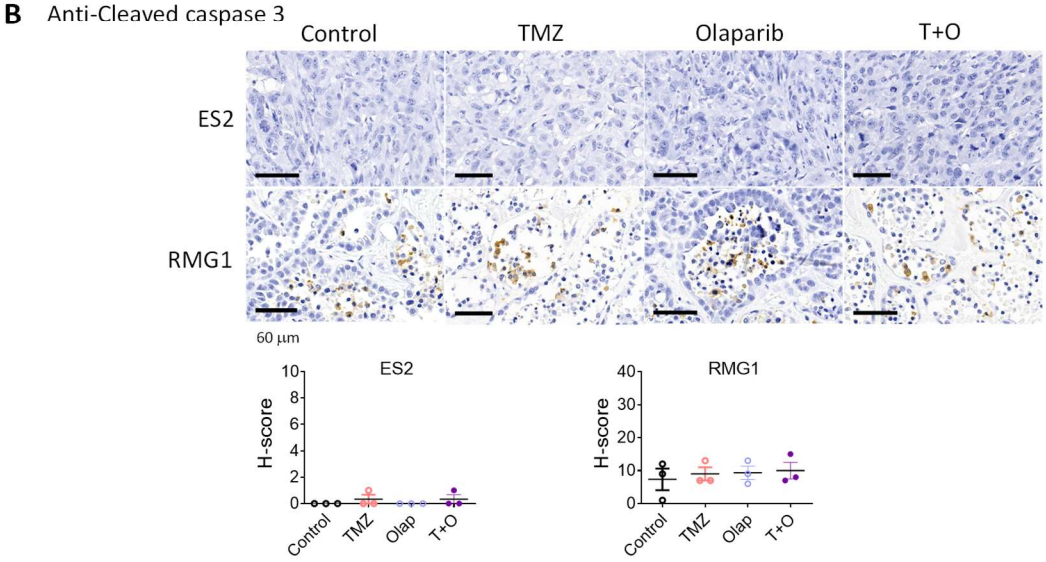


Figure S3. Anti-tumor potency of different PARP inhibitor in combination with TMZ.
(A) PARP inhibitors with different PARP trapping efficacy are evaluated in the TMZ+PARPi treatment regimen. Percent cell survival of hEM3 ARID1A-WT and ARID1A-KO cells under the treatment of TMZ and PARP inhibitor: Olaparib, Veliparib, or Niraparib which exhibit different PARP trapping efficacies. (B) The logarithmic combination index (CI) plots of DNA alkylating agent methyl methanesulfonate (MMS) in combination with PARP inhibitor, Olaparib (Olap), assessed in hEM3 ARID1A-WT and ARID1A-KO cells. (C) Cell viabilities of Type I ovarian cancer cell lines treated with a serial dilution of TMZ + 5 μM Olaparib (Olap). ES2 and KK are ARID1A-wildtype cell lines whereas OVTOKO, TOV21G and SKOV3 are ARID1A-mutated lines (Table S1 summarizes mutation status of these cancer cell lines).


A
Anti-γH2A.X
Control
TMZ
Olaparib
T+O
ES2
RMG1
60 μm
ES2
RMG1
H-score
Control
TMZ
Olap
T+O


B
Anti-Cleaved caspase 3
Control
TMZ
Olaparib
T+O
ES2
RMG1
60 μm
ES2
RMG1
H-score
Control
TMZ
Olap
T+O

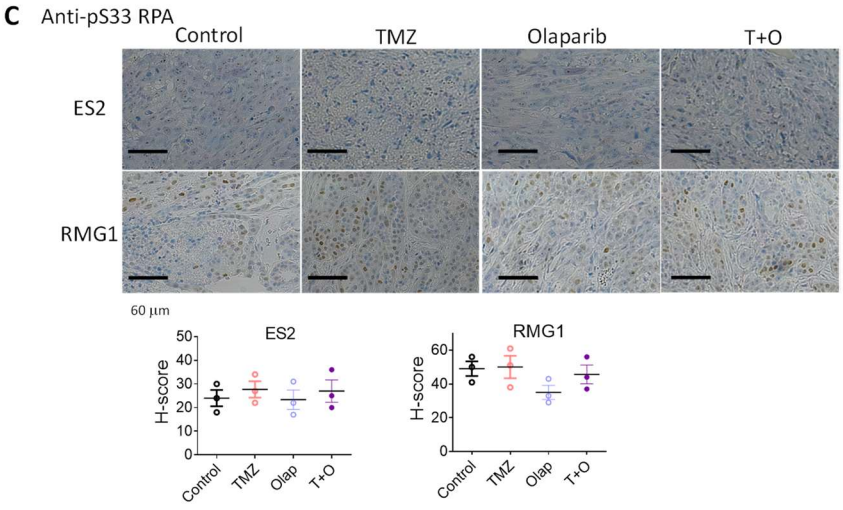

C
Anti-pS33 RPA
Control
TMZ
Olaparib
T+O
ES2
RMG1
60 μm
ES2
RMG1
H-score
Control
TMZ
Olap
T+O

Figure S4. TMZ+Olap combination treatment does not generate synergistic effect on wildtype ARID1A-bearing ovarian xenograft tumors.
(A-C) In the two ARID1A-wildtype xenograft tumors, ES2 and RMG1, the effect of *in vivo* treatment on replication stress and apoptotic tendency is evaluated using three different markers, γH2A.X (A), cleaved caspase 3 (B), and pS33 RPA (C) Top, photomicrographs of the immunostaining results. Bottom, H-scores were used to quantify immunostaining signals. Scale bar in each photomicrograph represents 60 μm.

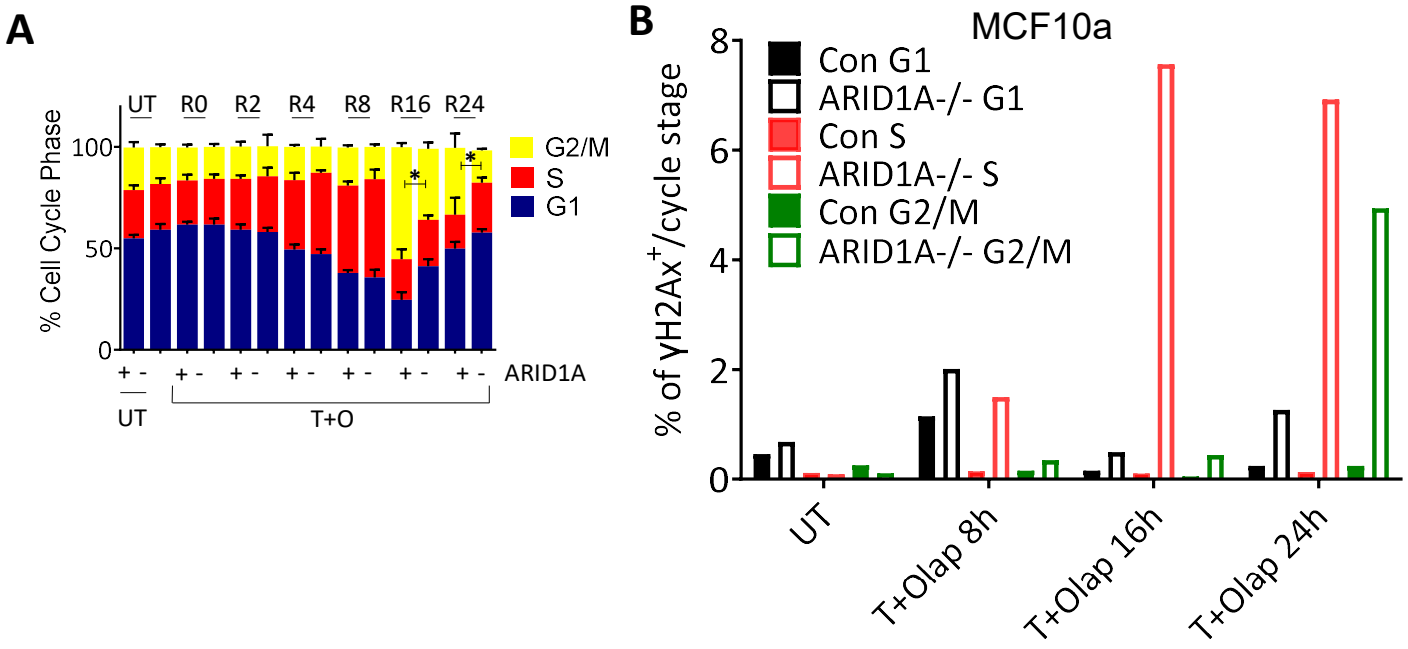


Figure S5. Delay of S phase progression in the ARID1A-KO cells.
(A) Percentage of cells in G1, S, and G2/M phases based on the flow cytometry data collected in Fig. 7A. Data are presented as mean ± SEM, n = 3, *P < 0.05, Student's *t*-test. (B) Cell cycle distribution coupled with γH2A.X signals of MCF-10a ARID1A-KO and control cells during 0-24 hours after TMZ+Olap treatment. Quantification of γH2A.X- positive cells normalized to each cell cycle stage.

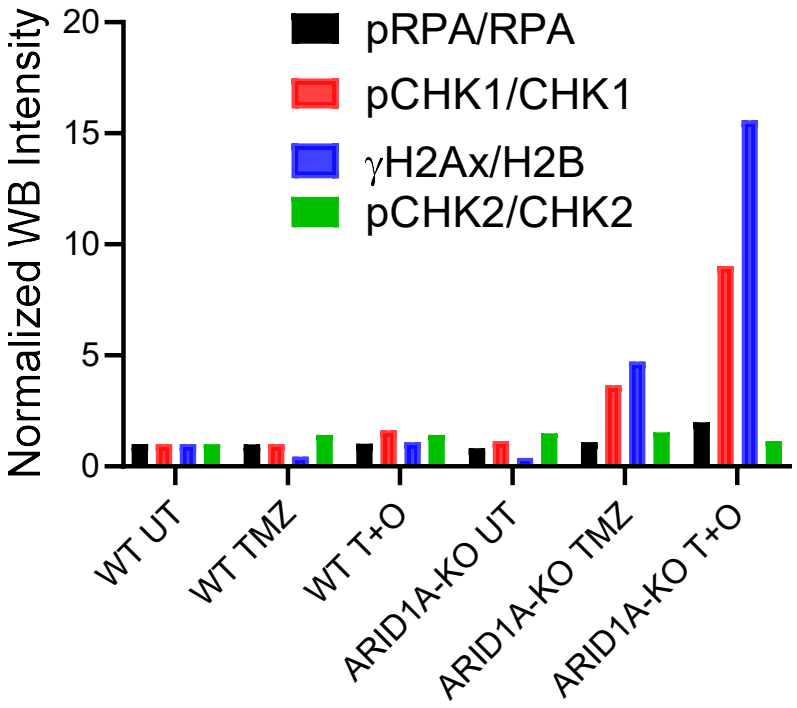


Figure S6. Quantification of Western Blot data as shown in Fig. 6E. Image J was used for quantifying protein band intensities in Fig. 6E. Relative amounts ae expressed as a ratio of each phospho-protein band relative to the total protein intensity. The results (y-axis) were normalized to the WT un-treated (UT) control group.