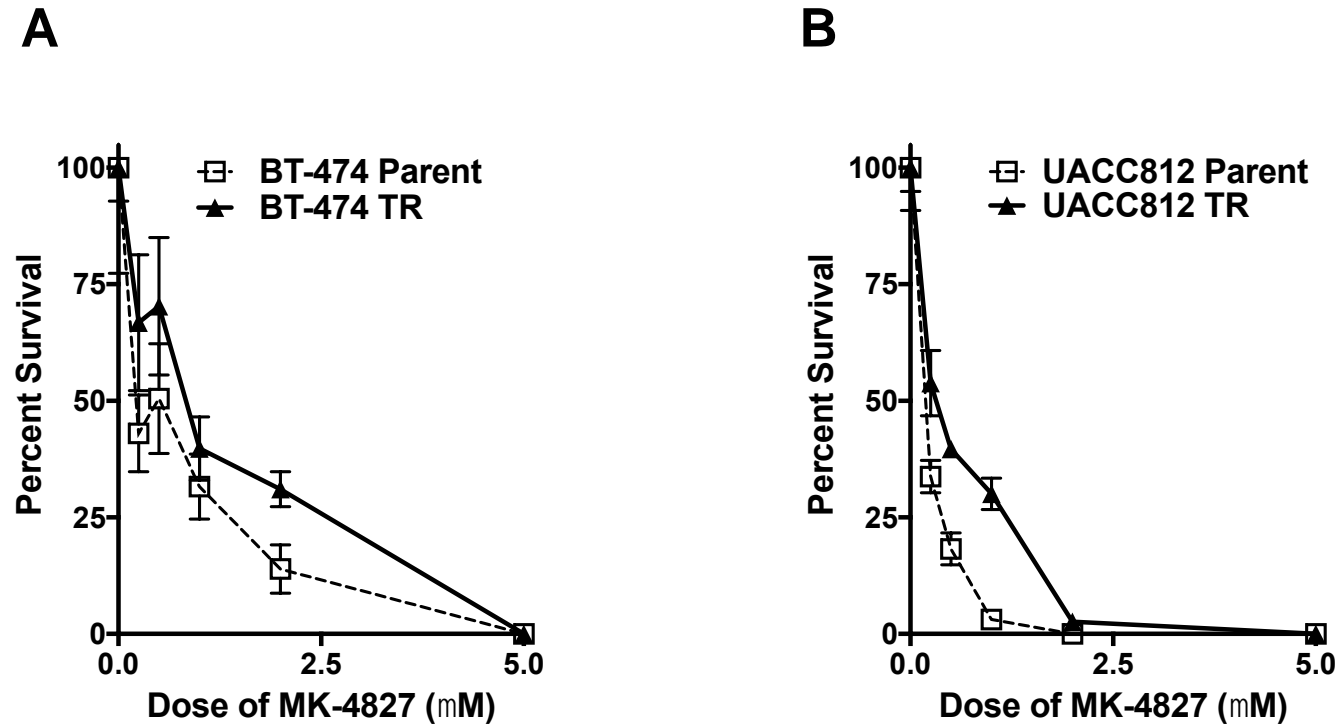
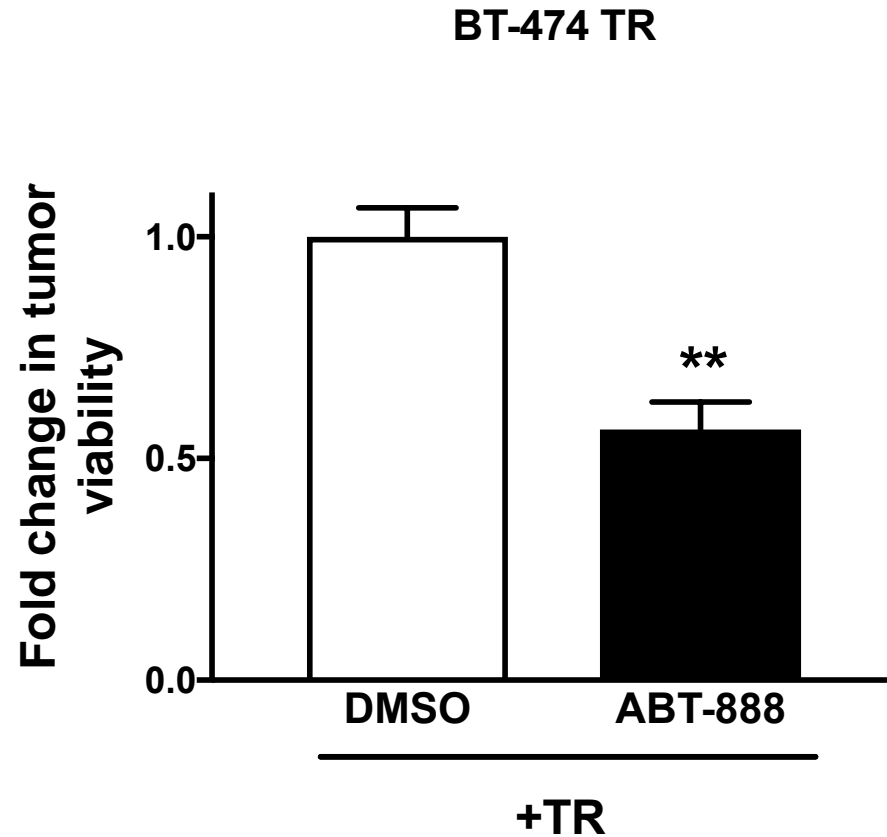


# Supplementary Figure S1



Supplementary Figure S1. MK-4827 (Niraparib) treatment decreased the survival fraction in both HER2+ trastuzumab resistant and parental breast cancer cell lines. HER2+ breast cancer cells were exposed to different doses of MK-4827 or vehicle control and then subjected to a colony formation assay. Shown is the mean survival fraction from one independent experiment performed in triplicate.

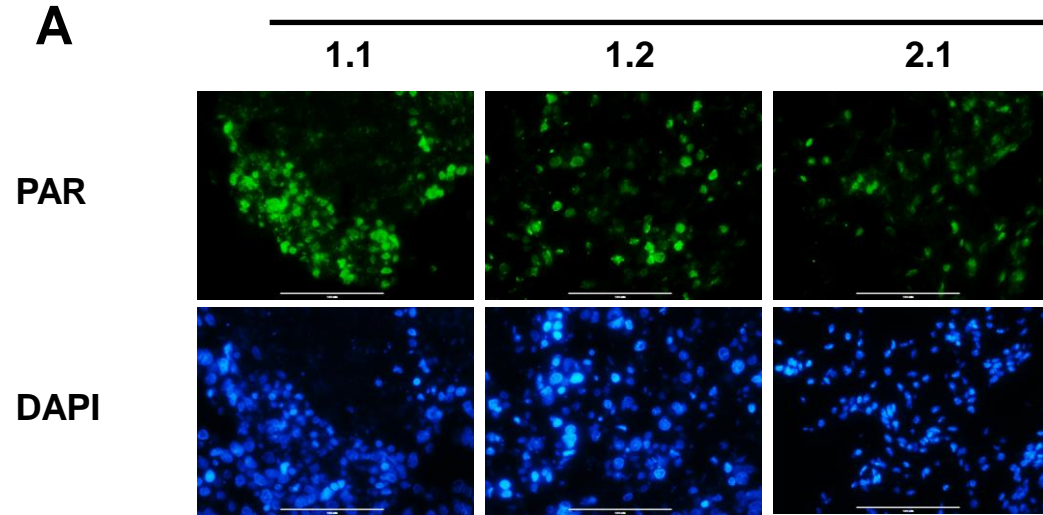
# Supplementary Figure S2



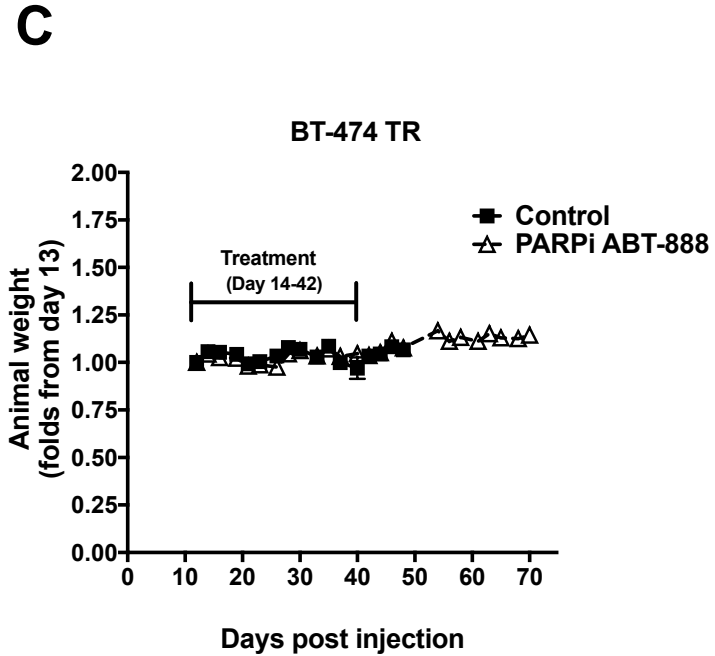
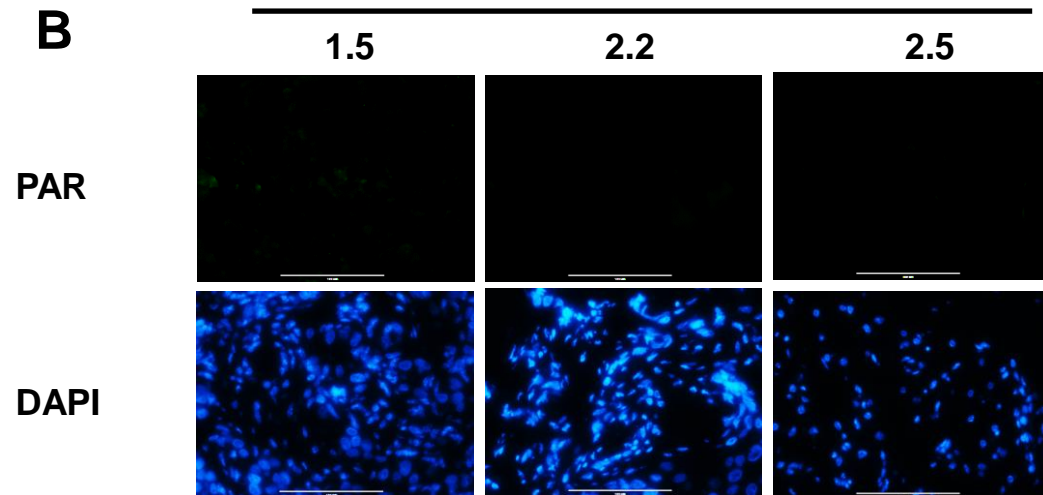
Supplementary Figure S2. PARPi reduces tumor viability in the presence of trastuzumab in BT-474 trastuzumab resistant microtumors. BT-474 TR microtumors were treated with a vehicle control (DMSO) or 10  $\mu$ M ABT-888 for 14 days. Half the media was changed every 3-4 days and then replenished with fresh drug. Tumor viability was then analyzed by a CellTiter-Glo Luminescent Cell Viability Assay. Data shown are from one independent experiment performed in pentuplicate. A one-way ANOVA test was performed to calculate the significance between groups. \*\* $p < 0.01$  and \*\*\* $p < 0.001$

# Supplementary Figure S3

Tumors of Control Animals

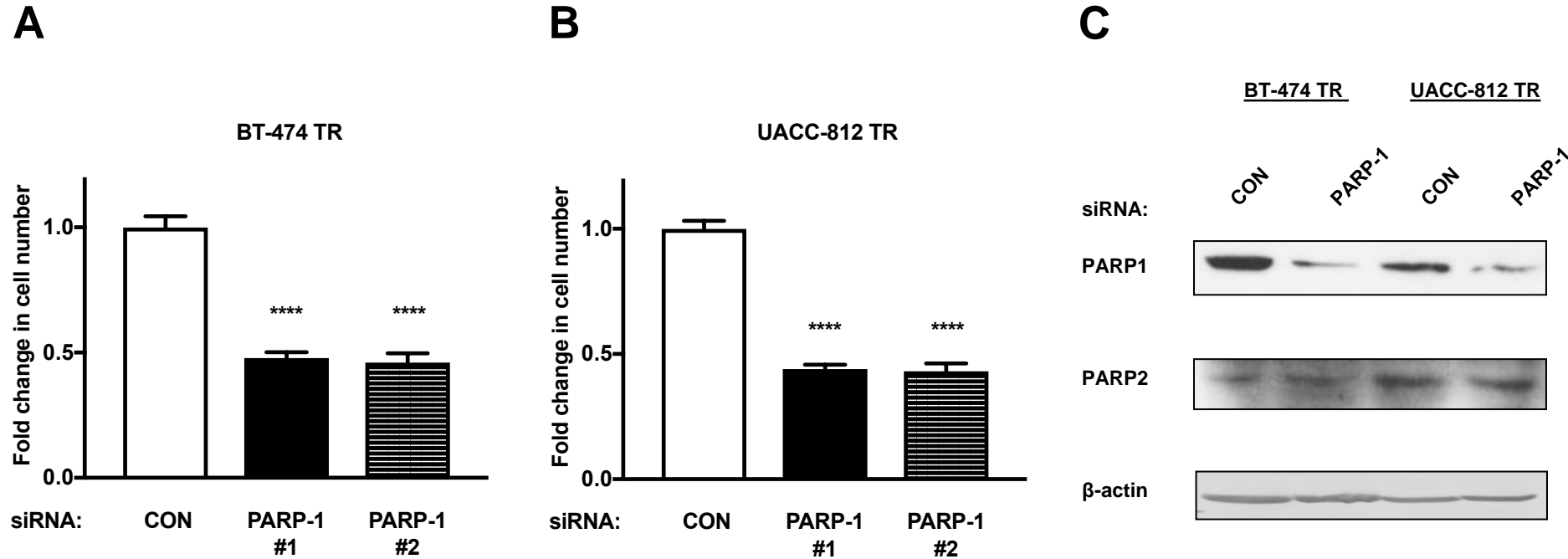


Tumors of ABT888-treated Animals



Supplementary Figure S3. PAR levels and animal body weights from control and ABT-888 treated animals. Representative immunofluorescence staining of PAR protein levels in tumors extracted from (A) control treated animals and (B) ABT-888 treated animals. (C) Mean fold change in body weight (grams) was measured three times per week.

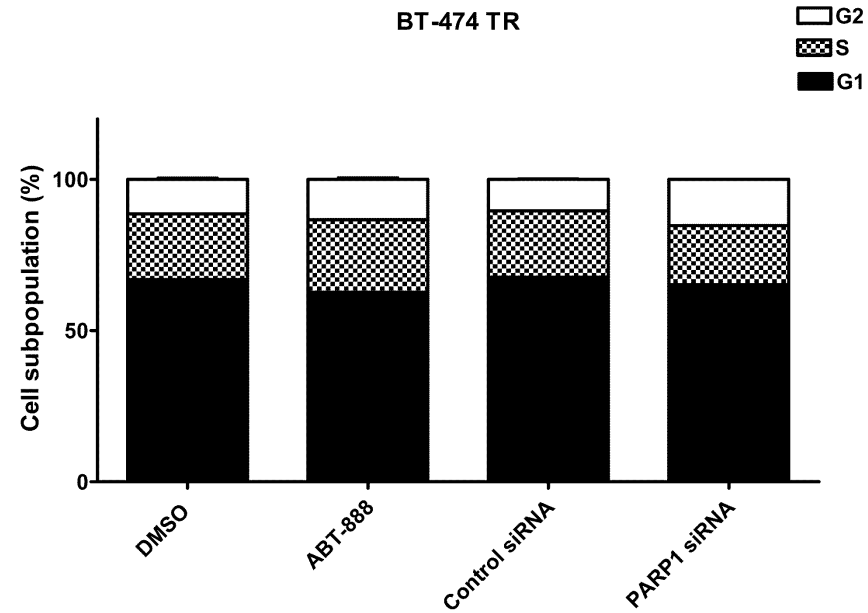
# Supplementary Figure S4



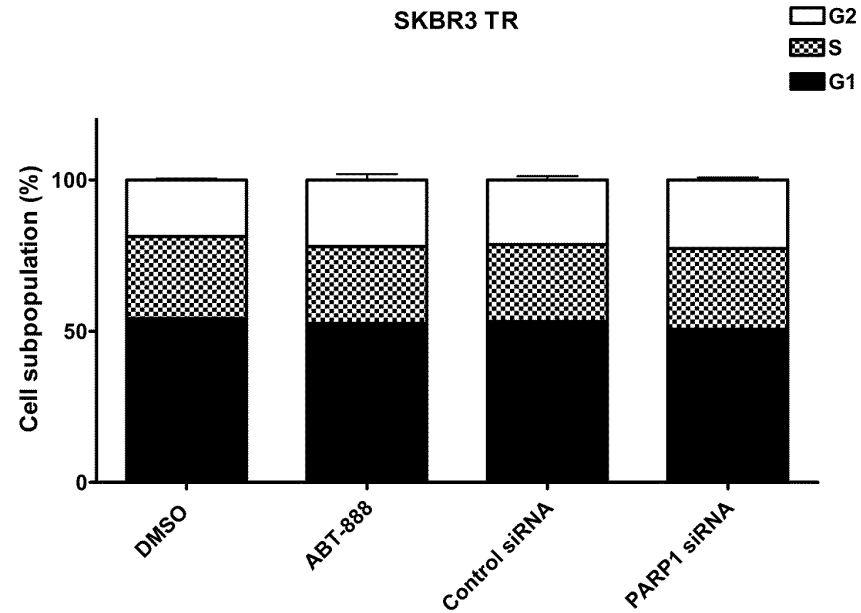
Supplementary Figure S4. Two different PARP-1 siRNAs decrease cell proliferation in HER2+ trastuzumab resistant breast cancer cells. (A,B) Cells were seeded and transfected with control (CON) or PARP-1 siRNA #1 (Santa-Cruz) or PARP-1 siRNA #2 (Sigma-Aldrich). Cellular proliferation was accessed forty-eight hours after transfection and normalized to control treated cells. The data shown are from one experiment. A one-way ANOVA test was performed to calculate the significance between groups. \*\*\*\*p<0.0001

# Supplementary Figure S5

**A**

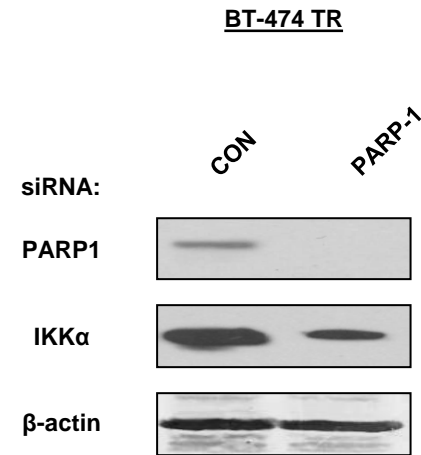


**B**



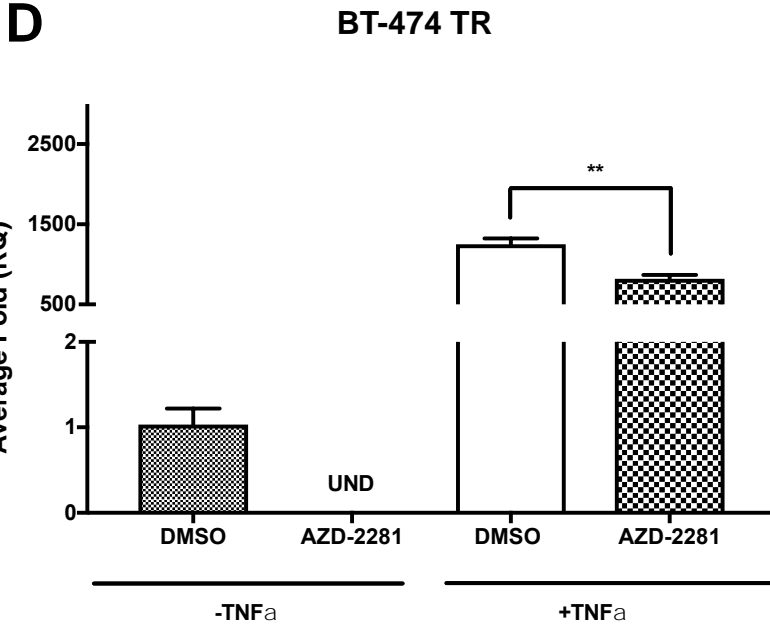
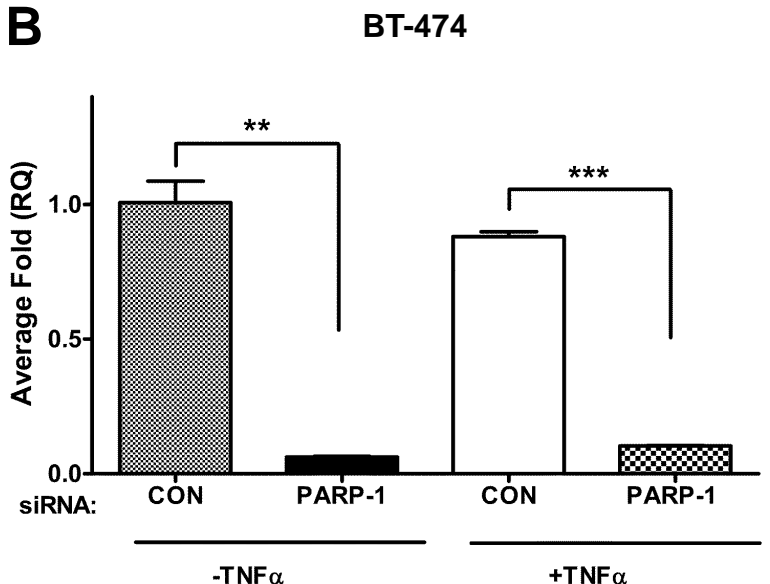
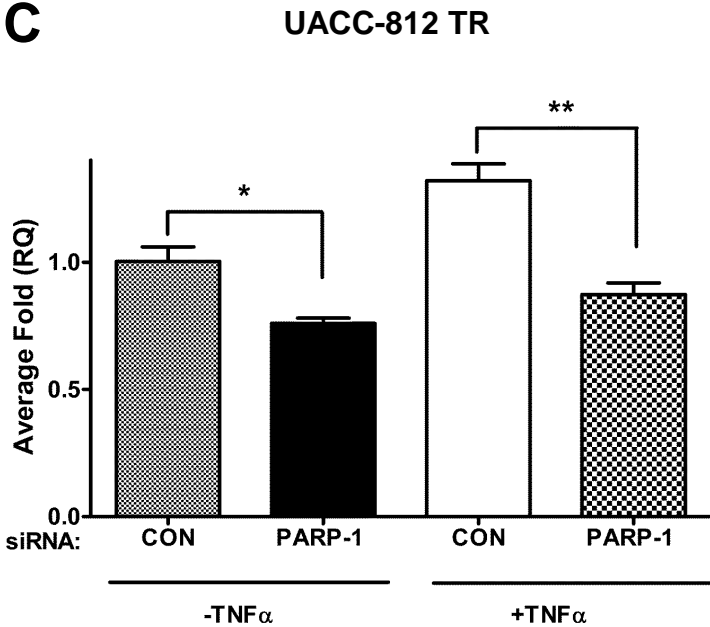
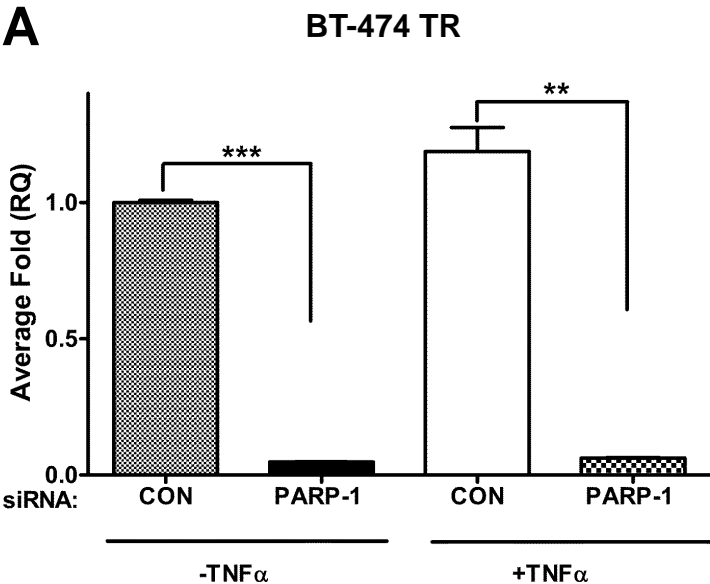
Supplementary Figure S5. Cell cycle distribution is not affected by PARPi in HER2+ trastuzumab resistant cell lines. (A) BT-474 TR and (B) SKBR3 TR were treated with DMSO or 10  $\mu$ M ABT-888 or transfected with control (CON) or PARP-1 siRNA for 72 hours and then subjected to FACS analysis after propidium iodide staining. The representative images shown are from one experiment performed in triplicate.

# Supplementary Figure S6



Supplementary Figure S6. IKKα protein levels were decreased after treatment with Sigma-Aldrich's PARP-1 siRNA. The BT-474 trastuzumab resistant breast cancer cell line was transfected with a control (CON) or PARP-1 siRNA. Forty-eight hours post transfection, protein lysates were collected and IKKα levels were detected by western blot analysis. Results shown are from one experiment.

# Supplementary Figure S7

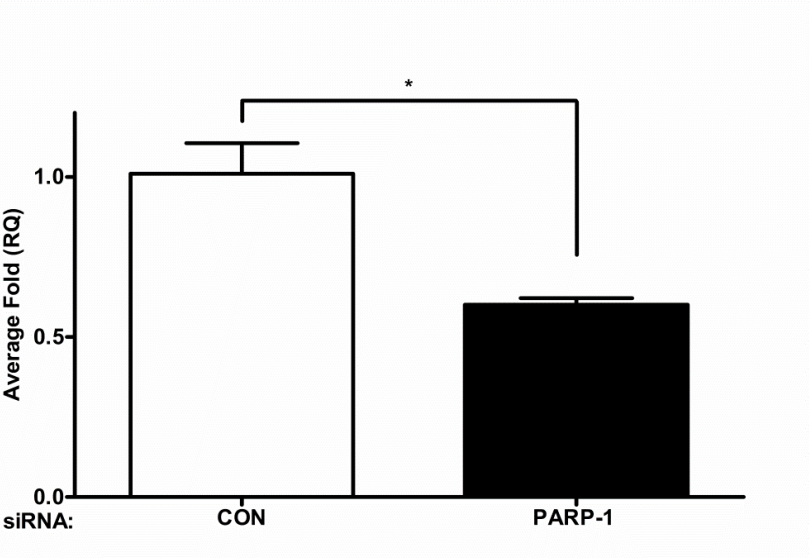


Supplementary Figure S7. PARP-1 and IL-8 gene expression levels after PARP-1 knockdown or inhibition in HER2+ parental and trastuzumab resistant breast cancer cell lines. (A) BT-474 trastuzumab resistant, (B) BT-474 parental, and (C) UACC-812 trastuzumab resistant cells were transfected with control (CON) or PARP-1 siRNA for 48 hours, serum-starved for 18 hours, and then treated with TNF- $\alpha$  for an additional 2 hours. Total RNA was isolated, reverse transcribed, and analyzed by qRT-PCR for PARP-1 and GAPDH expression. (D) BT-474 TR were serum starved and treated for 72 hours with DMSO or 1  $\mu$ M AZD-2281 and then treated with TNF- $\alpha$  for an additional 2 hours. Total RNA was isolated, reverse transcribed, and analyzed by qRT-PCR for IL-8 and GAPDH expression. Shown is the average fold change from untreated TNF- $\alpha$  cells treated with control siRNA (+/- SEM) from (A-C) one of three independent experiments or (D) a single experiment performed in triplicate. \* $p$ <0.05, \*\* $p$ <0.01, and \*\*\* $p$ <0.001

# Supplementary Figure S8

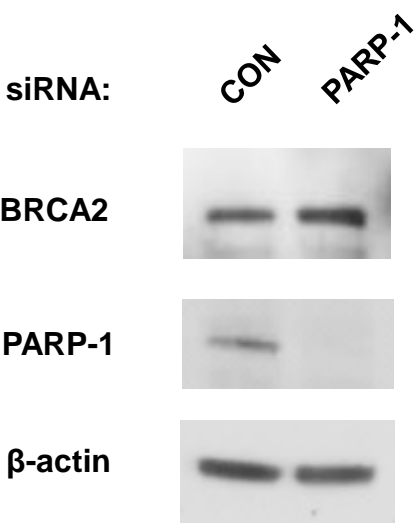
**A**

BT-474 TR



**B**

BT-474 TR



Supplementary Figure S8. BRCA2 gene and protein expression levels in BT-474 trastuzumab resistant breast cancer cell lines after PARP-1 knockdown. The expression of BRCA2 was measured by (A) qRT-PCR and (B) western blot analysis 72 hours after PARP-1 knockdown in the BT-474 TR. Results shown are from one of (A) three experiments performed in triplicate or (B) two independent experiments. \*p<0.05.