Supplementary Material for

PARP inhibitor and PRMT5 inhibitor synergy is independent of *BRCA1/2* and *MTAP* status in breast cancer cells

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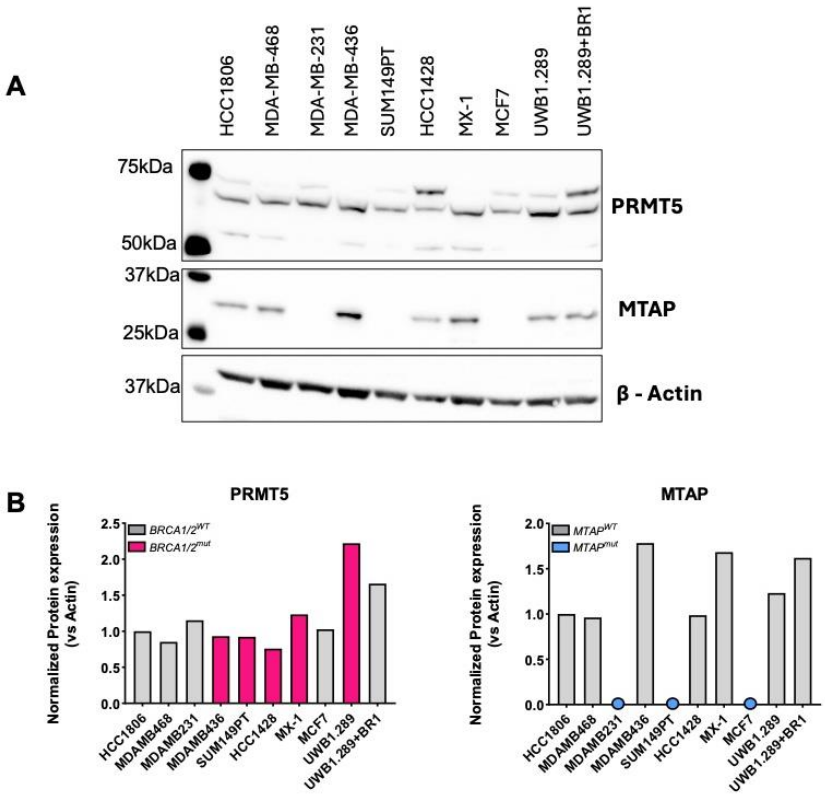
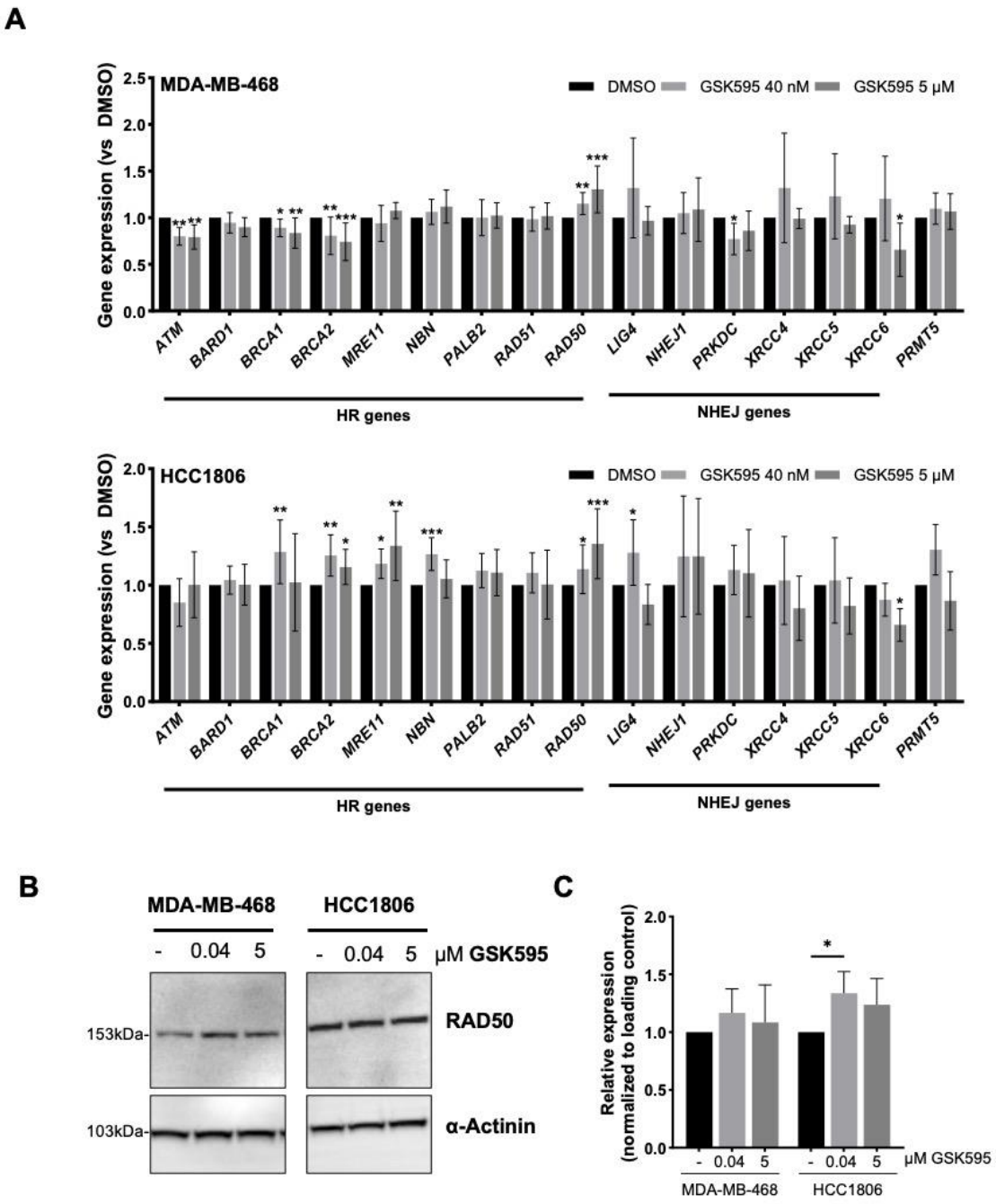
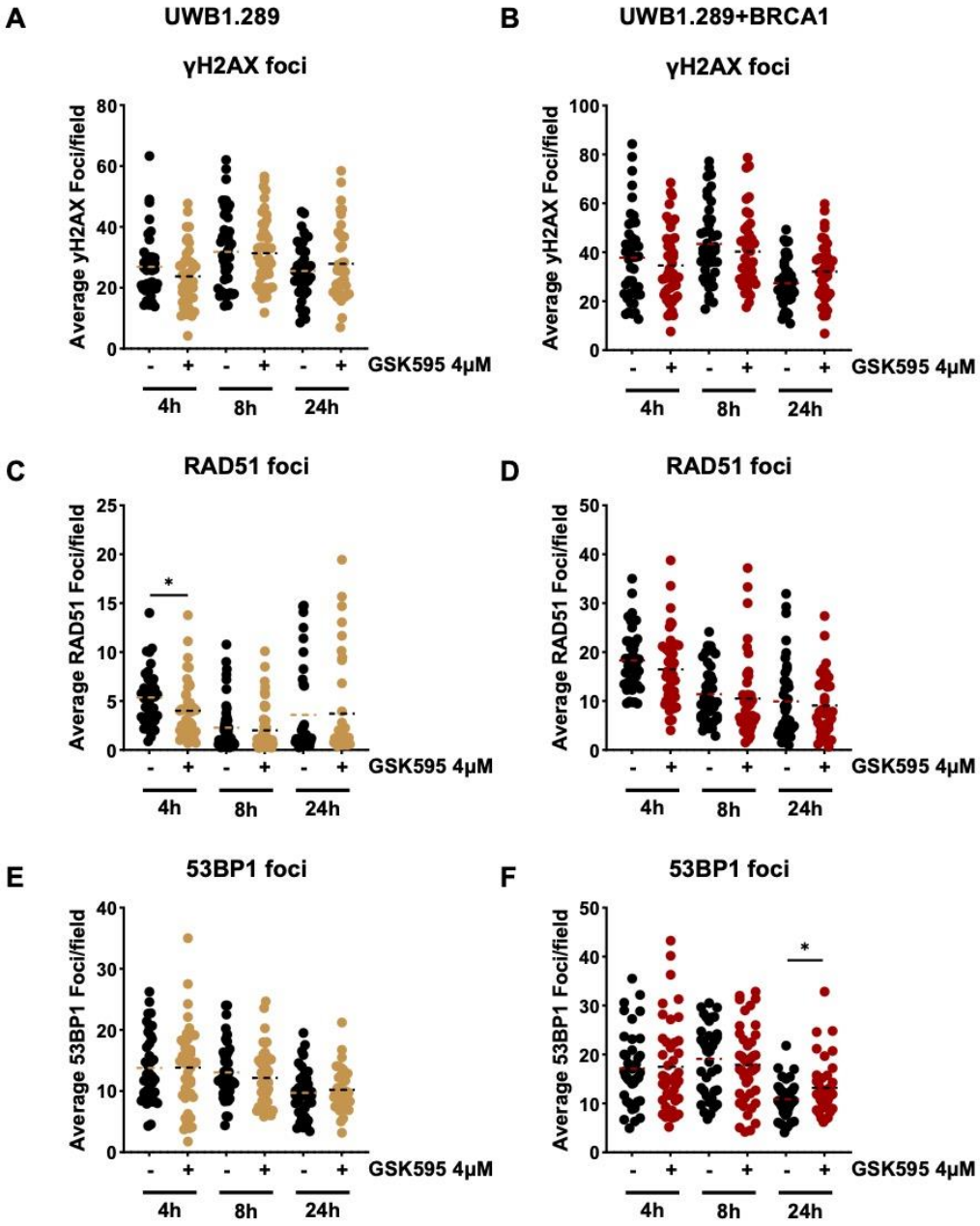


Supplemental Figure 1: PRMT5 and MTAP protein expression in a panel of breast and ovarian cancer cell lines. (A) Proteins were harvested using RIPA lysis buffer from each cell line. Anti-PRMT5 and anti-MTAP antibodies were used to detect the expression of PRMT5 and MTAP, and anti-β-actin was used as a loading control. Presented western blot is representative of three independent biological replicates. Uncropped blot can be found in Supplemental Figure 9. **(B)** Relative quantitation of PRMT5 (left) and MTAP (right) protein bands normalized to loading control (β-actin).

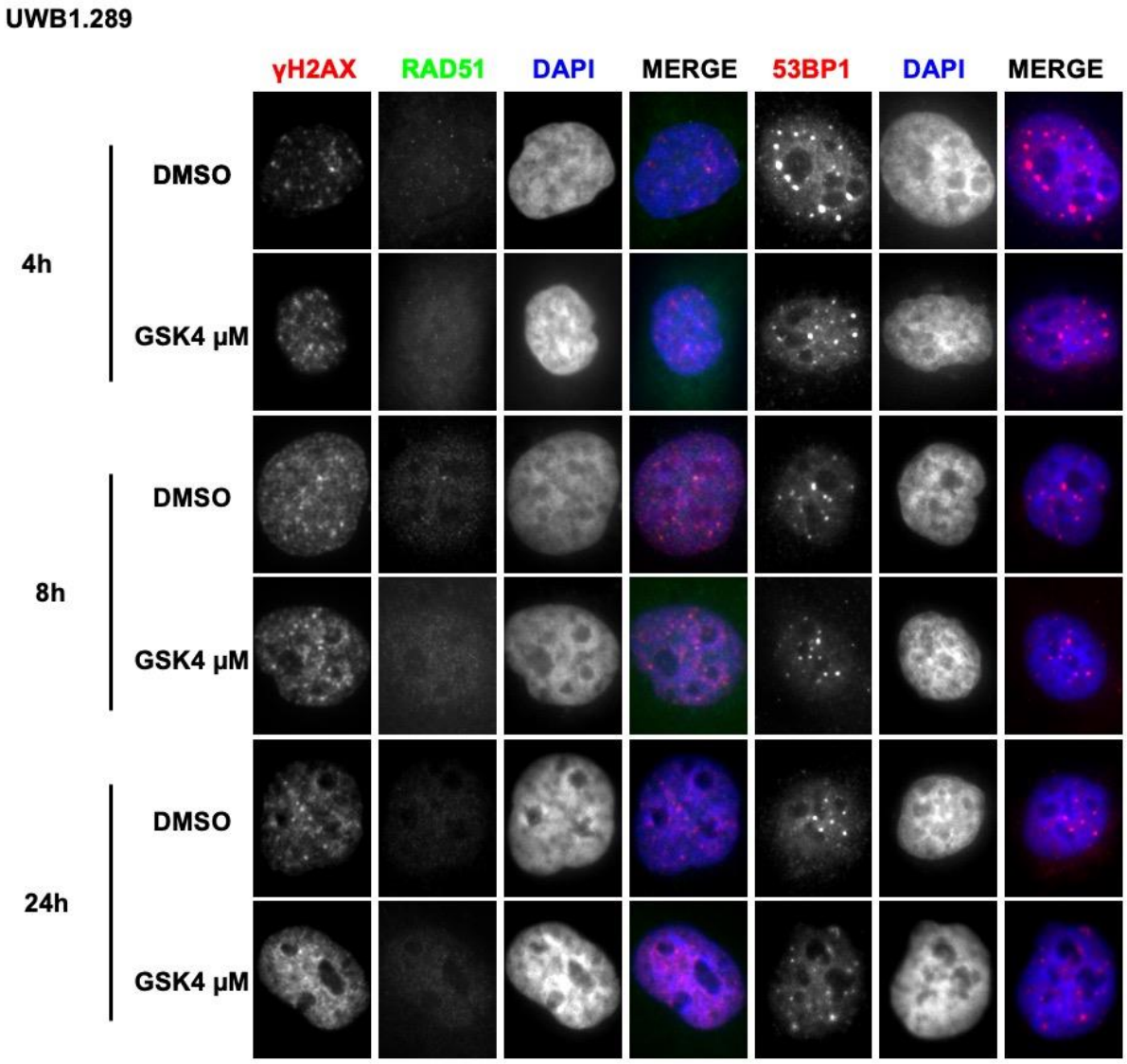


Supplemental Figure 2: Relative mRNA expression of homologous recombination and non-homologous end-joining pathway genes with or without GSK595 treatment. MDA-MB-468 and HCC1806 cells were treated with two doses of GSK595 or equivalent amounts of DMSO for 24h. (**A**) RT-qPCR was performed to determine the mRNA expression of different genes relative to GAPDH. Bars represent mean ± SD from three independent experiments done in technical triplicates. Students T test was used to determine statistical significance with * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$. (B) Proteins were harvested using RIPA lysis buffer from each cell line. Anti-RAD50 antibody was used to detect the expression of RAD50, and anti-α-actinin was used as a

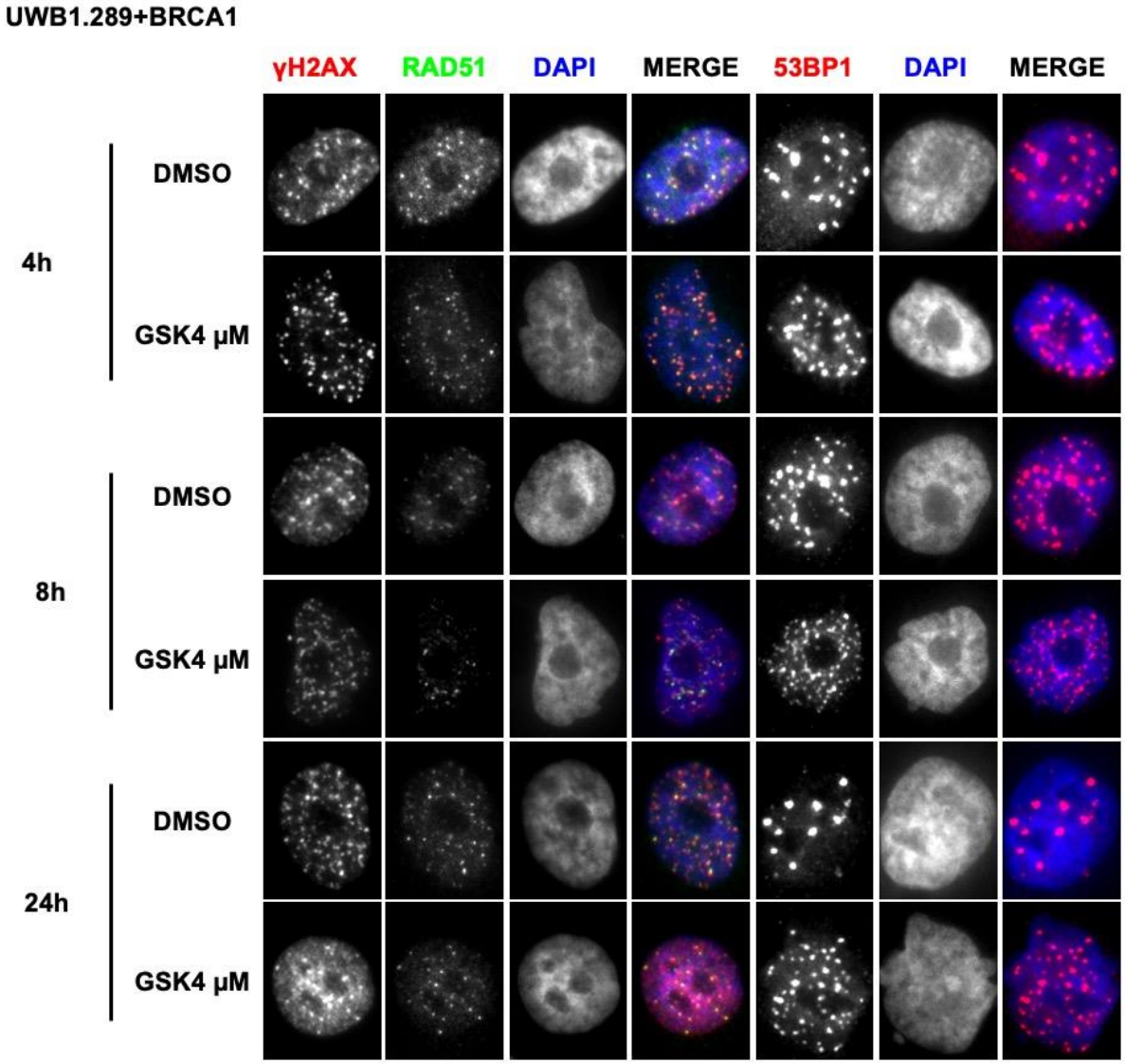
loading control. Presented western blot is representative of three independent biological replicates. Uncropped blot can be found in Supplemental Figure 10. (C) Relative quantitation of RAD50 protein bands normalized to loading control (α-actinin). Bars represent mean ± SD from three independent experiments. Students T test was used to determine statistical significance with * $p < 0.05$.



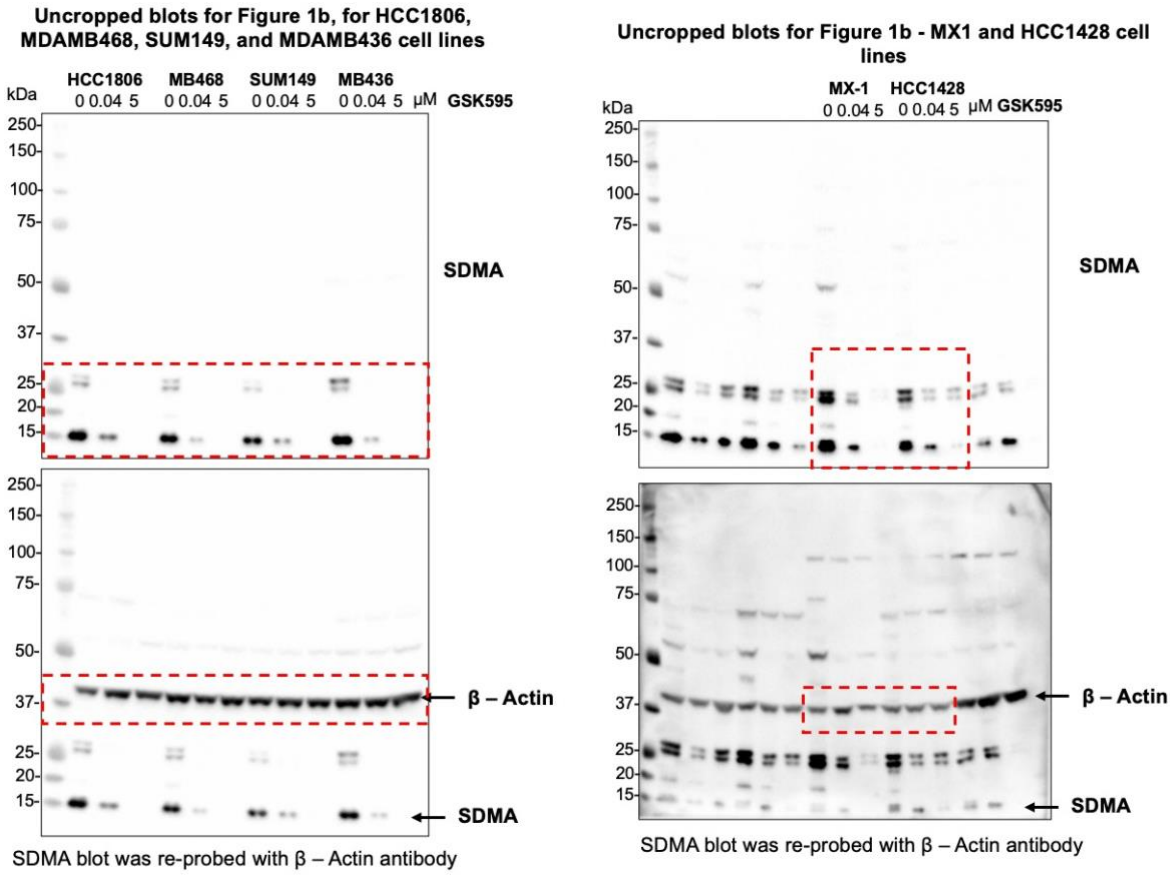
Supplemental Figure 3: RAD51, 53BP1 and γH2AX foci count in UWB1.289 and UWB1.289+BRCA1 cells after 4h, 8h, or 24h of GSK595 or DMSO treatment. Average number of foci per field of imaging were counted for each of RAD51, 53BP1, and γH2AX markers in both UWB1.289 and UWB1.289+BRCA1 cells after 4h, 8h, or 24h of GSK595 4μM or DMSO treatments. Statistical significance was determined using a Student's T Test and * represents $p < 0.05$.



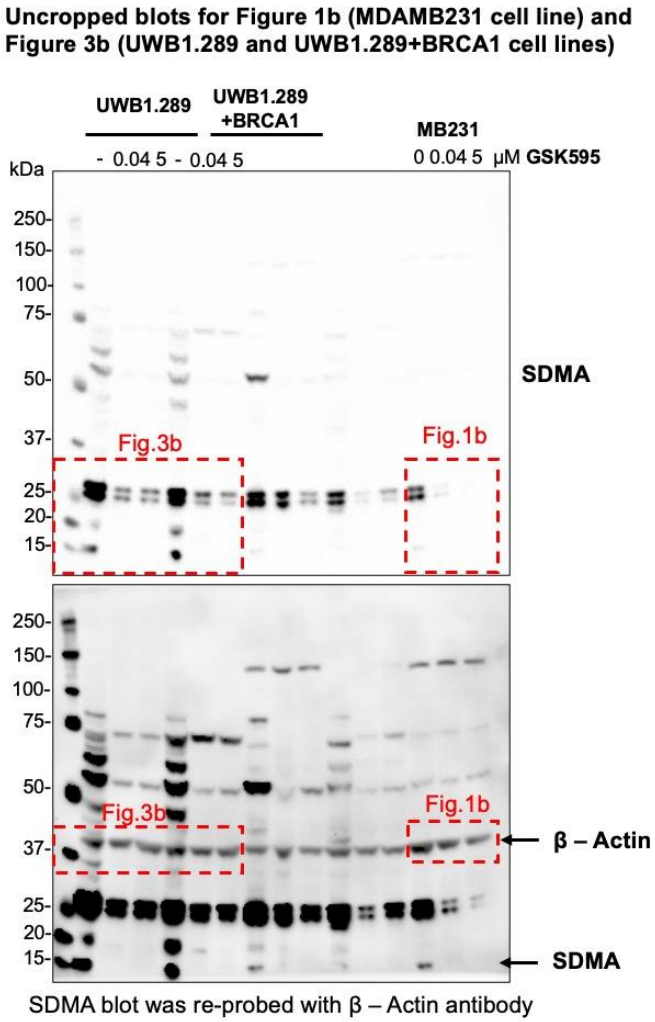
Supplemental Figure 4: Representative images of RAD51, 53BP1 and γH2AX foci in UWB1.289 cells after 4h, 8h, or 24h of GSK595 or DMSO treatment.



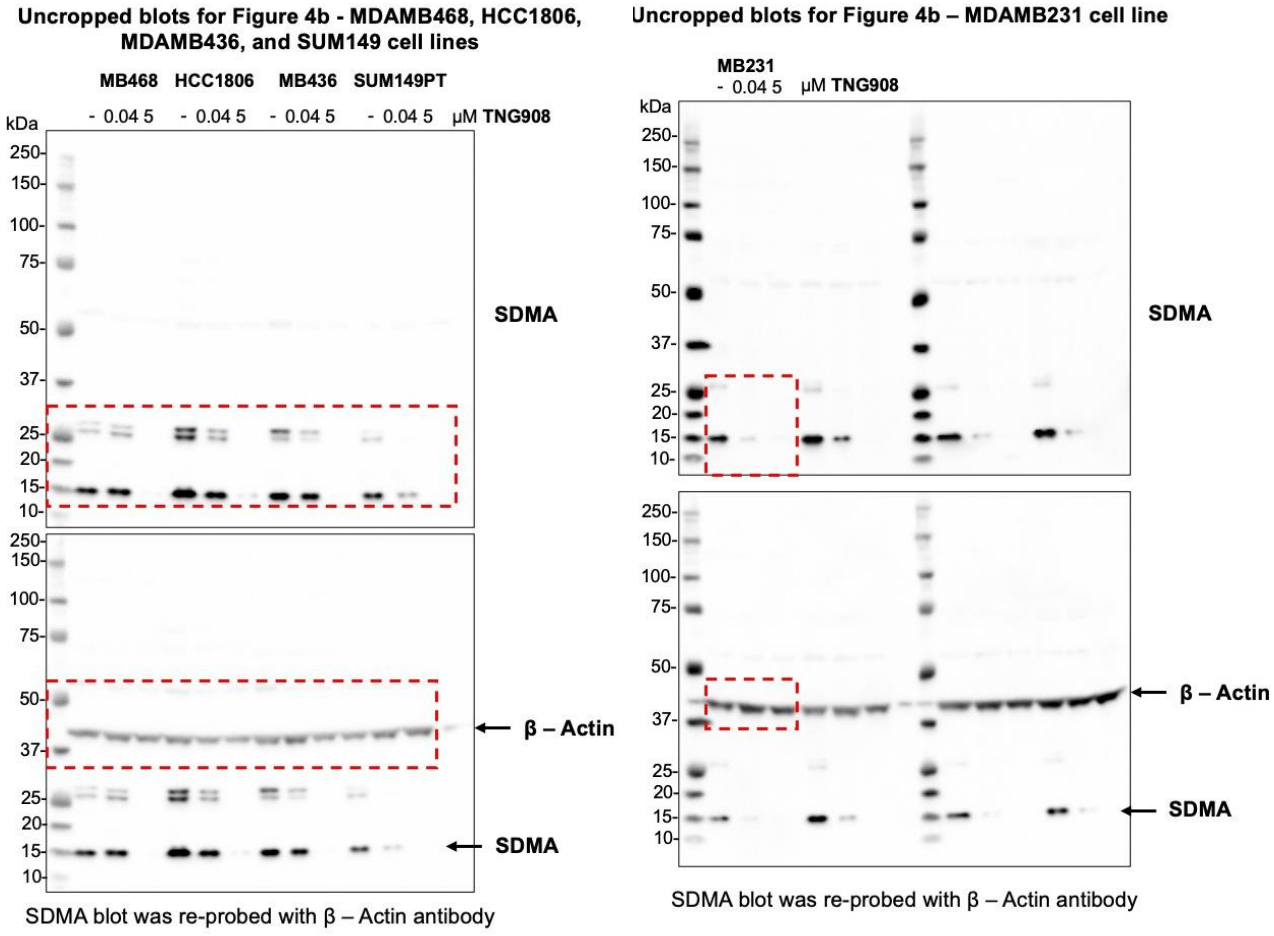
Supplemental Figure 5: Representative images of RAD51, 53BP1 and γH2AX foci in UWB1.289+BRCA1 cells after 4h, 8h, or 24h of GSK595 or DMSO treatment.



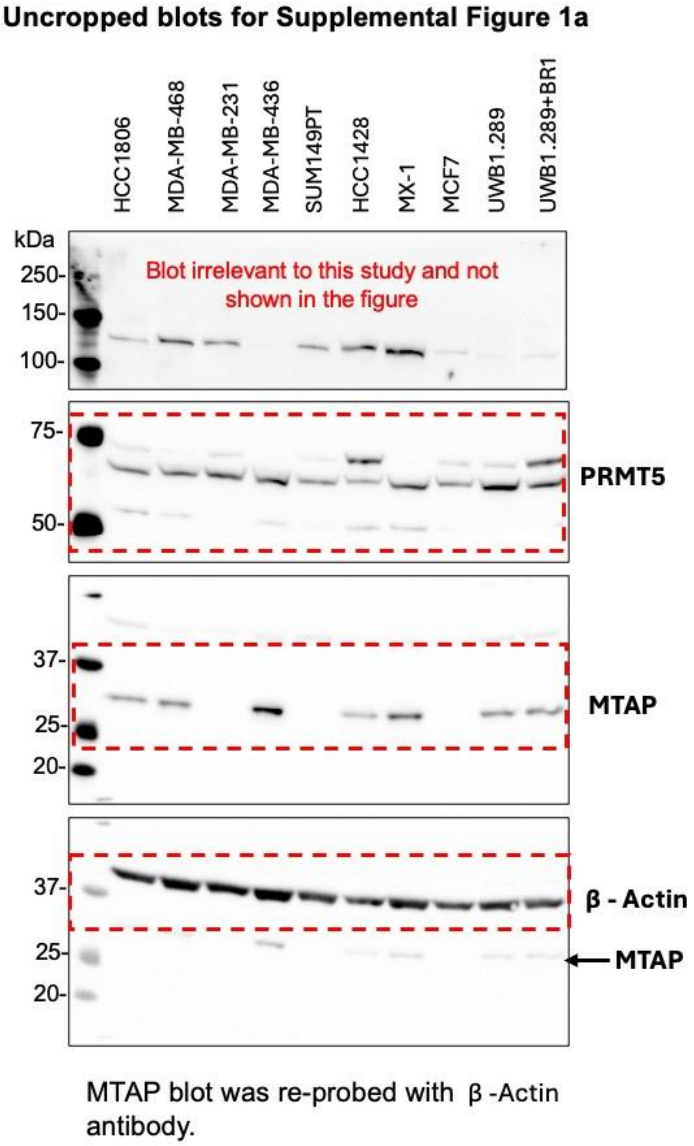
Supplemental Figure 6: Uncropped blots of the western blots shown in Figure 1B for HCC1806, MDAMB468, SUM149PT, MDAMB436, MX1, and HCC1428 cell lines. The red dashed box marks the part of the blot shown in the main figure.



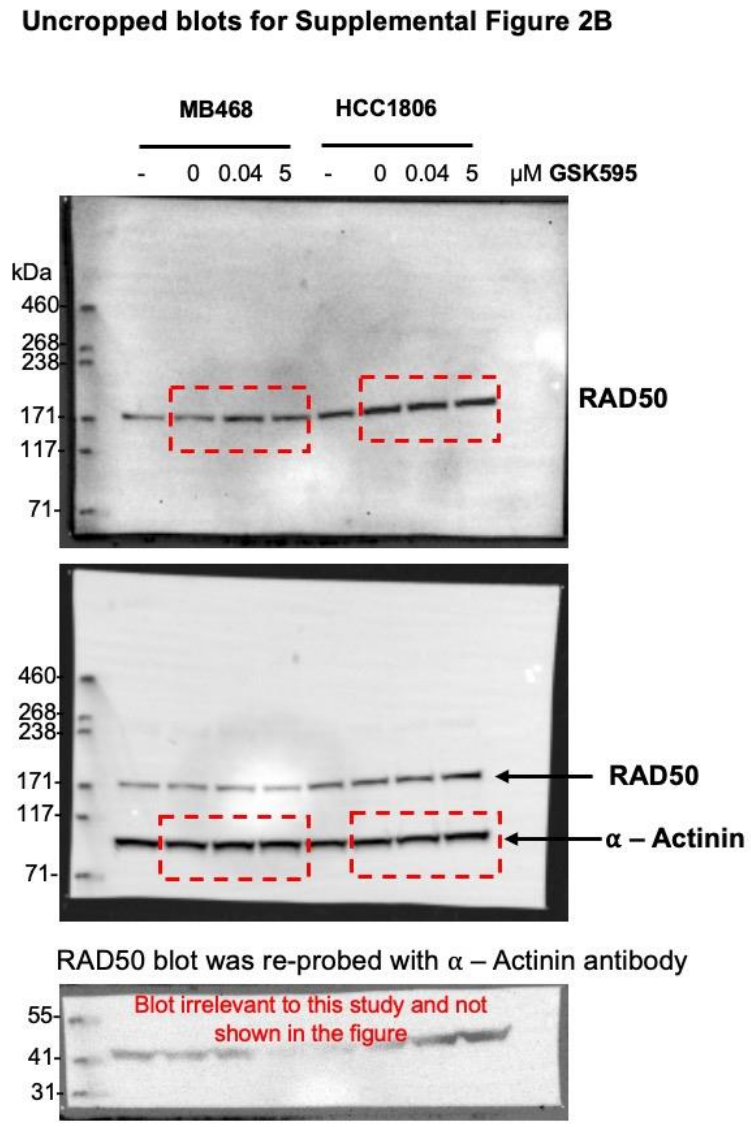
Supplemental Figure 7: Uncropped blots of the western blots shown in Figure 1B for the MDAMB231 cell line and for the UWB1.289 and UWB1.289+BRCA1 cell lines shown in Figure 3B. The red dashed boxes mark the parts of the blots shown in the main figures.



Supplemental Figure 8: Uncropped blots of the western blots shown in Figure 4B for MDAMB468, HCC1806, SUM149PT, MDAMB436, and MDAMB231 cell lines. Red dashed boxes mark the parts of the blots shown in the main figure.



Supplemental Figure 9: Uncropped blots of the western blots shown in Supplemental Figure 1A. The red dashed boxes mark the parts of the blots shown in the main figure. As shown, the membrane was cut after 100kDa and 50kDa after protein transfer to hybridize with different antibodies. The upper blot (250-100kDa) is irrelevant to this study and not shown in the main figure.



Supplemental Figure 10: Uncropped blots of the western blots shown in Supplemental Figure 2B. The red dashed boxes mark the parts of the blots shown in the main figure. After protein transfer, the membrane was cut below 71kDa and hybridized with RAD50 antibody. The lower part of the membrane (55-31kDa) is irrelevant to this study and not shown in the main figure.

Supplementary Table 1: List of Primers used for qPCR in this study.

Target	Forward Primer	Reverse Primer
ATM	GAGAGGAGACAGCTTGTTAAGG	CCTCTTCCTAGTTTCCGTGTTT
BARD1	GATGTCTAGTCCCTCAGCAATG	CAGAAGGTATGTCGCCCTTAAT
BRCA1	CAGTCGGGAAACAAGCATAGA	GCACATTCCTCTTCTGCATTTC
BRCA2	GAAGCCCTTTGAGAGTGGAA	CTCCATCTGGGCTCCATTTAG

GAPDH	AGCCACATCGCTCAGACAC	GCCCAATACGACCAAATCC
MRE11	GATGAAGTCCGTGAGGCTATG	AGCCATCTGTTCTGCTAAATCT
NBN	GCAAGGGAGTTAGGGAAATGA	CTGGTCTCAATGCCTGTAGTAG
PALB2	CCGGTTGTAAAGAGCCATGTA	CTGCGAAGTGCCAGGTATAA
PRMT5	GTTTCCCATCCTCTTCCCTATT	CCACTCATACCACACCTTCTT
RAD50	GCTTGGTCACTCCCTCTTATTT	GAGAGGCCAAGGAGTTGTATTAG
RAD51	GGCAGTGATGTCCTGGATAATG	CGGTGGCACTGTCTACAATAAG
XRCC6 (KU70)	CCAAGACCCGGACCTTTAATAC	AGTATAATCTGACGACTCCCATAGA
XRCC5 (KU80)	CCATGAGCTTGGCAAAGAAAG	GTGCAGCAGACACTGAAATAATC
PRKDC(DNA-PKcs)	GAACATGGCAGGAGAGAATCA	GAAGACACAGCAGATGACAGATA
LIG4	TTAAAGCAGCAGAGATCGTACC	GCCACTCCTTGTCATCTCTTATC
XRCC4	GGAAGCTTTGGAGACTGATCTT	TCTCGTTCTTGAGCTGCATTTA
NHEJ1	GTCTCCATCTTTCCCTGATTCC	CAGGCTAGACTCTTTCCAGTTC

Supplementary Table 2: List of Primary and Secondary Antibodies used in this study.

Target	Application	Dilution	Supplier	Catalog Number	RRID
α-Actinin	WB	1:5000	Proteintech	11313-2-AP	AB_2223815
SDMA	WB	1:1000	Cell Signaling Technologies	13222	AB_2714013
β-Actin	WB	1:5000	Proteintech	66009-1-Ig	AB_2687938
MTAP	WB	1:1000	Proteintech	11475-1-AP	AB_2147094
PRMT5	WB	1:1000	SantaCruz Biotech	sc-376937	AB_2904201
RAD50	WB	1:1000	Cell Signaling Technologies	3427	AB_2176936
γ-H2AX	IF	1:1000	Cell Signaling Technologies	9718	AB_2118009
RAD51	IF	1:200	Novus Biological	NB100-148	AB_10002131
53BP1	IF	1:200	Novus Biological	NB100-904SS	AB_1290520
Goat anti-Rabbit IgG (H+L) HRP-conjugated Secondary Antibody	WB	1:10000	Invitrogen	31460	AB_228341
Goat anti-Mouse IgG (H+L) HRP-conjugated Secondary Antibody	WB	1:10000	Invitrogen	31432	AB_228302

Goat anti-Rabbit IgG (H+L) Alexa Fluor 594 Secondary Antibody	IF	1:200 & 1:500	Invitrogen	A11012	AB_2534079
Goat anti-Mouse IgG (H+L) Alexa Fluor 488 Secondary Antibody	IF	1:200 & 1:500	Invitrogen	A11001	AB_2534069

Abbreviations: WB: Western Blot, IF: Immunofluorescence.