

PI3K inhibitors in HER2-positive breast cancer

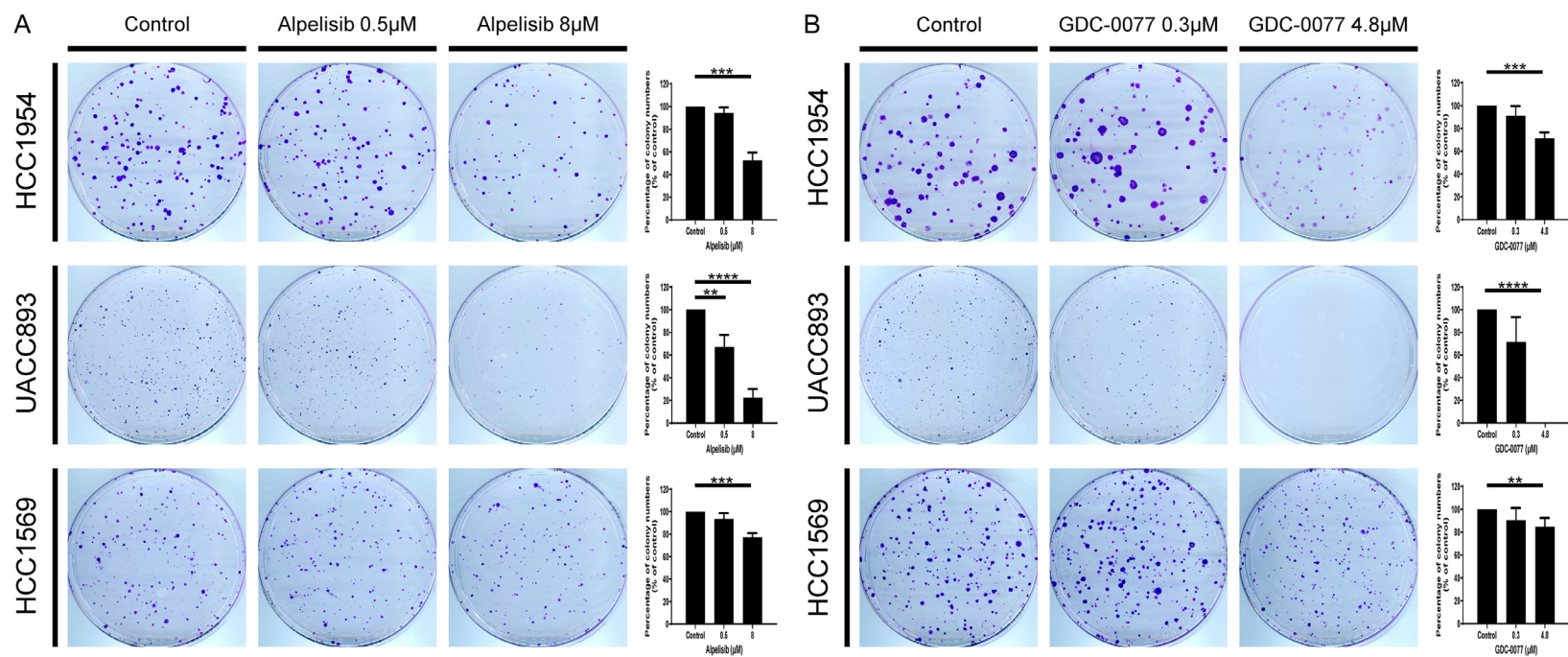


Figure S1. Colony formation assays. A. HCC1954, UACC893, and HCC1569 cells were treated with DMSO, alpelisib (0.5 μ M), and alpelisib (8 μ M). B. Cells were treated with DMSO, GDC-0077 (0.3 μ M), and GDC-0077 (4.8 μ M). Bar charts represent quantification of the colonies and are shown as the mean \pm SD. *P*-value: ***P*<0.01, ****P*<0.001, and *****P*<0.0001.

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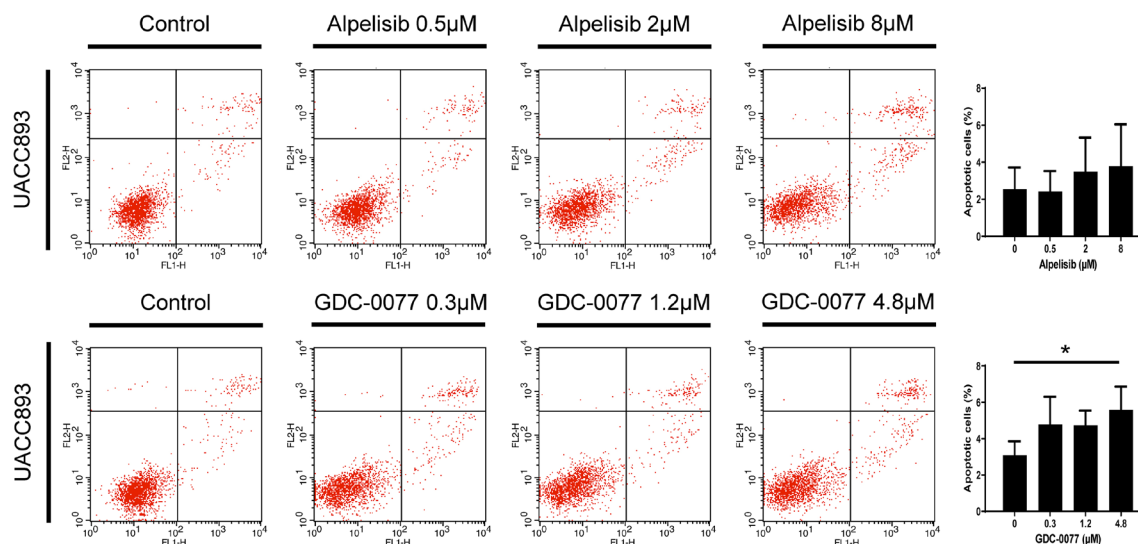


Figure S2. PI3K inhibitors induce apoptosis in UACC893 cells. Cells were treated with alpelisib and GDC-0077 at the indicated concentrations then stained with annexin V/PI. Apoptotic events were analyzed by flow cytometry 48 hours after treatment. Bar charts represent the mean percentage of apoptotic cells \pm SD. *P*-value: **P*<0.05.

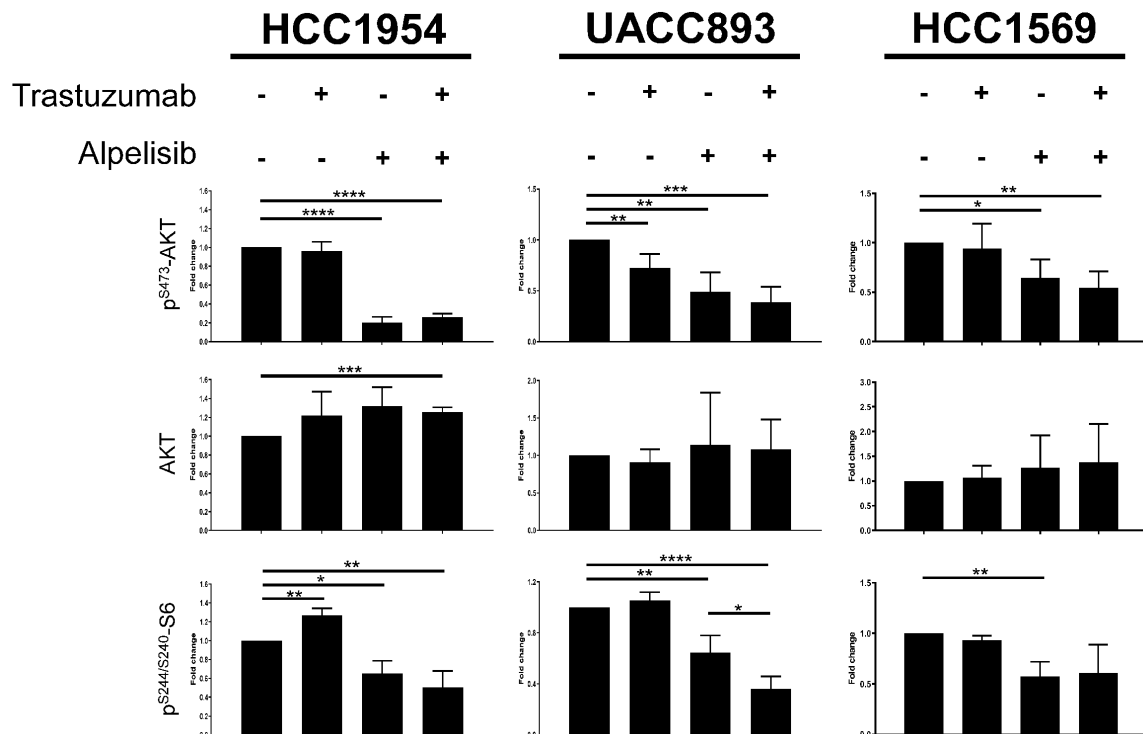
Table S1. Combination index of alpelisib plus trastuzumab in HCC1954, UACC893, and HCC1569 cells

HCC1954			
Trastuzumab ($\mu\text{g/mL}$)	Alpelisib (μM)	Effect	Combination index
0.5	0.125	0.7777	0.07750
1.0	0.25	0.7385	0.14249
2.0	0.5	0.6969	0.26286
4.0	1.0	0.647	0.48090
8.0	2.0	0.5279	0.79202
16.0	4.0	0.3742	1.23856
UACC893			
Trastuzumab ($\mu\text{g/mL}$)	Alpelisib (μM)	Effect	Combination index
0.5	0.125	0.8003	0.27131
1.0	0.25	0.6761	0.31380
2.0	0.5	0.5638	0.41967
4.0	1.0	0.4629	0.59725
8.0	2.0	0.3509	0.80744
16.0	4.0	0.2163	0.91832
HCC1569			
Trastuzumab ($\mu\text{g/mL}$)	Alpelisib (μM)	Effect	Combination index
0.5	0.125	0.8732	0.18533
1.0	0.25	0.8488	0.24848
2.0	0.5	0.84	0.43589
4.0	1.0	0.7923	0.46663
8.0	2.0	0.7433	0.54423
16.0	4.0	0.5975	0.29471

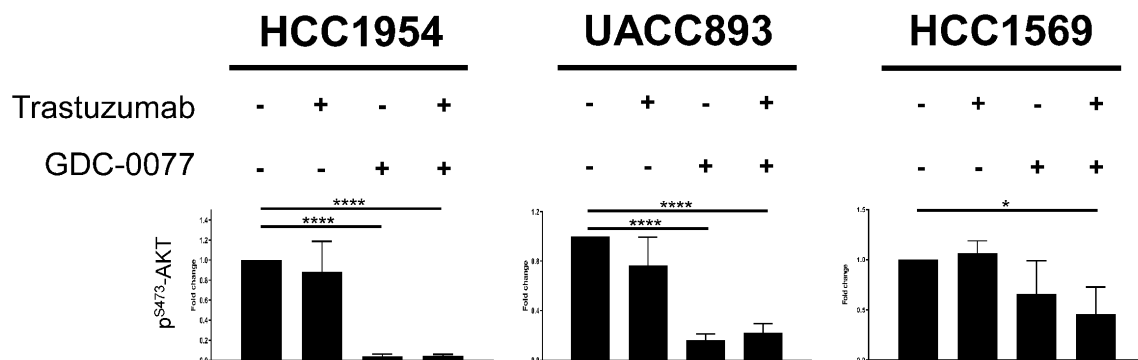
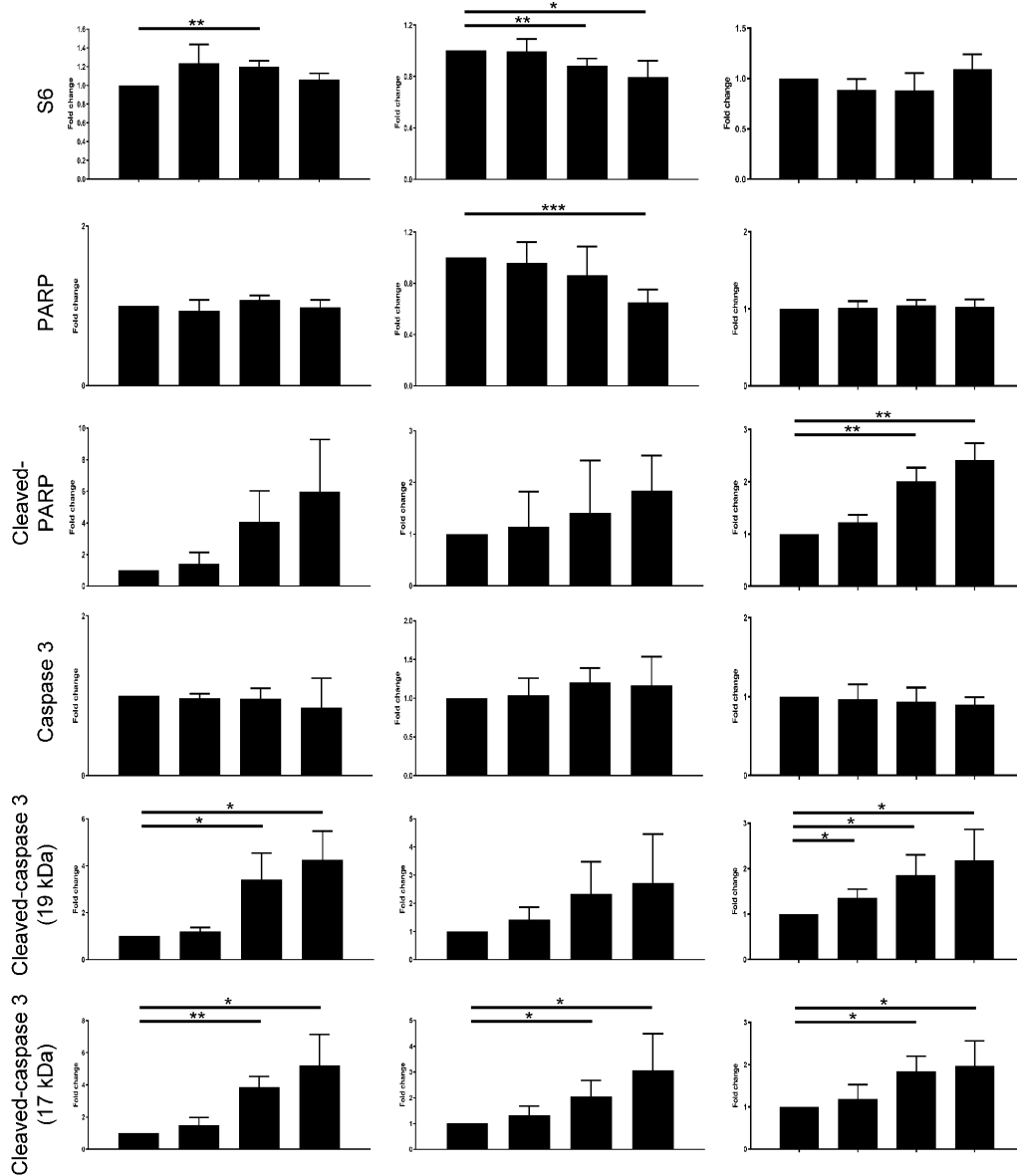
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Table S2. Combination index of GDC-0077 plus trastuzumab in HCC1954, UACC893, and HCC1569 cells

HCC1954			
Trastuzumab (µg/mL)	GDC-0077 (µM)	Effect	Combination index
0.5	0.05	0.8286	0.40245
1.0	0.1	0.734	0.19876
2.0	0.2	0.6709	0.18681
4.0	0.4	0.6485	0.29128
8.0	0.8	0.5579	0.22590
16.0	1.6	0.4418	0.14113
UACC893			
Trastuzumab (µg/mL)	GDC-0077 (µM)	Effect	Combination index
0.5	0.0125	0.8938	0.60198
1.0	0.025	0.8358	0.77614
2.0	0.05	0.6681	0.69091
4.0	0.1	0.4937	0.73441
8.0	0.2	0.3376	0.83433
16.0	0.4	0.2487	1.14560
HCC1569			
Trastuzumab (µg/mL)	GDC-0077 (µM)	Effect	Combination index
0.5	0.1	0.8722	0.15071
1.0	0.2	0.8397	0.22781
2.0	0.4	0.8306	0.42484
4.0	0.8	0.7281	0.44795
8.0	1.6	0.6111	0.50962
16.0	3.2	0.3995	0.41043



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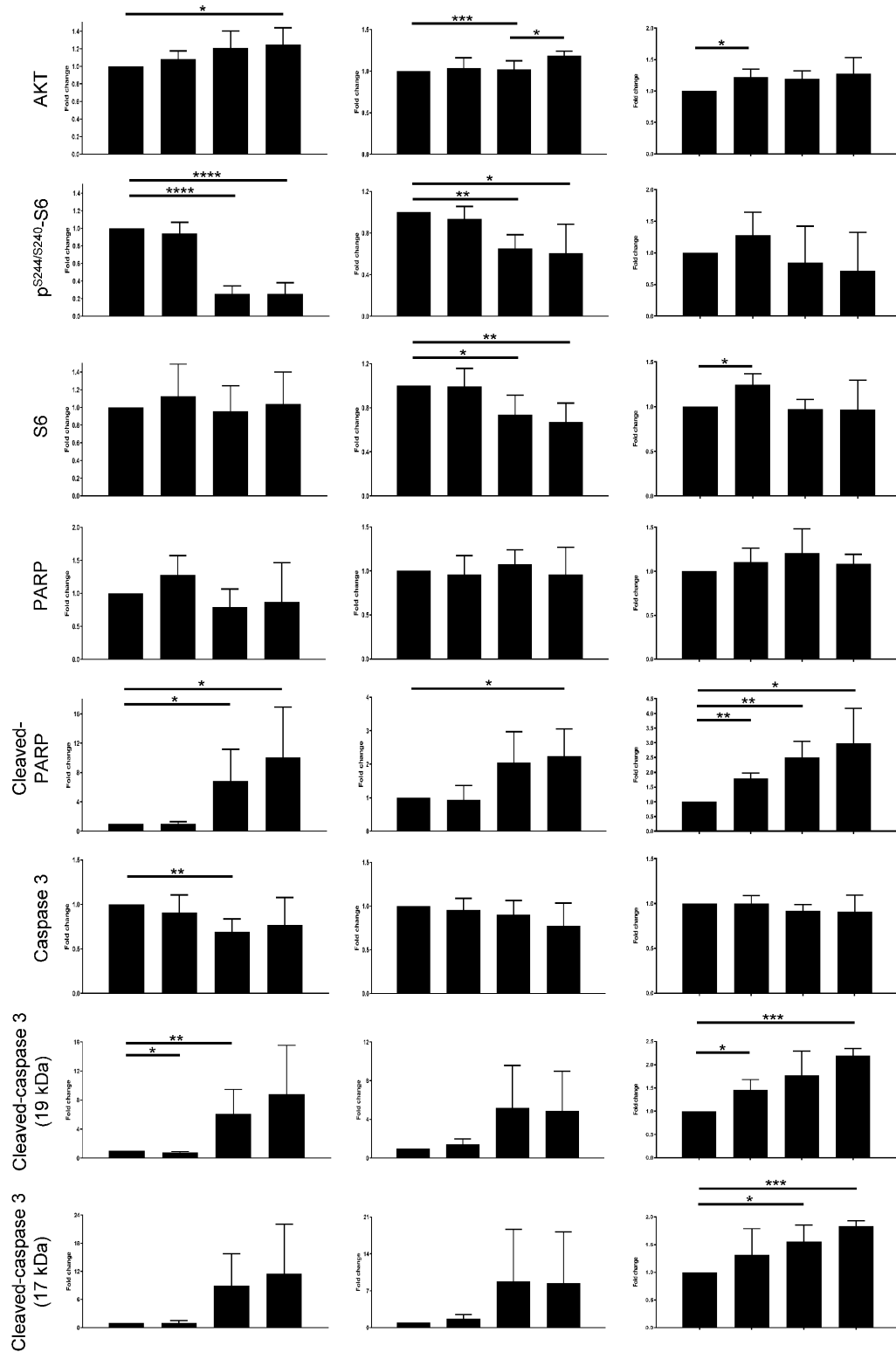


Figure S4. Quantification of western blots for cells treated with GDC-0077 and trastuzumab. The intensity of each indicated protein relative to the control was calculated. Bar charts represent the mean \pm SD. *P*-value: **P*<0.05, ***P*<0.01, ****P*<0.001, and *****P*<0.0001.