

SUPPLEMENTARY INFORMATION

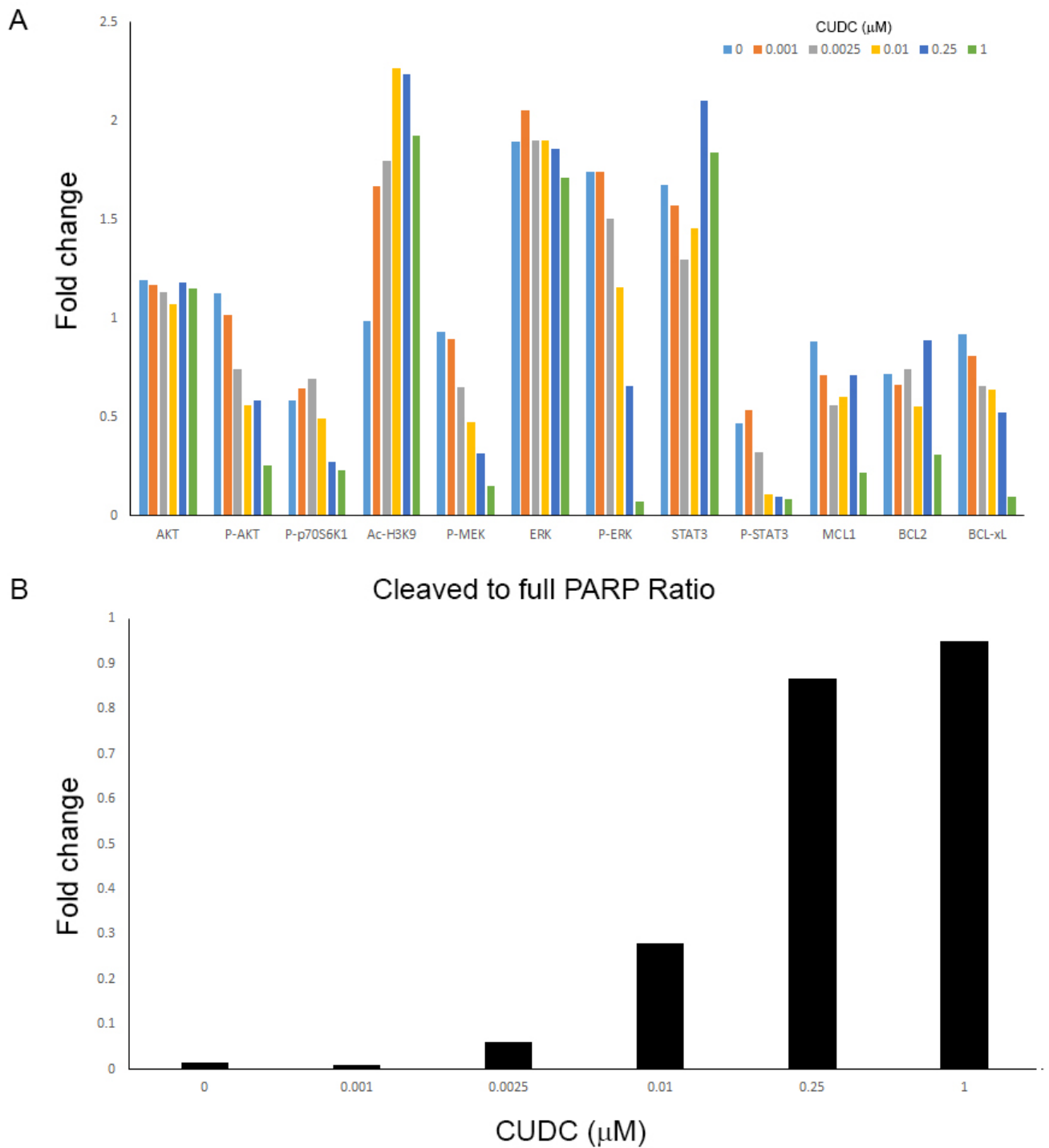


Figure S1. CUDC-907 inhibits pro-survival signals in CLL cells. Densitometry analysis of Figure 2A performed with Image J, showing values related to actin expression (**A**) or the ration between cleaved and non-cleaved PARP (**B**).

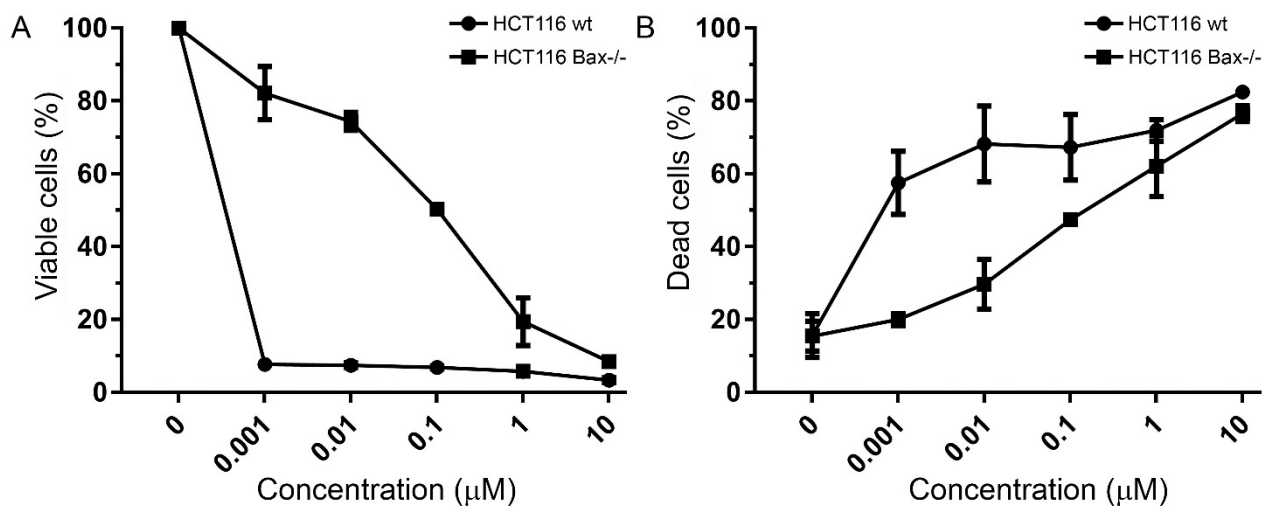


Figure S2. CUDC-907 induces cell death through Bax-dependent and -independent pathways. (A) HCT116 and HCT116 Bax^{-/-} cell viability measured by MTS assay, normalized to Control samples (0μM). Cells were treated with different concentrations of CUDC-907 for 48 hours. All graphics show mean values of two independent experiments and error bars represent standard deviation. (B) Induction of cell death in the same cells, as measured by FACS analysis of Annexin V/PI-stained cells. Graph shows the percentage of double positive cells (apoptotic).

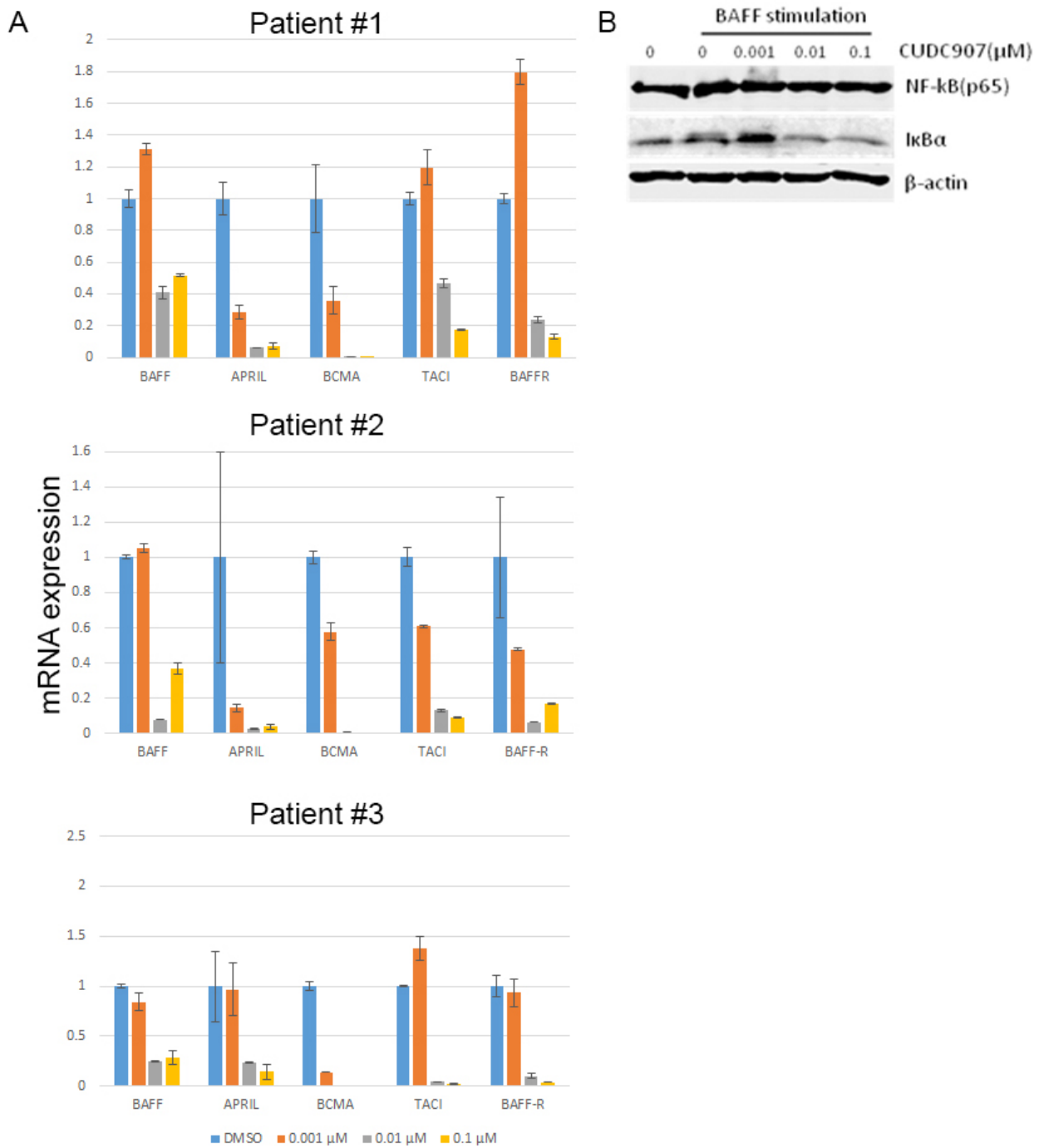


Figure S3. CUDC-907 induces cell death through Bax-dependent and -independent pathways. (A) Same as Figure 2C, using three more patient samples. (B) Same as Figure 2D, using another patient sample.

Gene	Forward primer (5'→3')	Reverse primer (5'→3')
BAFF	GGGAGCAGTCACGCCTTAC	GATCGGACAGAGGGGCTTT
APRIL	GTGTGGACGGGACAGTGAG	GCATCGGAACTCTGACAGTACAG
BCMA	ACCTTGTCAACTTCGATGTTCTT	CAGAGAATCGCATTTCGTTTCCTT
TACI	CAGGAGCCCAGTGAACCTTC	CCTTCCCGAGTTGTCTGAATTG
BAFFR	GGGTAGAGGCTCCGTACTIONCA	GGGCTTCATTTGACGGAGGA
CCL3	AGTTCTCTGCATCACTTGCTG	CGGCTTCGCTTGGTTAGGAA
CCL4	CTGTGCTGATCCAGTGAATC	TCAGTTCAGTTCAGGTCATACA
CCL17	CCAGGGATGCCATCGTTTTTG	AGTCAGGAGTCTGGGGTGAG
CCL22	ATCGCCTACAGACTGCACTC	GACGGTAACGGACGTAATCAC

Table S1. qPCR primers used in this study.

MEC-1

CUDC	IMD	CI	CUDC	Ibrutinib	CI	CUDC	ABT-199	CI
0.001	1	0.80	0.001	2.5	0.56	0.001	0.1	1.80
0.001	5	0.67	0.001	10	0.24	0.001	5	1.51
0.005	1	0.31	0.01	2.5	0.86	0.005	0.1	0.88
0.005	5	0.08	0.01	10	0.40	0.005	5	0.58
0.025	1	0.04	0.05	2.5	0.29	0.025	0.1	0.59
0.025	5	0.11	0.05	10	0.11	0.025	5	0.24
AVERAGE		0.33	AVERAGE		0.41	AVERAGE		0.93

PATIENT CELLS

CUDC	IMD	CI	CUDC	Ibrutinib	CI	CUDC	ABT-199	CI
0.005	0.25	2.83	0.0025	2.5	0.57	0.005	0.005	0.30
0.005	1	0.97	0.0025	10	0.43	0.005	0.025	0.51
0.01	0.25	0.49	0.01	2.5	0.75	0.01	0.005	0.31
0.01	1	0.55	0.01	10	0.49	0.01	0.025	0.51
0.1	0.25	0.42	0.05	2.5	0.83	0.1	0.005	0.33
0.1	1	0.47	0.05	10	0.53	0.1	0.025	0.42
AVERAGE		0.95	AVERAGE		0.60	AVERAGE		0.40

Table S2. Combination Index (CI) values calculated using the CalcuSyn software. CI is used as an indication of synergy in the combination treatments shown in Figure 4. Values represent: < 0.1, Very strong synergism; 0.1–0.3, Strong synergism; 0.3–0.7, Synergism; 0.7–0.85, Moderate synergism; 0.85–0.9, Slight synergism; 0.90–1.1, Nearly additive; 1.1–1.2, Slight antagonism; 1.2–1.45, Moderate antagonism; 1.45–3.3, Antagonism; 3.3–10, Strong antagonism; >10, Very strong antagonism. In green, synergistic combinations. In red, non-synergistic combinations. All concentrations are in μM . The results show average synergy in all combinations, with some of the concentrations reaching very strong or strong synergism and only three having a degree of antagonism.