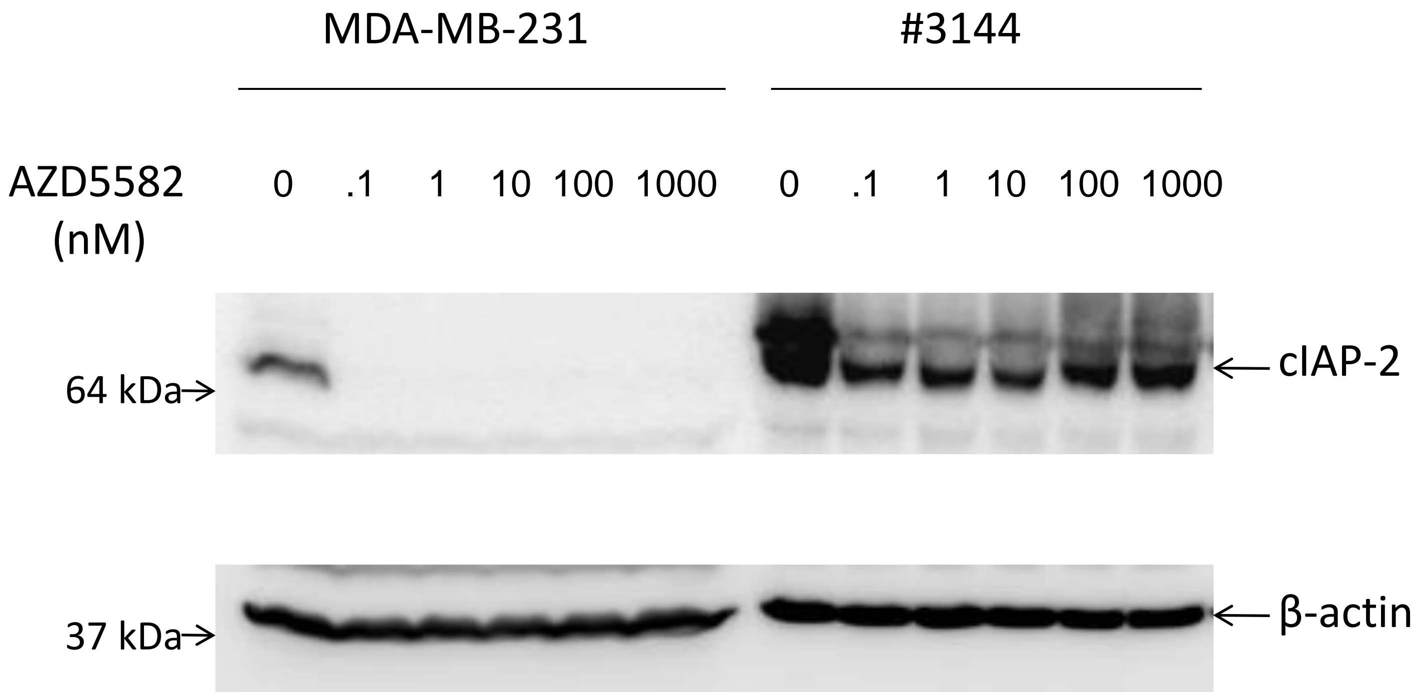
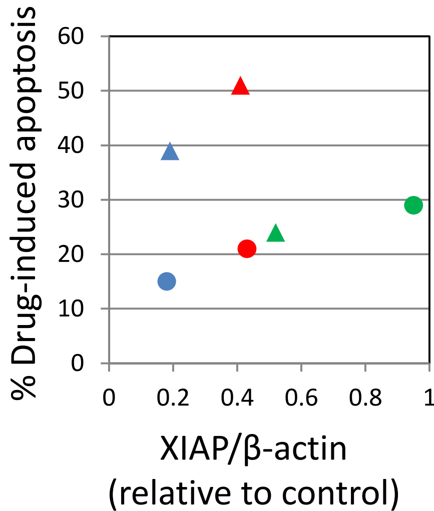


Supplementary Figure S1. AZD5582 is potent in inducing degradation of IAP proteins. Primary CLL cells (#3144) were incubated for 4h with AZD5582 at the indicated concentrations and then examined for expression of cIAP-2 by Western blotting. β-actin was used as control for protein loading. The human breast cancer cell line MDA-MB-231 was used as a positive control as it has been shown that IAPs were extensively degraded by SMAC mimetic IAP inhibitor AZD5582 (Hennessey et al., J Med Chem, 2013).

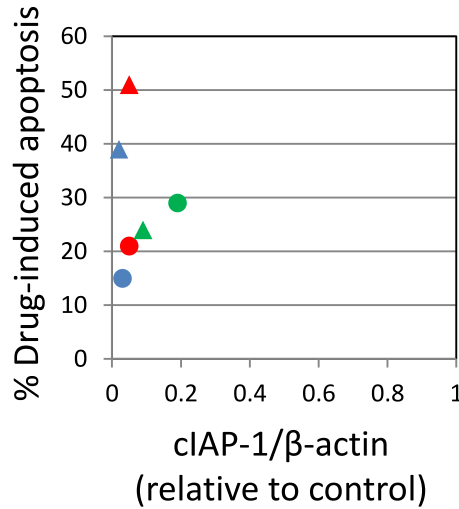
Supplementary Figure S2

Pearson's correlation analysis

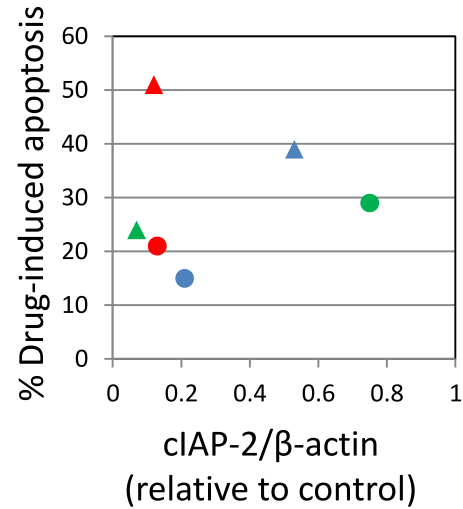
R^2=0.001, *P*=0.99



R^2= 0.06, *P*=0.881



R^2=0.014, *P*=0.826

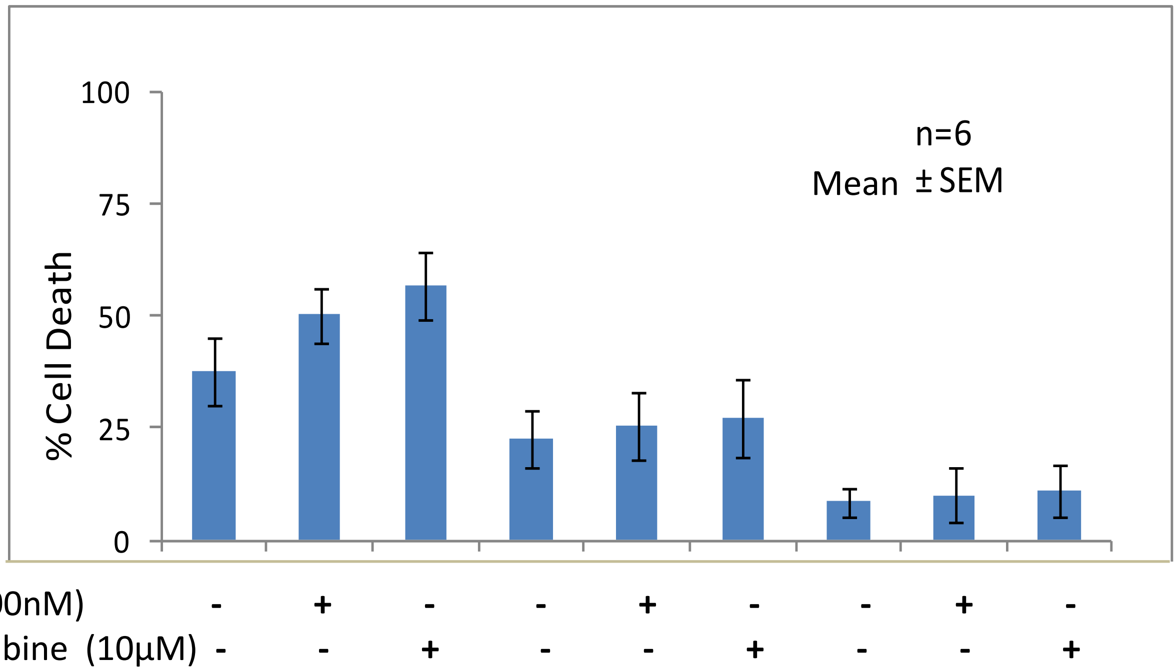


● #2096 (17p-) ● #2263 (11q-) ● #2441 (no 17p-/11q-)

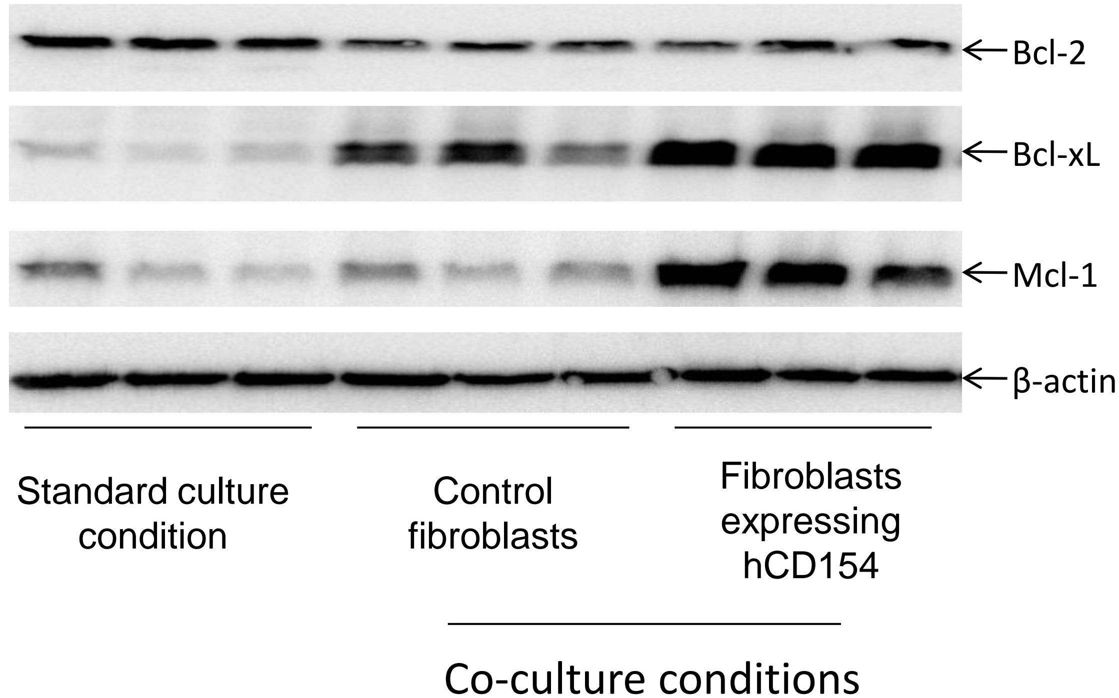
▲ #2103 (17p-) ▲ #2474 (11q-) ▲ #2968 (no 17p-/11q-)

Supplementary Figure S2. Lack of correlation between levels of individual IAPs after AZD5582 treatment and sensitivity to TRAIL-induced apoptosis. Primary CLL cells were co-incubated for 48h with 1 nM AZD5582 and recombinant human TRAIL (500 ng/ml) and cell death measured by flow cytometry. Pearson's correlation analysis was performed to determine the statistical significance of the correlation between the AZD5582-induced reduction in levels of XIAP, cIAP-1 and cIAP-2 and sensitivity to TRAIL-induced killing among the six cases examined.

a



b



Supplementary Figure S3. CD40 stimulation protects CLL cells from spontaneous apoptosis and killing induced by fludarabine and dexamethasone. (a) CLL cells were cultured for 48 h under standard conditions or on parental or CD154-expressing fibroblasts in the absence or presence of fludarabine (10µM) or dexamethasone (Dex) (100nM). CLL cells were then harvested for analysis of viability by flow cytmetry. (b) CLL cells cultured for 48 h under the same conditions as in (a) were also examined for the expression of Bcl-xL, Mcl-1 and Bcl-2 proteins by Western blotting