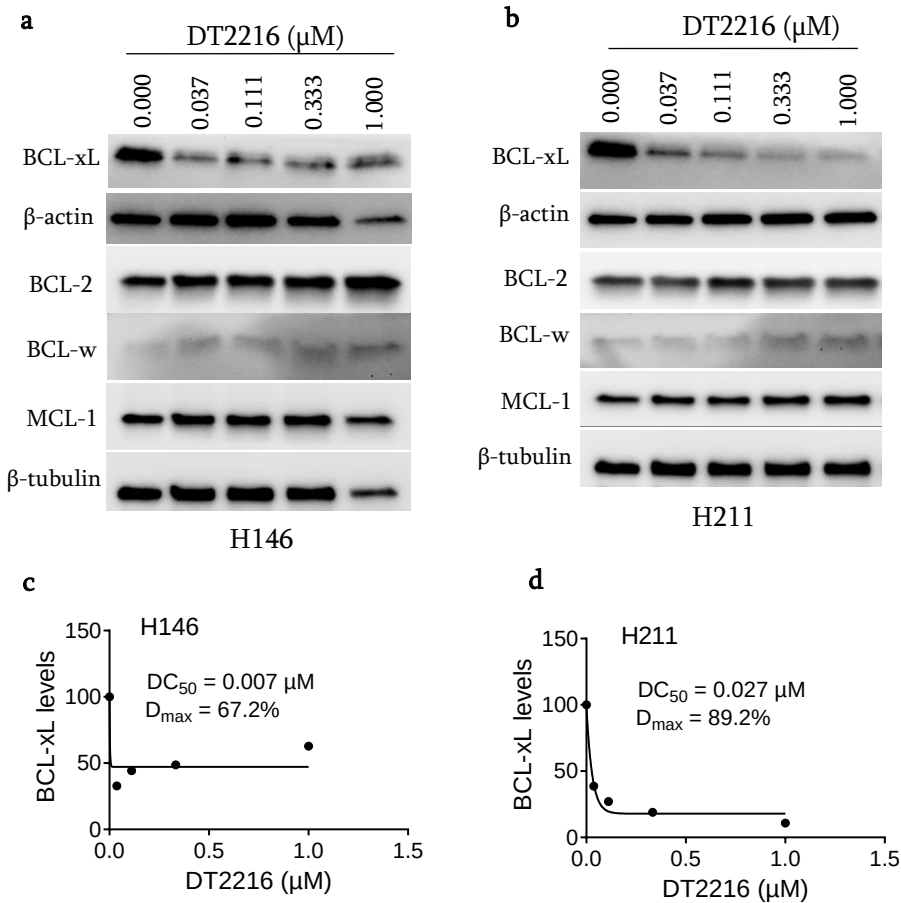


SUPPLEMENTARY INFORMATION

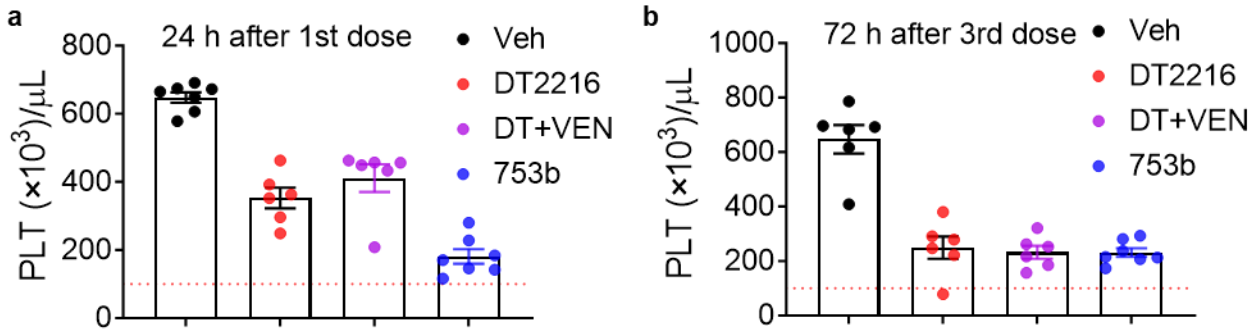
PROTAC-mediated dual degradation of BCL-xL and BCL-2 is a highly effective therapeutic strategy in small-cell lung cancer

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SUPPLEMENTARY FIGURES



Supplementary Figure S1. DT2216 degrades BCL-xL in SCLC cells. **(a,b)** Immunoblot analyses of BCL-xL, BCL-2, BCL-w and MCL-1 in H146 **(a)** and H211 **(b)** cells after they were treated with increasing concentrations of DT2216 for 48 h. β -actin and β -tubulin were used as equal loading controls. **(c,d)** Densitometric analysis of BCL-xL along with DC_{50} and D_{max} values in H146 **(c)** and H211 **(d)** cells are shown.



Supplementary Figure S2. 753b did not cause appreciable platelet toxicity in mice. **(a)** Enumeration of platelets (PLT) in mice blood 24 h after the 1st dose with vehicle, DT2216, DT2216+venetoclax, or 753b. Data are presented as mean $\pm$ SEM ($n = 7, 6, 6,$ and 7 mice in vehicle, DT2216, DT2216 + venetoclax, and 753b groups, respectively). **(b)** Enumeration of platelets in mice blood 72 h after the 3rd weekly dose with vehicle, DT2216, DT2216+venetoclax, or 753b. Data are presented as mean $\pm$ SEM ($n = 7, 6, 6,$ and 7 mice in vehicle, DT2216, DT2216 + venetoclax, and 753b groups, respectively).

Supplementary Table S1. Antibodies used in immunoblotting.

Antibody	Clone	Antibody isotype	Catalog #	Concentration
BCL-xL	–	Rabbit IgG polyclonal	2762	1:1000
BCL-2	50E3	Rabbit IgG monoclonal	2870	1:500
MCL-1	D35A5	Rabbit IgG monoclonal	5453	1:1000
BCL-w	31H4	Rabbit IgG monoclonal	2724	1:500
PARP/Cleaved PARP	46D11	Rabbit IgG monoclonal	9532	1:1000
Full-length caspase-3	–	Rabbit IgG polyclonal	9662	1:1000
cleaved caspase-3	–	Rabbit IgG polyclonal	9661	1:1000
β -tubulin	–	Rabbit IgG polyclonal	2146	1:3000
β -actin	D6A8	Rabbit IgG monoclonal	8457	1:5000
Secondary antibody		Anti-rabbit IgG, HRP	7074	1:3000

Footnotes: All the antibodies were purchased from Cell Signaling Technology, Danvers, MA.