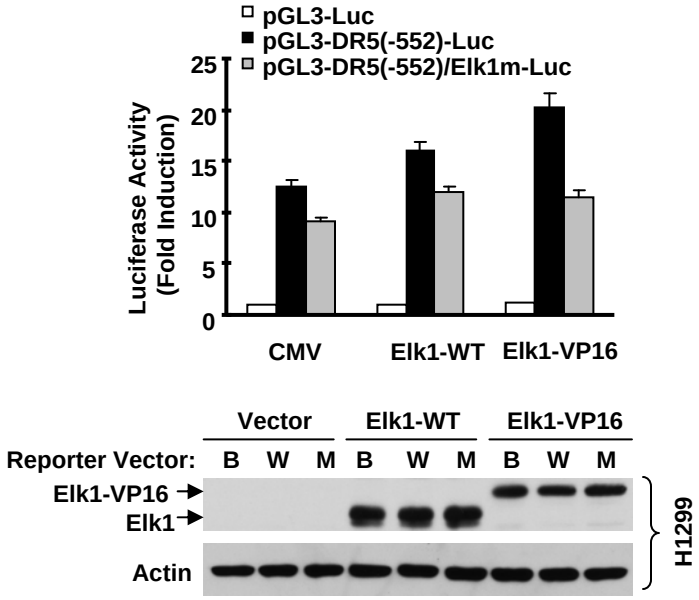

Fig. S1. Elk1 increase DR5 promoter activity. H1299 cells were co-trasnfected with the given DR5 promoter reporter and Elk1 expression plasmids for 36 h and then harvested for luciferase assay and Western blot analysis, respectively.

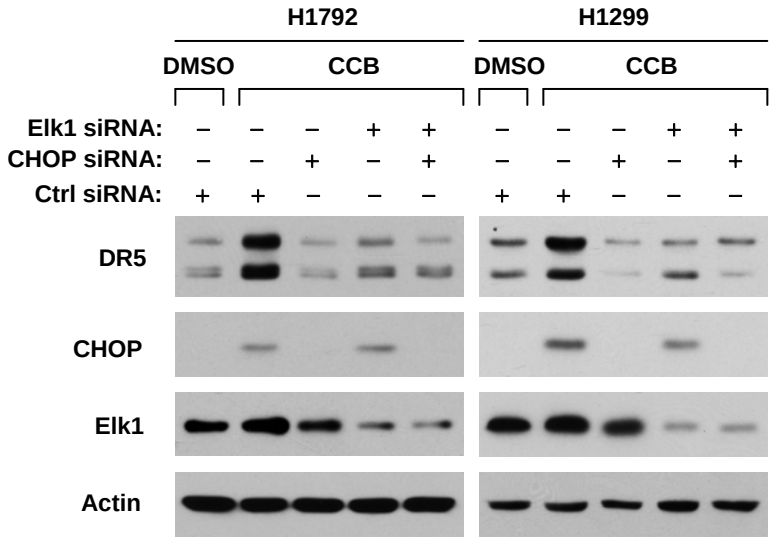

Fig. S2. Simultaneous knockdown of CHOP and Elk1 abolishes celecoxb-induced DR5 induction. The given cell lines were transfected with control (Ctrl), CHOP, Elk1 or CHOP plus Elk1 siRNAs for 40 h and then treated with and without 50 μM celecoxib (CCB) for an additional 10 h. The indicated proteins were detected with Western blot analysis.

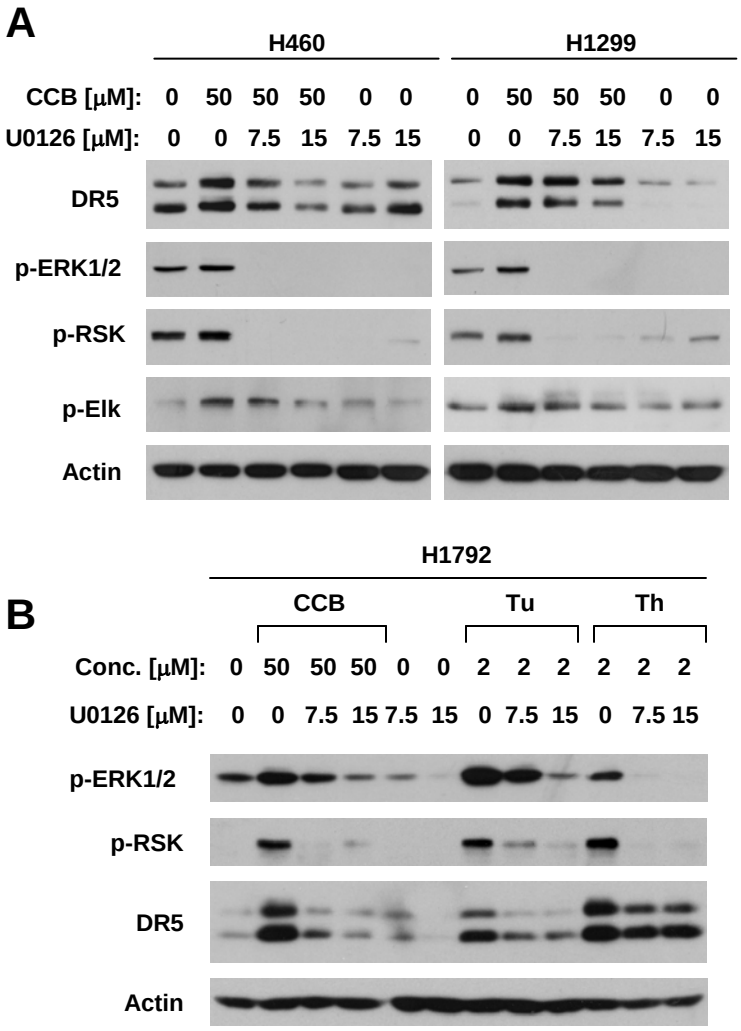

Fig. S3. The MEK inhibitor U0126 attenuates DR5 upregulation induced by celecoxib (*A* and *B*) and other drugs (*B*). The indicated cell lines were pretreated with U0126 for 30 min and then co-treated with the given concentrations of celecoxib (CCB), tunicamycin (Tu) and thapsigargin (Th) for additional 12 h. The cells were then harvested for preparation of whole cell protein lysates and subsequent Western blot analysis for the given proteins

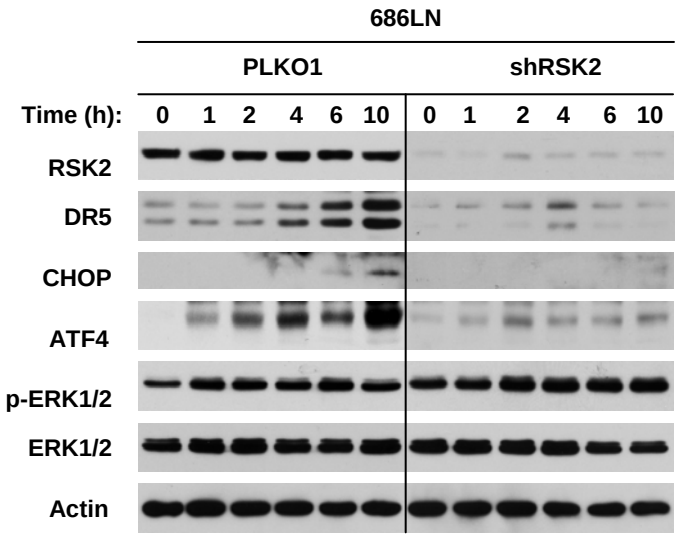

Fig. S4. Stable silencing of RSK2 abolishes celecoxib-induced DR5, CHO and ATF4 upregulation in 686LN cells. The indicated stable cell lines derived from 686LN cells were treated with 50 μM celecoxib for the given times and then subjected to preparation of whole cell protein lysates and subsequent Western blot analysis.

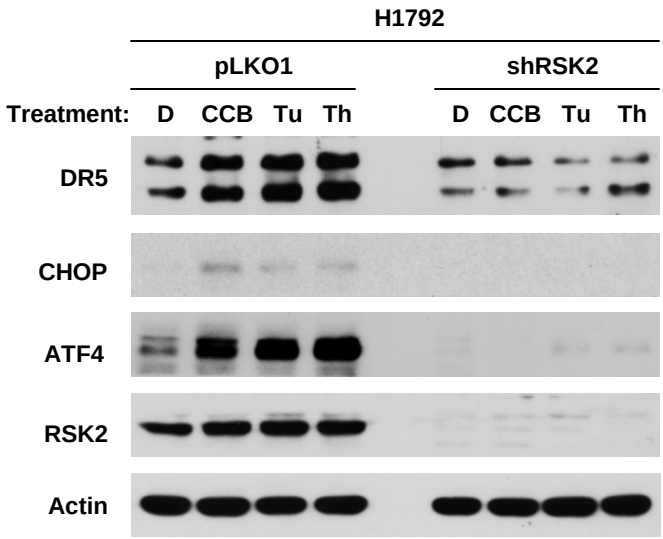

Fig. S5. RSK2 knockdown abolishes upregulation of DR5, CHOP and ATF4 induced by other agents. The indicated stable cell lines were treated with DMSO (D), 50 μM celecoxib (CCB), 2 μM tunicamycin (Tu) or 2 μM thapsigargin (Th) for 10 h. The cells were then harvested for preparation of whole-cell protein lysates and subsequent Western blot analysis for the given proteins

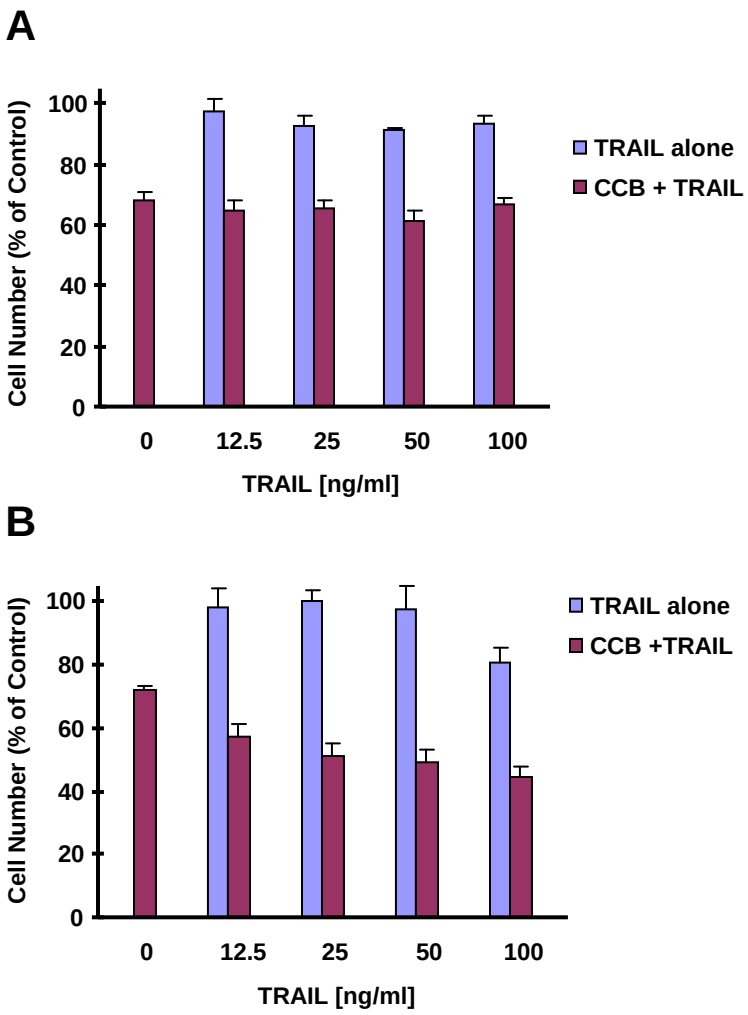

Fig. S6. Celecoxib and TRAIL combination exhibit enhanced effect on decreasing cell survival in H1299 lung cancer cells (B), but not in HBEC3KT normal human bronchial epithelial cells (A). Both H1299 (B) and HBEC3KT (A) cell lines were seeded in 96-well plates and next day treated with the indicated concentrations of TRAIL alone in the absence and presence of 25 μM celecoxib (CCB). After 24 h, the cell numbers were estimated with the SRB assay. Columns represent means ± SDs of triplicate determinations.

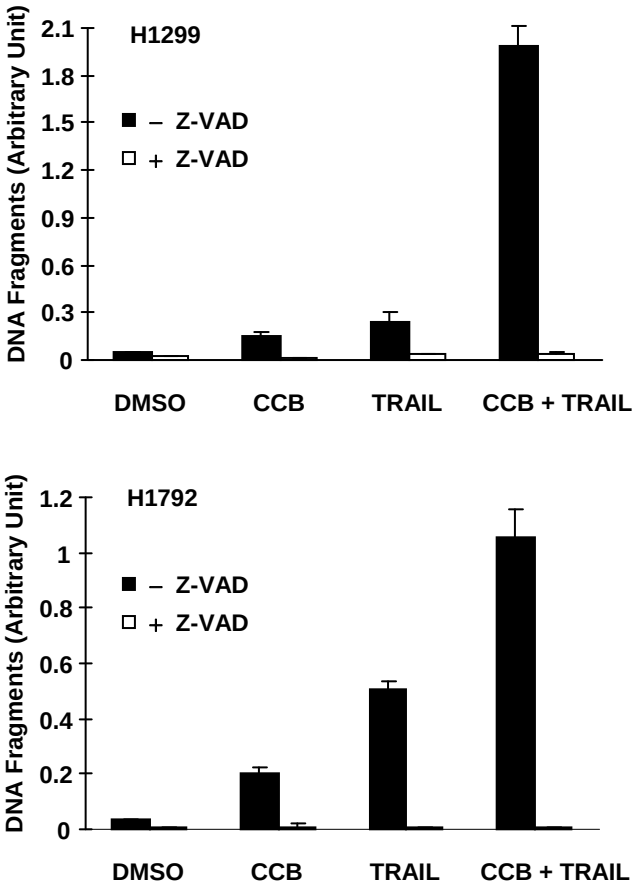

Fig. S7. The pan-caspase inhibitor, Z-VAD-FMK, abolishes cooperative induction of apoptosis by celecoxib and TRAIL combination. The indicated cell lines were plated in 96 well plates and treated on the next day with DMSO, 50 μM celecoxib (CCB), 20 ng/ml TRAIL, or celecoxib plus TRAIL in the absence and presence of 50 μM z-VAD-FMK (30 min pretreatment). After 16 h, the cells were subjected to DNA fragmentation assay using the Cell Death Detection ELISA^{Plus} kit. Columns represent means ± SD of triplicate determinations.