Legends for Supplementary Figures:

Figure S1: Silencing of ERK rescues cells from LY30-induced sensitization to TRAIL:

SHEP-1 cells were transfected with siERK1 or siERK2 as described in Materials and Methods. 72 hours after transfection, cells were treated with LY30 (25uM) for 2 hours followed by the addition of TRAIL (50ug/ml) for 4 hours and cell viability was determined by the crystal violet assay as described in Materials and Methods.

Figure S2: LY30 sensitizes glioblastoma cell line T98G to TRAIL

(A) Glioblastoma cell line (T98G) was pre-treated with LY30 for 1 hour followed by treatment with TRAIL for 48 hours and cell viability was determined by Crystal Violet assay as described in Materials and Methods. (B) Photomicrograph of T98G cells; a: control; b: LY30 50 μmol/L; c: TRAIL 100ng/ml; d: LY30 50μmol/L+TRAIL 100ng/ml. (C). Intracellular H_2O_2 generation upon LY30 treatment was measured by loading with the redox sensitive dye DCFH-DA (5μmol/L for 15 minutes) and analyzed by flow cytometry. (D) A representative histogram indicating the increase in surface expression of DR4 and DR5 following 18 hours of LY30 treatment was analyzed using PE-conjugated mouse monoclonal anti-human DR4 and DR5 (10μg/ml). Non-specific mouse IgG2B was used as an isotype control.

Figure S3: Sensitization of Jurkat cells to TRAIL by LY30 pre-treatment

(A) Jurkat cells ($1x10^6$) were seeded onto 12 well plates and exposed to LY30 for 1 hour followed by TRAIL treatment for 18-24hours before washing with cold 1X PBS and cell viability was determined by MTT assay. Briefly, cells were incubated with

MTT (3-(4, 5-dimethylthiazolyl-2)-2, 5-diphenyltetrazolium bromide, Sigma Aldrich) for 2 hours followed by dissolution of the formazan crystals with Sorenson's glycine and DMSO (Sigma Aldrich) buffer. After solubilizing, quantification was done with a TECAN spectrophotometer using an absorbance wavelength of 570nm. (B) Intracellular H_2O_2 was detected by flow cytometry as described in Figure S2. (C) Time course of MAPKs activation in Jurkat cells at ~90% confluence was observed in cells treated with LY30 (25μmol/L) for up to 6 hrs. Activation of JNK and ERK was detected by Western blotting using antibodies specific for their phosphorylated forms. (D) A representative histogram indicating the increase in surface expression of DR4 and DR5 following 4 hours of LY30 treatment was analyzed using PE-conjugated mouse monoclonal anti-human DR4 and DR5 (10ug/ml). Non-specific mouse IgG2B was used as an isotype control.

Figure S4: LY30 sensitizes a variety of human tumor cell lines to TRAIL

(A) Ovarian carcinoma cells (HeLa) and (B) Neuroblastoma cells (SH-SY5Y) were pre-treated with the indicated concentrations of LY30 for 1 hour prior to the addition of TRAIL and cell viability was determined by the crystal violet assay as described in Materials and Methods. (C) Cell cycle profiles after PI staining of colorectal carcinoma cells (HT29) following treatment of cells with TRAIL (50ng/ml) with or without pretreatment with LY30 (25μmol/L) for 1 hr. (D) Leukemia cells (CEM) were pre-treated with the indicated concentrations of LY30 for 1 hour prior to the addition of TRAIL (24 hours) and cell viability was determined by the MTT assay as described. Intracellular H_2O_2 generated after DCFH-DA (5μmol/L) staining for 15 minutes was indicated by the shift in fluorescence and detected by flow cytometry.