

Figure S1. TPL treatment promotes intracellular accumulation of GPx4 in Huh7 cells. Upregulation of GPx4 in Huh7 cells following TPL treatment was assessed by western blot analysis. Grayscale analysis was conducted with an ImageJ 1.52a software. Quantitative data are presented as the mean  $\pm$  standard deviation (n=3). \*P<0.05 vs. 0 ng/ml TPL group. GPx4, glutathione peroxidase 4; TPL, triptolide.

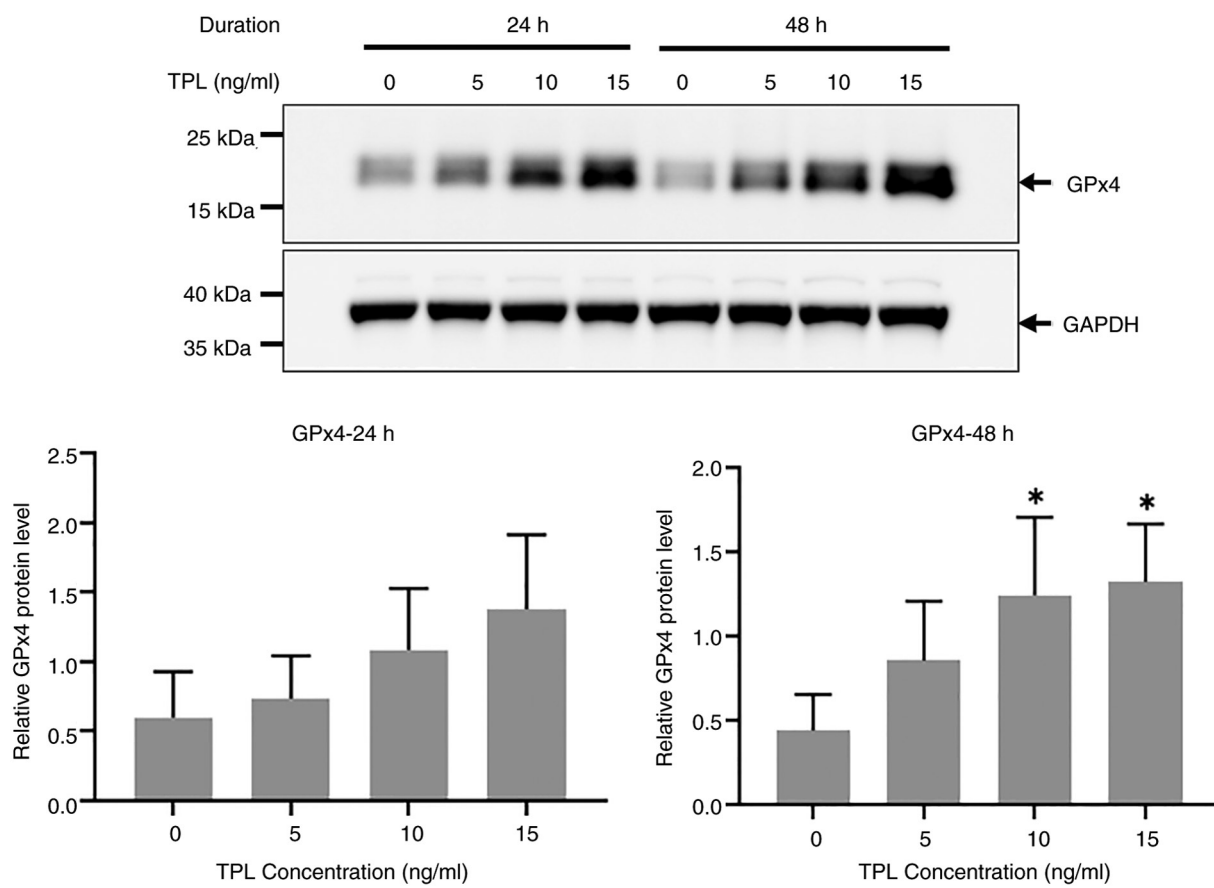


Figure S2. Huh7 cell viability was complementarily inhibited by TPL and RSL3 co-treatment. Cell Counting Kit-8 was used to evaluate the effects of (A) RSL3 and (B) TPL treatment for 24 h at various concentrations, and the effect of (C) co-treatment with RSL3 (0.5/1  $\mu\text{M}$ )  $\pm$  TPL (10 ng/ml) for 24 and 48 h, on Huh7 cell viability. Quantitative data are presented as the mean  $\pm$  standard deviation (n=3). \*\*P<0.01 vs. RSL3 (0  $\mu\text{M}$ ) group in (A); \*\*P<0.01 vs. TPL (0 ng/ml) group in (B); \*P<0.05 and \*\*P<0.01 vs. TPL (10 ng/ml) group in (C) at 24 h; \*P<0.05 vs. RSL3 (0.5  $\mu\text{M}$ ) group, \*\*P<0.01 vs. RSL3 (1  $\mu\text{M}$ ) group, \*P<0.05 and \*\*P<0.01 vs. TPL (10 ng/ml) group in (C) at 48 h. RSL3, RAS-selective lethal 3; TPL, triptolide.

