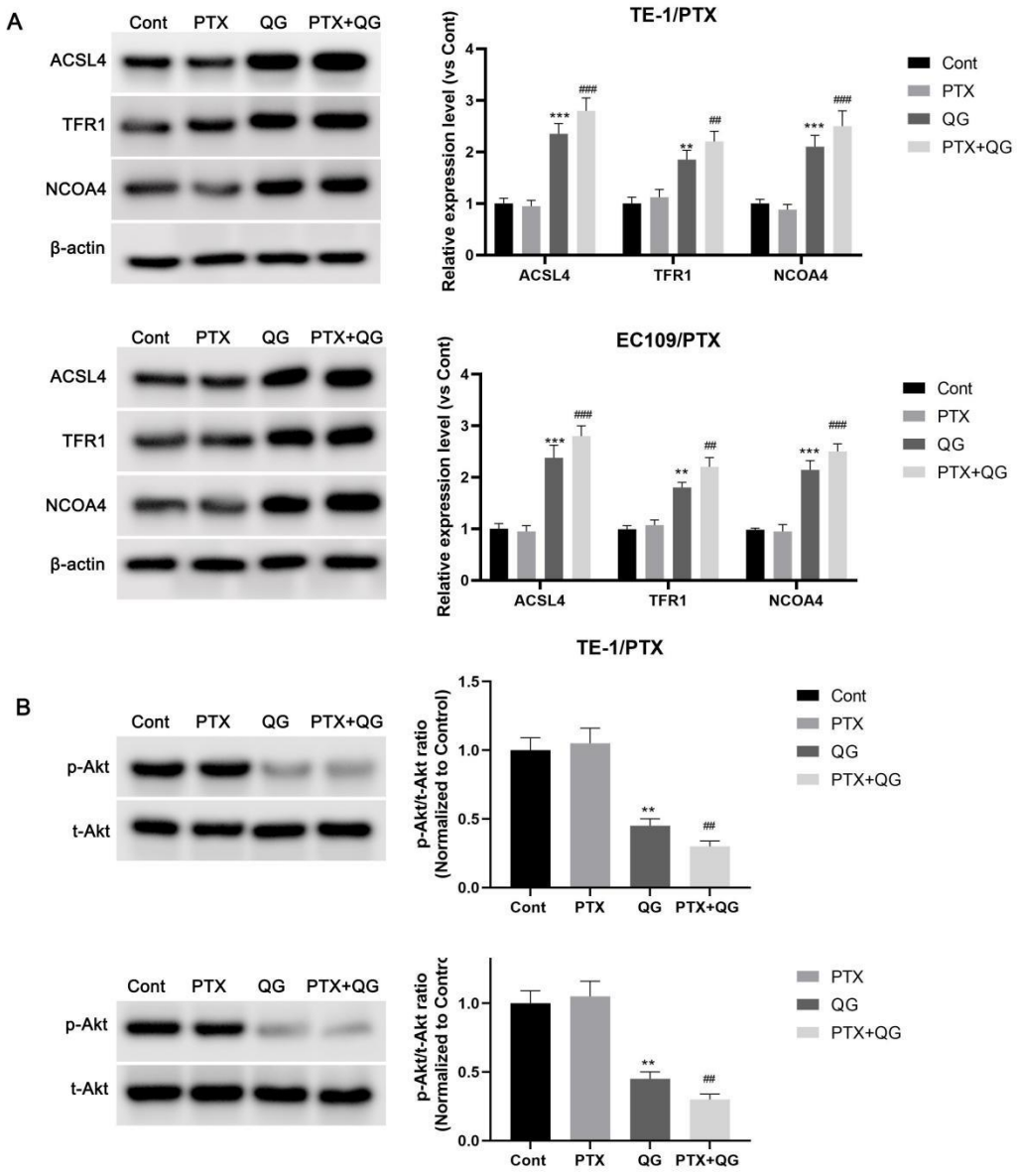
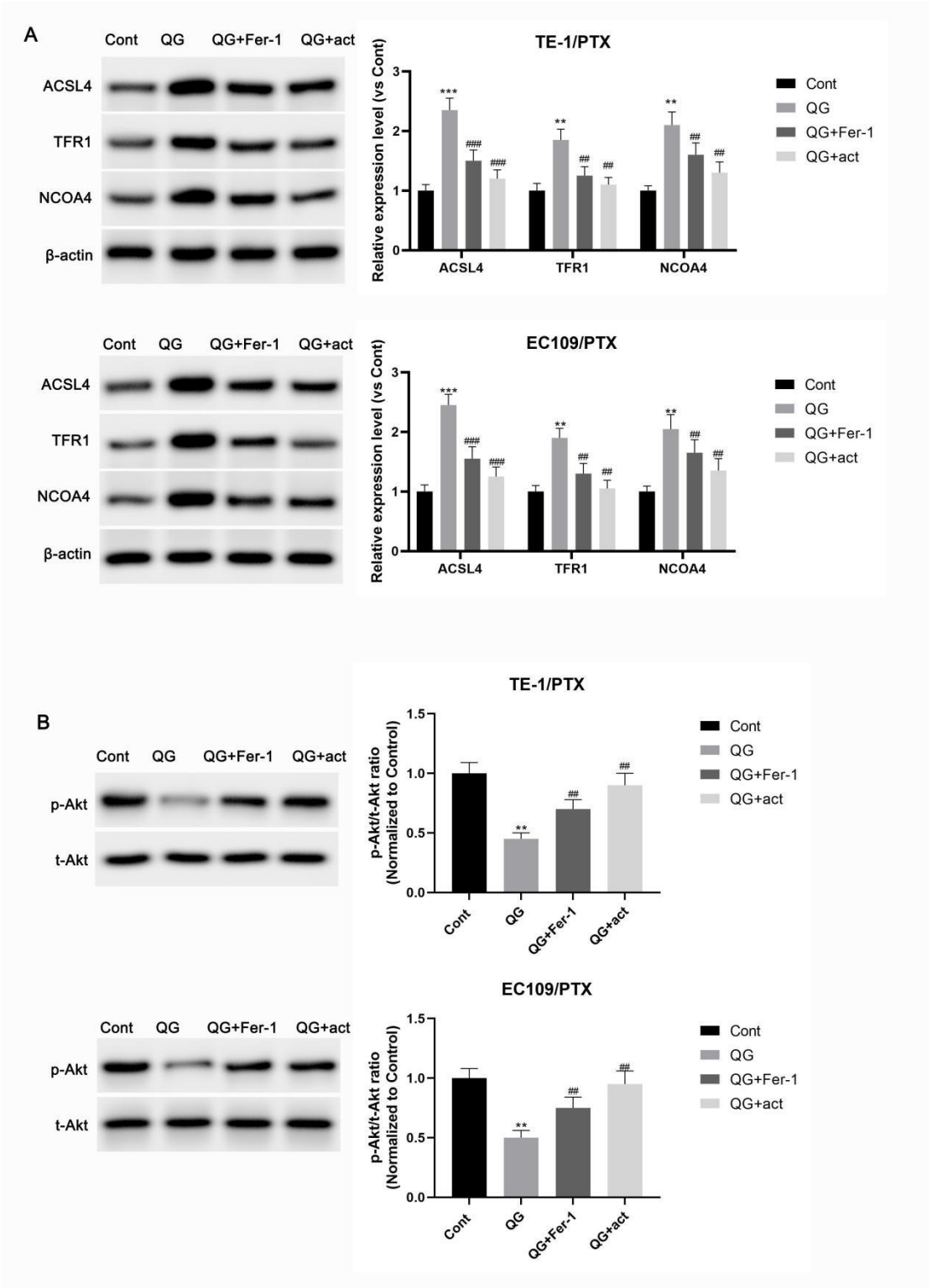


Supplementary Figure 1 Qige San modulates ferroptosis markers and Akt phosphorylation in paclitaxel-resistant esophageal cancer cells

(A) Protein expression levels of ferroptosis-related markers (ACSL4, TFR1, NCOA4) in TE-1/PTX and EC109/PTX cells. Left panels: Representative Western blot images. Right panels: Quantification of protein expression normalized to Control (set as 1.0).

(B) p-Akt/t-Akt ratio in TE-1/PTX and EC109/PTX cells. Left panel: Western blot analysis of p-Akt (Ser473) and total Akt. Right panel: Quantification of p-Akt/t-Akt ratio normalized to Control.

Data are mean ± SEM (n = 3). **p < 0.01, ***p < 0.001 *vs* Control; ##p < 0.01, ###p < 0.001 *vs* PTX (one-way ANOVA with Tukey's test).



Supplementary Figure 2 Inhibition of ferroptosis or PI3K activation reverses Qige San's effects

(A) Protein expression levels of ferroptosis-related markers (ACSL4, TFR1, NCOA4) in TE-1/PTX cells. Left panels: Western blot images. Right panels: Quantitative analysis normalized to Control.

(B) p-Akt/t-Akt ratio in TE-1/PTX cells. Left panel: P-Akt and total Akt blots. Right panel: Normalized p-Akt/t-Akt ratio.

Data are mean ± SEM (n = 3). **p < 0.01, ***p < 0.001 *vs* Control; ##p < 0.01, ###p < 0.001 *vs* QG (one-way ANOVA with Tukey's test).

Supplementary Table 1. Top 5 active components of Qige San and their targets

Compound	OB (%)	DL	Key Targets	Source Plant
Tanshinone IIA	38.9	0.55	AKT1, MAPK1, GPX4	Salvia miltiorrhiza
Emodin	45.6	0.21	PTGS2, NOS2, NCOA4	Rheum palmatum
Curcumin	52.8	0.18	STAT3, NF-κB	Curcuma aromatica
Baicalin	40.3	0.25	SLC7A11, HIF-1 α	Scutellaria baicalensis
Ginsenoside Rg3	36.7	0.42	PI3K, mTOR	Panax ginseng