

Figure S1. Representative flow cytometry histograms of Miaapaca2 cells stained with C11 BODIPY 581/591. Cells were either left untreated (black line) or treated with erastin (red line). The proportion of the oxidized population is indicated.

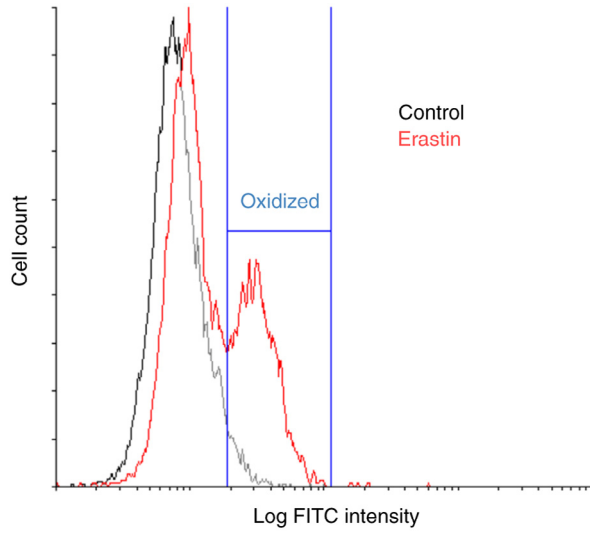


Figure S2. Erastin does not induce apoptosis, necroptosis or autophagy in T3M4 cells. (A) T3M4 cell viability following erastin and cell death inhibitor treatment. (B) Flow cytometric analysis of cell death type following erastin treatment in T3M4 cells. The data are presented as the mean  $\pm$  SD; n=3. Cells cultured under standard conditions were used as the control. Era, erastin; Ferr-1, ferrostatin-1; ZVAD, Z-VAD-FMK; Nec-1, necrostatin-1; SBI, SBI-0206965.

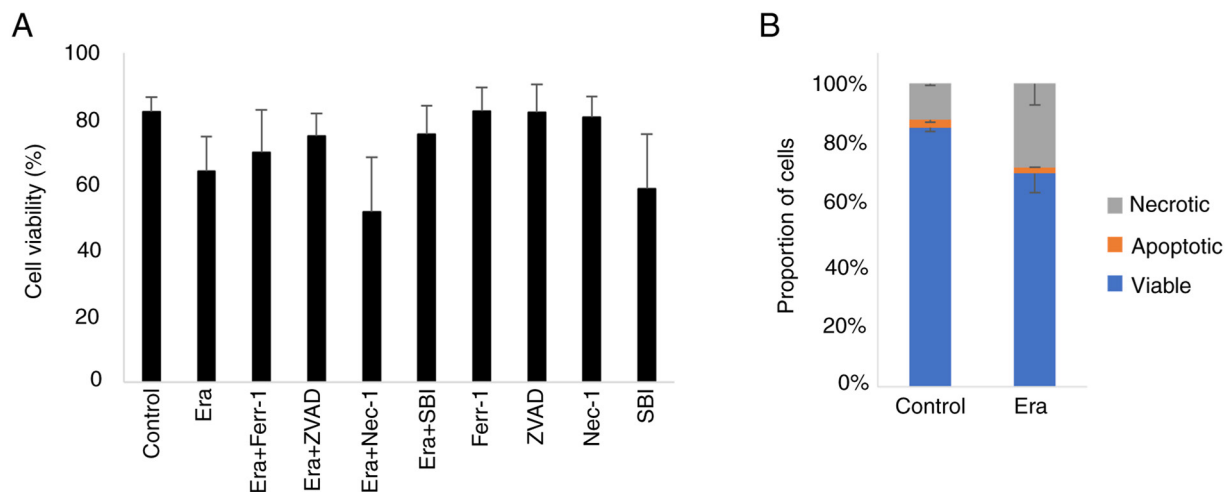


Figure S3. ERK1/2 is translocated to the nucleus in starved Miapaca2, Su.86.86 and T3M4 cells. Representative fluorescence microscopy images of (pseudo)starved (rapamycin-treated) cells, either treated with erastin or left untreated. Magnification, x20.

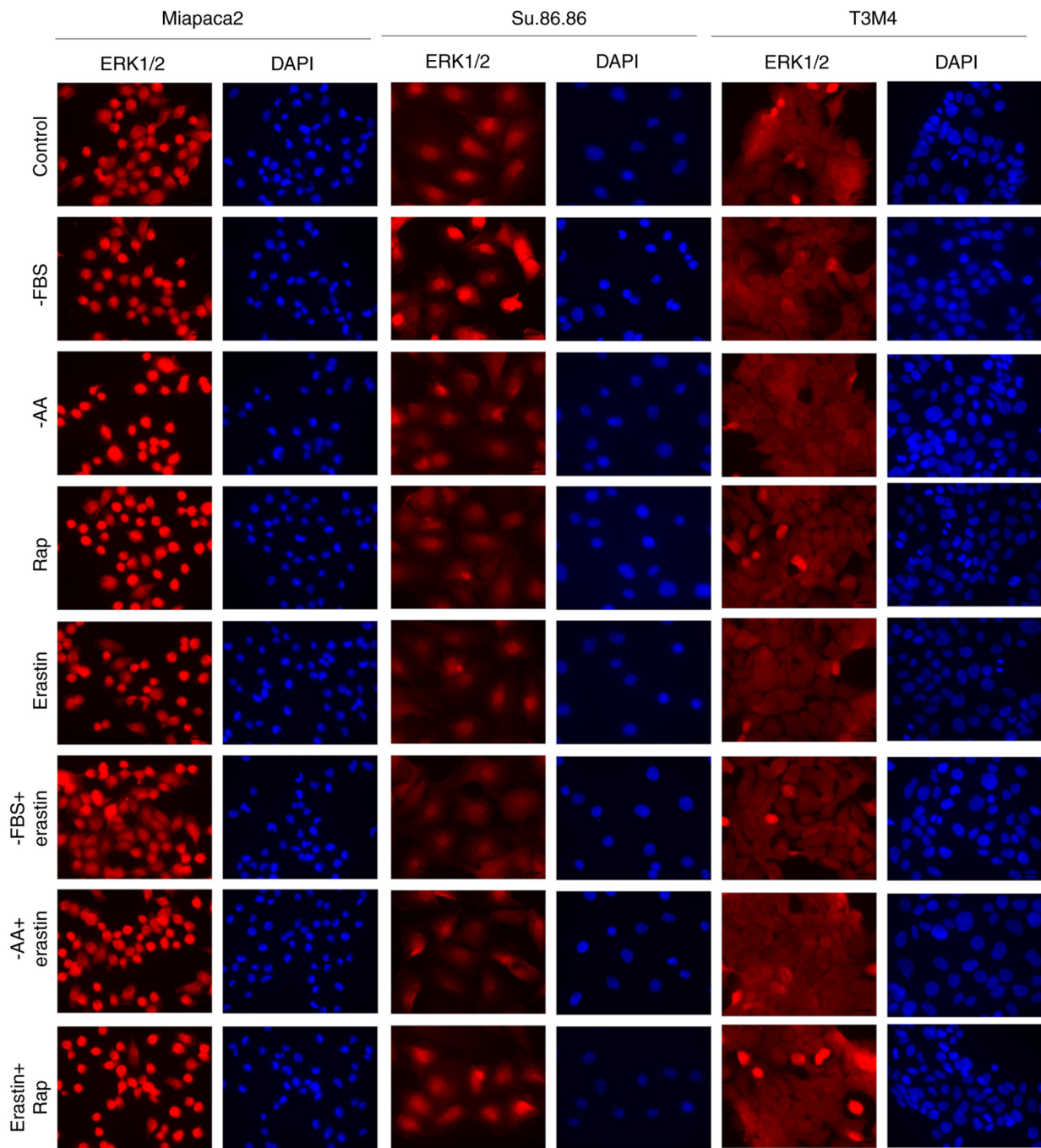


Figure S4. Measurement of lipid peroxidation of (A) Miapaca2, (B) Panc-1, (C) Su.86.86 and (D) T3M4 cells, cultured without FBS, without the amino acids L-glutamine, L-lysine and L-arginine and treated with the ERK1/2 inhibitor, SCH (1  $\mu$ M). Ferroptosis was induced by erastin and inhibited by Ferr-1. The data are presented as the mean  $\pm$  SD; n=3. Cells cultured under standard conditions were used as the control. \*P<0.05, \*\*P<0.01 and \*\*\*P<0.001, vs. control of each group. -AA, cells cultured without L-glutamine, L-lysine and L-arginine; SCH, SCH772984; Ferr-1, ferrostatin-1.

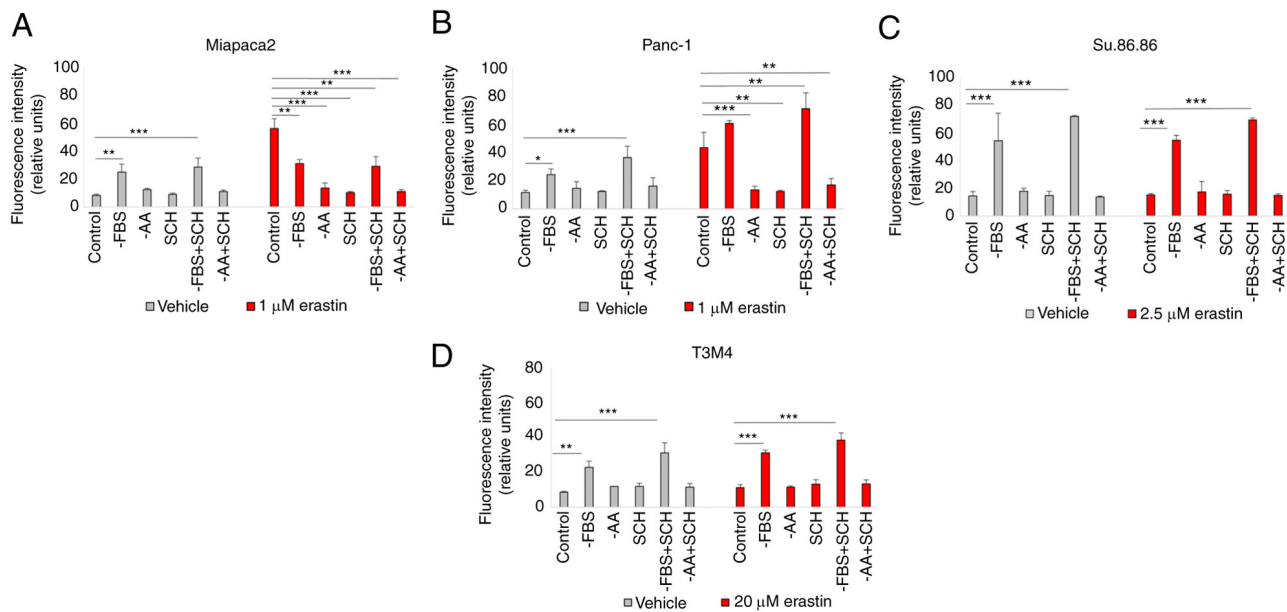


Figure S5. Expression of epithelial-to-mesenchymal transition markers in pancreatic cancer cells during starvation. (A) YAP1 expression in Miapaca2 cells with or without starvation for 1-7 days. (B) Quantification of western blots in panel A. (C) Western blot analysis of vimentin expression in Capan-26 cells starved for 1-5 days. C12 primary stromal cell culture was used as a positive control. The data are presented as the mean  $\pm$  SD.  $n=3$ . \* $P<0.05$  vs. 0 days of starvation. YAP1, yes-associated protein 1.

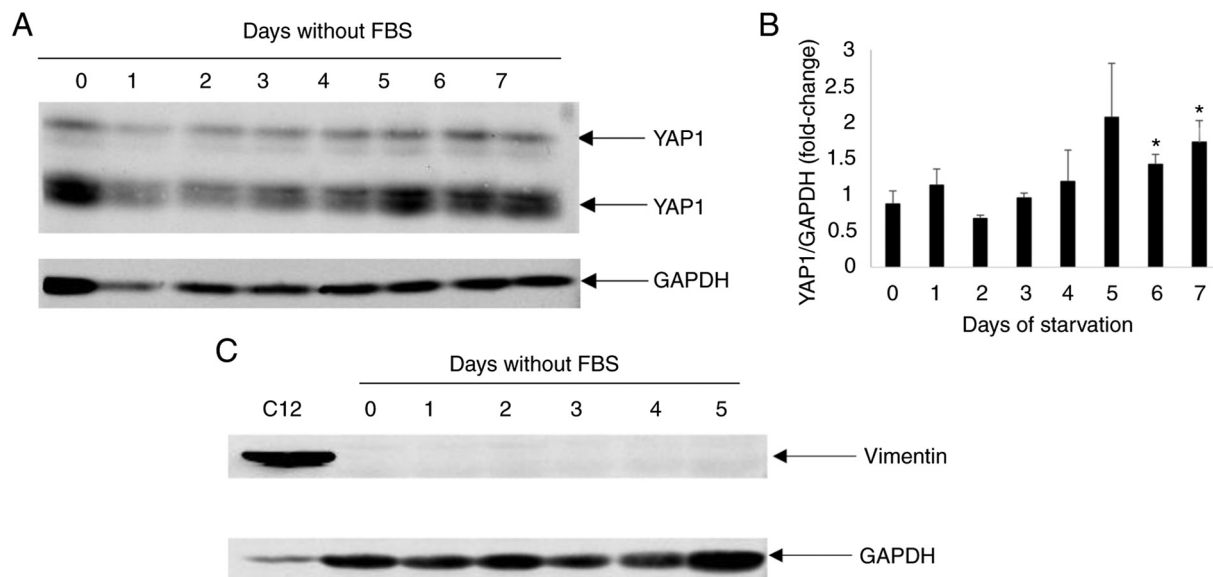


Figure S6. FBS starvation does not induce morphology changes in Panc-1, Su.86.86 and T3M4 cells. Representative images of different cell lines in the absence of FBS for the indicated time period. Scale bar, 50  $\mu$ m.

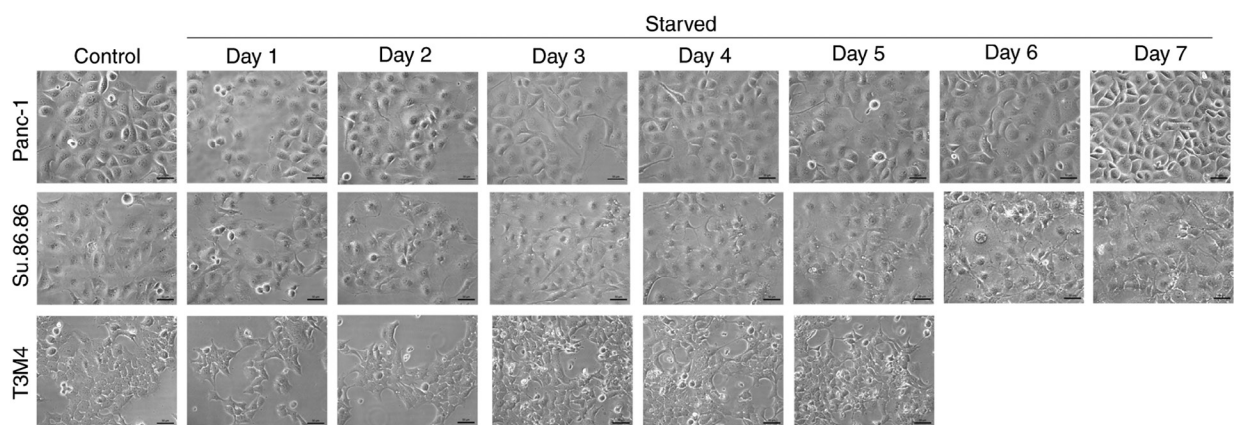


Figure S7. Starvation elevates GSH levels in Miapaca2, but not in Panc-1 and Su.86.86 cells. The data are presented as the mean  $\pm$  SD; n=3. Cells cultured under standard conditions were used as the control. \*P<0.05 and \*\*P<0.01 vs. control (non-starved) cells. GSH, glutathione; -AA, cells cultured without L-glutamine, L-lysine and L-arginine.

