Supplemental Figure Legends

Figure S1. Ferroptosis inducers trigger differential cell death in pancreatic tumor cells.

(**A**). Relative viability of pancreatic tumor cell lines assessed by Crystal Violet staining after control or erastin (E) treatment for 48 hours.

(**B**). Representative cell morphology of erastin-sensitive cell lines PANC-1 (18 hrs) and MIAPaCa-2 (21 hrs) after control or erastin (2.5 μM) treatment respectively.

(**C**). Relative viability of pancreatic tumor cell lines measured by the CellTiter-Glo® assay after treatments with increasing concentrations of RSL3 treatments for 48 hours (n=3, #, $p<0.002$).

(**D**). Relative viability of MIAPaCa-2 cells assessed by Crystal Violet staining under control, erastin (E, 2.5 μM), Ferostatin-1 (Fer-1, 5 μM) or E + Fer-1 conditions for 48 hours.

Figure S2. Phenotypic cysteine dependence correlates with the EMT status of pancreatic tumor cells

(**A**). Summary of various tumor associated genetic mutations across different pancreatic tumor cell lines.

(**B**). Immunoblot analysis of Smad4 protein expression in vector control (Vec) or Smad4 overexpressing CFPAC-1 cells (Left panel); Relative viability of CFPAC-1 Vec or Smad4 cells after control or erastin treatment for 72 hours (Right panel).

(**C**). RT-qPCR expression analysis of selected EMT gene markers in CFPAC-1 Vec or Smad4 cells; β-Actin serves as a normalization control.

(**D**). RT-qPCR expression analysis of selected selenoprotein genes in pancreatic tumor cells.

Figure S3. Selenite protects erastin-sensitive cells from ferroptosis inducers.

(**A**). Relative viability of PANC-1 and MIAPaCa-2 cells treated with control, erastin (E, 2.5μM), selenite (Se, 200 nM), or E+Se for 18 hrs (n=3, #, $p<0.0001$).

(**B**). Relative viability of PANC-1 and MIAPaCa-2 assessed by Crystal Violet staining with similar treatments in (**A**) for 48 hrs.

(**C**). Relative viability of PANC-1 and MIAPaCa-2 treated with control or selenite (SeO_3) and increasing concentrations of RSL3 for 48 hrs.

(**D**). RT-qPCR analysis of gene expression in PANC-1 cells with similar treatments in (**A**) for 16 hrs (n=2, #, $p<0.01$).

Figure S4. Thioredoxin reductase inhibitors synergize with erastin to induce cell death in erastin-resistant cells

(**A**). Relative viability assessed by the CellTiter-Glo® assay and Crystal Violet staining in CFPAC-1 cells treated with control (Con), erastin (E, 2.5 μM), D9 (8 μM), or E+D9 for 72 hrs.

(**B**). Relative viability assessed by the CellTiter-Glo® assay and Crystal Violet staining in BXPC3 cells with similar treatments as (**A**) for 72 hrs.

(**C**). Immunoblot analysis of phosphorylated H2AX (p-H2AX) in ASPC1 cells treated with control, erastin (E, 5 μM), D9 (2 μM), or E+D9 for 36 and 48 hrs.

(**D**)**.** RT-qPCR analysis of gene expression in CAPAN-2 cells treated as (**C**) for 48 hrs.

(**E**). Immunoblot analysis of phosphorylated histone (pH2AX) in ASPC1 cells treated with control, erastin (E, 5 μM), Auranofin (Au, 5 μM), or E+Au for 48 hrs.