



**Figure S2**

**Figure S2: Anti-proliferative effect of SLC7A11 knockdown in CAFs and the effect of SLC7A11 inhibition in MiaPaCa-2 PDAC cells and normal human pancreatic ductal epithelial (HPDE) cells.** A) Live cell counts (trypan blue exclusion) of CAFs expressing low (CAF line 6 in Figure 1B) or high basal levels of SLC7A11 (CAF line 1 in Figure 1B), 72h post-transfection with control siRNA (ns-siRNA), SLC7A11-siRNA pool or SLC7A11-siRNA single sequence (SLC7A11-siRNA single seq). Circles indicate replicate experiments (n=3). B-C) Peak areas as assessed by mass spectrometry for (B) unlabelled cystine and (C) C<sub>13</sub>-glutamate in immortalised CAFs stably expression scramble-shRNA (ctl-shRNA) or SLC7A11-shRNA (slc-shRNA), 1 hour post release from labelling medium. Lines show mean±s.e.m, circles indicate replicates (n=3). D) Cell proliferation (cell counting kit 8 absorbance) of MiaPaCa-2 PDAC cells treated with sulfasalazine (SSZ) ± 66µM 2-mercaptoethanol (2-ME), as a % of controls. Circles indicate replicates (n=3). E) Live cell counts (trypan blue exclusion) of MiaPaCa-2 cells treated with erastin, as a fraction of controls. Circles indicate replicates (n=3). F) Representative Western blot and qPCR for SLC7A11 knockdown in HPDE cells, 72h post-transfection. Circles indicate replicates (n=3). G) Cell proliferation (cell counting kit 8 absorbance) of HPDE cells 72h post-transfection with ns-siRNA or SLC7A11-siRNA pool, as a % of controls. Circles indicate replicates (n=3). One-way ANOVA used for (A, D), student t-test used for (B-C, E-G). Asterisks in all graphs indicate significance (ns = not significant, \*p≤0.05, \*\*p≤0.01, \*\*\*p≤0.001, \*\*\*\*p≤0.0001). Replicate numbers for CAF experiments in panels (A) refer to independent transfections/treatments using primary CAF cells isolated from different PDAC patients. Replicate numbers for all HPDE and MiaPaCa-2 experiments refer to independent transfections and treatments. Replicate numbers for panels (B-C) refer to independent experiments using an immortalised CAF cell line.