Supplementary data

Figure S1. HMGA2 is highly expressed in pancreatic cancer and promotes cancer cell malignancy.

HMGA2 expression in cancer and normal tissue (**A**) and survival probability of cancer patients between high and low HMGA2 expression (**B**). Data were collected from the TCGA database. **C**. Comparison of HMGA2 expression in PAAD cancer samples and normal ones from TCGA database. **D.** Cell growth detection after HMGA2 deletion in BXPC-3 cells. Cell viability analysis was accessed using CCK-8 (n = 4). The efficiency of deletion was confirmed using western blot as listed. **E.** Evaluation of HMGA2 deletion on the clonal growth of PANC-1 cell. **F.** Xenograft tumor model investigating the growth of PANC-1 sgNC and PANC-1 sgHMGA2 cells in SCID mice. The graph bar represents the average tumor volume. Data are represented as mean ± SD for each group of mice. (n = 7). *$p < 0.05$, **$p < 0.01$.

Figure S2. HMGA2 confers resistance to ferroptosis cell death

Cell viability analysis of the effects of HMGA2 alternation in MIAPaCa-2 (**A**) and PANC-1 (**B**) cells with HMGA2 overexpression after erastin treatment. Cell viability analysis was accessed using CKK-8 at A450 (n = 4). The p-value was determined using a two-tailed unpaired Student's t-test. *$p < 0.05$; **$p < 0.01$

Figure S3. HMGA2 enhances GPX4 transcription

A. Correlation between HMGA2 and GPX4 mRNA expression using data from the TCGA database. **B.** H3K27Ac status of the cis-element in GPX4 promoter region from UCSC genome browser on humans (GRCh38/hg38).

Figure S4. HMGA2 promotes GPX4 protein synthesis through mTORC1 signaling

A. Detection of the GPX4 protein level in PANC-1 MOCK and HMGA2 cells after cycloheximide (CHX) treatment at different times. The correlation between GPX4 level and CHX time was analyzed using Image J. **B**. Western blotting analysis of the HMGA2 protein level in three pancreatic cell lines PANC-1, ASPC-1, and BXPC-3 cells treated with KRAS signaling inhibitor trametinib.

Supplementary Table: Primers for PCR

	Name	Sequence (5'-3')
RT-qPCR	HMGA2 S	GCGCCTCAGAAGAGAGGAC
	HMGA2 AS	GGTCTCTTAGGAGAGGGCTCA
	GPX4 S	GATACGCTGAGTGTGGTTTG
	GPX4 AS	ATCTTCATCCACTTCCACAGC
	GSS S	GACCAGCGTGCCATAGAGAATGA
	GSS AS	CATGTGACCTCTCCAGCAGTAGAC
	ACSL4 S	TCTGCTTCTGCTGCCCAATT
	ACSL4 AS	CGCCTTCTTGCCAGTCTTTT
	SLC7A11 S	GTTGCGTCTCGAGAGGGTCA
	SLC7A11 AS	GTCGAGGTCTCCAGAGAAGAGC
ChIP qPCR	enhancer1 S	CCGTGTTTTCCCCACTTCTG
	enhancer1 AS	TTGCCGGTGTTGTTTTCCTT
	enhancer2 S	CAAACCATCCATGACGCCTC
	enhancer2 AS	ACCTTTTCTGACCCTGCACT
	enhancer3 S	TTTTCTGAGCACATACCGCG
	enhancer3 AS	GTCAGTGACTCCCCATCCTG
	promoter S	AGGAGTTCGAGATCAGCCTG
	promoter AS	CGATTCTCCTGACTCAGCCT

Figure S1.

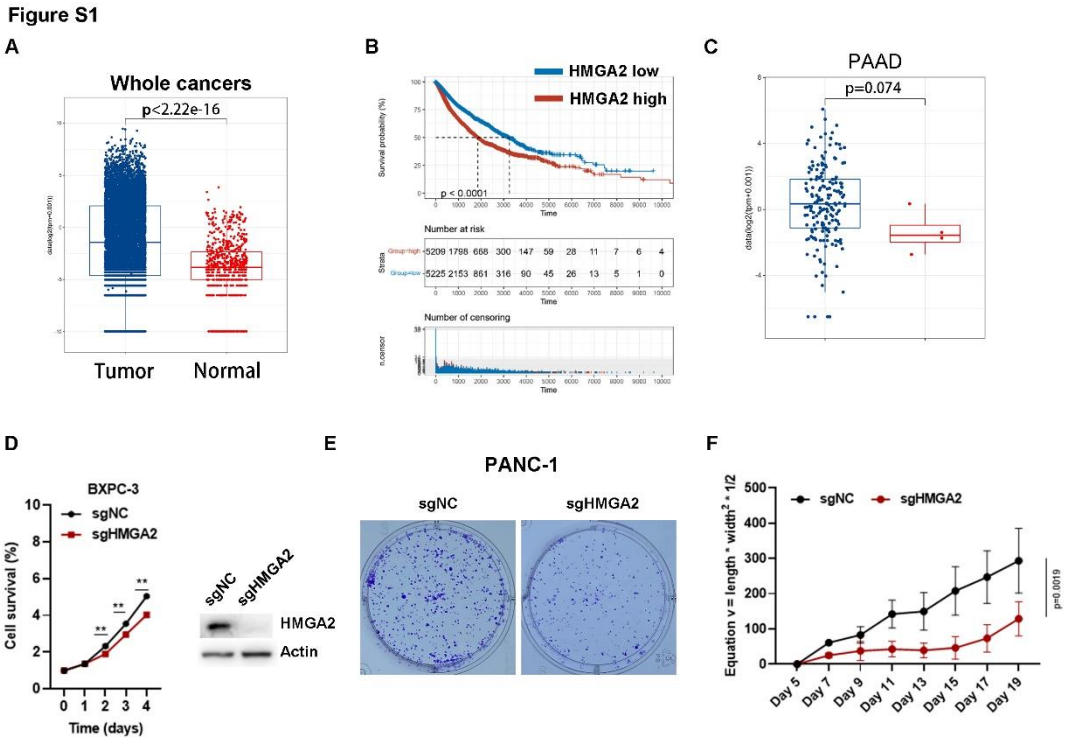
Figure S1
A
Whole cancers
p<2.22e-16
Tumor
Normal
B
HMGA2 low
HMGA2 high
p < 0.0001
Survival probability (%)
Time
Number at risk
Number of censoring
C
PAAD
p=0.074
D
BXPC-3
sgNC
sgHMGA2
Cell survival (%)
Time (days)
HMGA2
Actin
E
PANC-1
sgNC
sgHMGA2
F
sgNC
sgHMGA2
Equation v = length * width² * 1/2
p=0.0019
Day 5
Day 7
Day 9
Day 11
Day 13
Day 15
Day 17
Day 19

Figure S2.

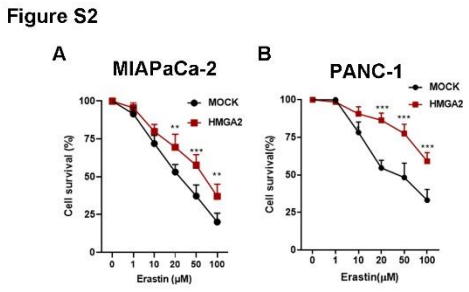
Figure S2
A
MIAPaCa-2
MOCK
HMGA2
Cell survival (%)
100
75
50
25
0
0 1 10 20 50 100
Erastin (μM)
**
***
**
B
PANC-1
MOCK
HMGA2
Cell survival(%)
100
75
50
25
0
0 1 10 20 50 100
Erastin(μM)
***
***
***

Figure S3.


Figure S3
A
B
p−value = 0.033
R = 0.16
log2(GPX4 TPM)
log2(HMGA2 TPM)
UCSC Genome Browser on Human (GRCh38/hg38)

Figure S4.

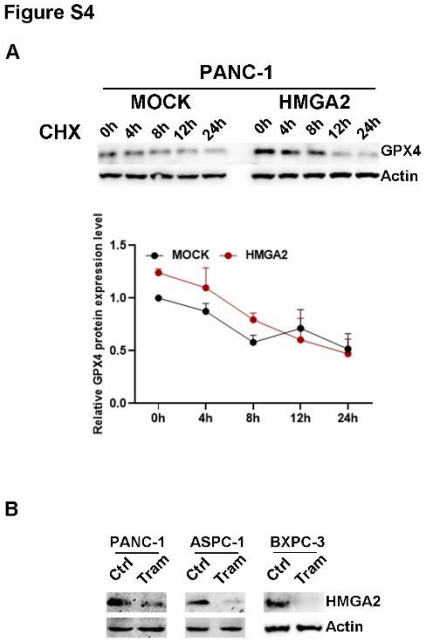
Figure S4
A
PANC-1
MOCK
HMGA2
CHX
0h 4h 8h 12h 24h
0h 4h 8h 12h 24h
GPX4
Actin
Relative GPX4 protein expression level
MOCK
HMGA2
1.5
1.0
0.5
0.0
0h 4h 8h 12h 24h
B
PANC-1
ASPC-1
BXPC-3
Ctrl
Tram
HMGA2
Actin