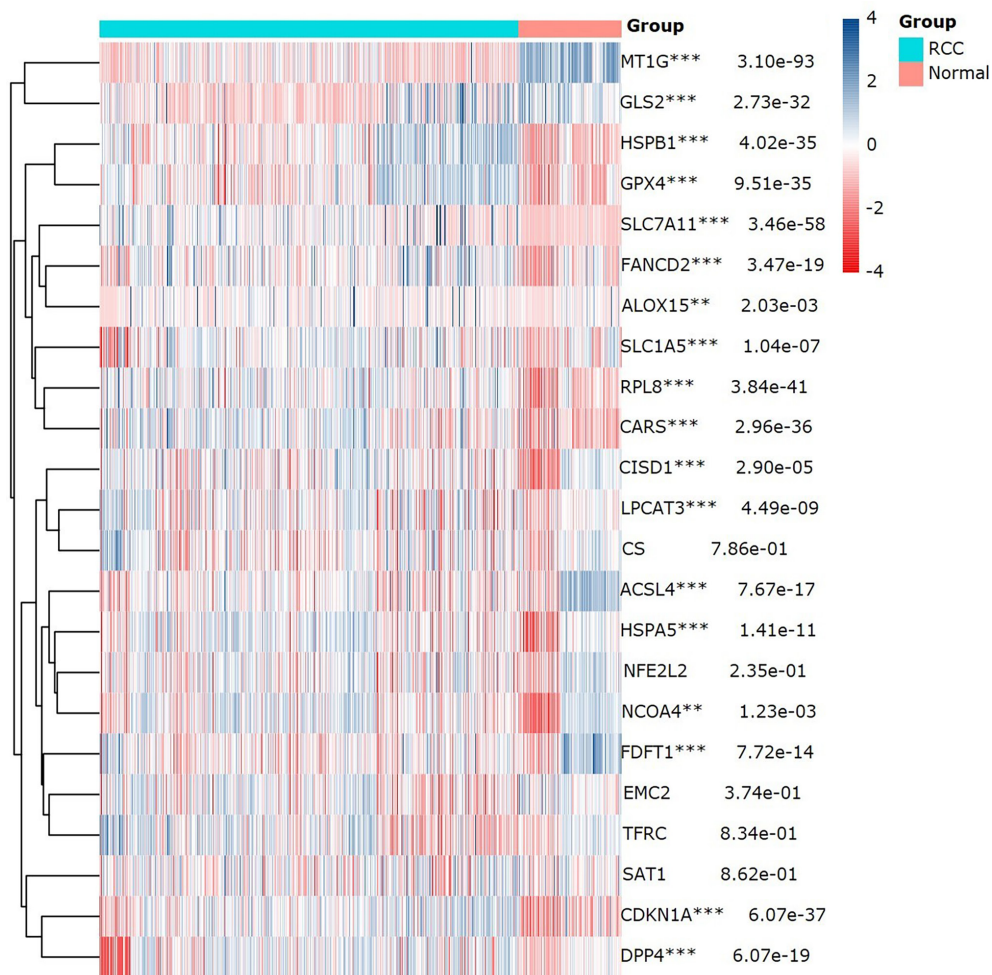
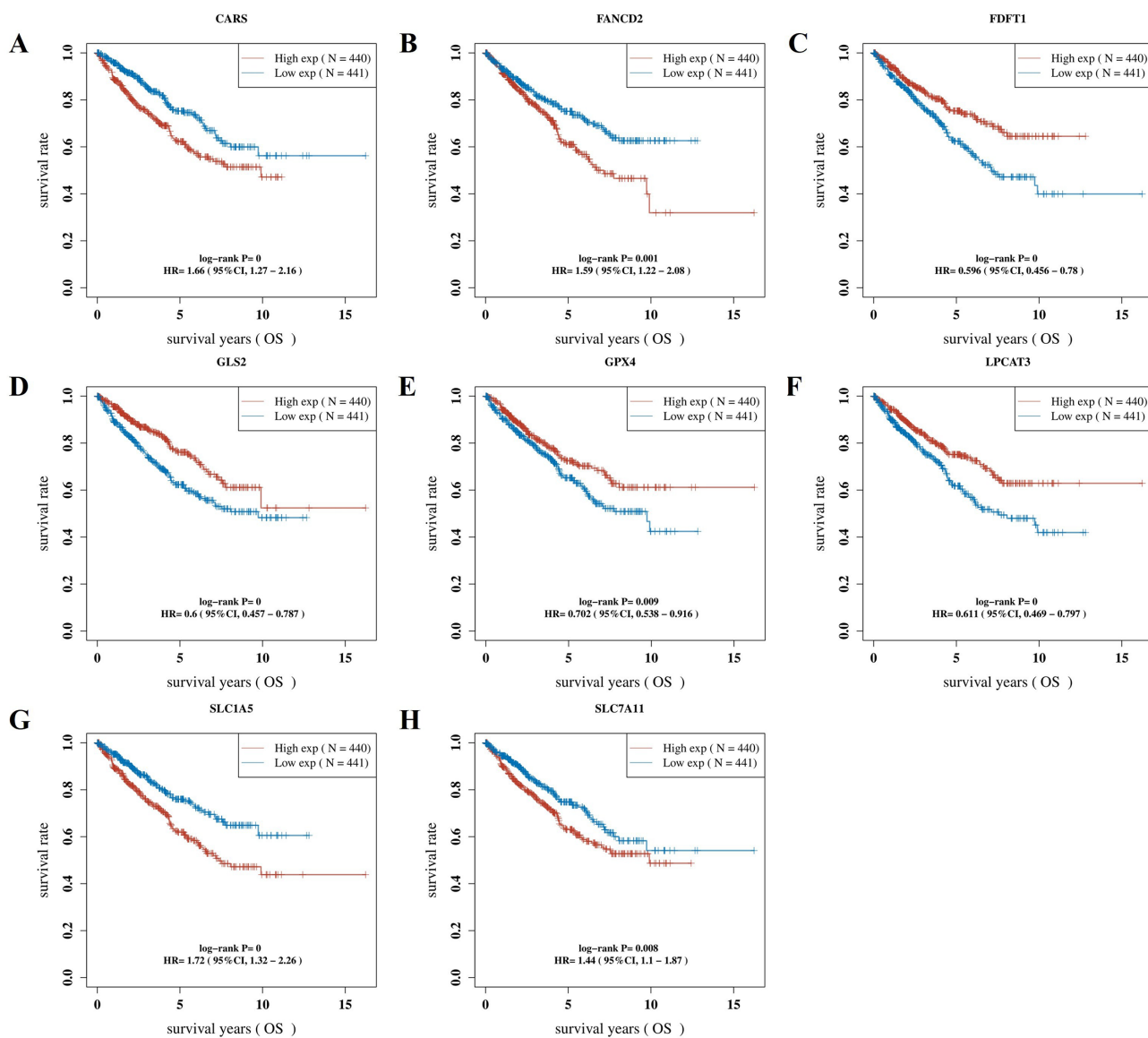


**Figure S1** The enriched KEGG signaling pathways are selected to demonstrate the primary biological actions of major potential mRNA. The abscissa indicates gene ratio and the enriched pathways are presented in the ordinate. GO analysis of potential targets of mRNAs. The BP, CC, and MF of potential targets are clustered based on the ClusterProfiler package in R software (version 4.2.0). (A) Enrichment results of differentially upregulated genes KEGG pathway. (B) Results of GO term enrichment of differentially upregulated genes. (C) Enrichment results of differentially down-regulated genes KEGG pathway. (D) Results of GO term enrichment of differentially down-regulated genes. KEGG, Kyoto Encyclopedia of Genes and Genomes; GO, Gene Ontology; BP, biological process; CC, cellular component; MF, molecular function.



**Figure S2** FRG expression heat map, where different colors represent the expression trend in different samples. The significance of the two groups of samples passed the Wilcoxon test, and the significance of the three groups and above passed the Kruskal-Wallis test. \*\*, P<0.01; \*\*\*, P<0.001. RCC, renal cell carcinoma; FRG, ferroptosis-related gene.



**Figure S3** The prognostic impact of a gene on a given sample, based on the amount of individual gene expression, using the median gene expression as a grouping, the poorer prognosis of high expression means that the gene may promote tumor development, while the opposite is a protective factor. (A) *CARS*. (B) *FANCD2*. (C) *FDFT1*. (D) *GLS2*. (E) *GPX4*. (F) *LPCAT3*. (G) *SLC1A5*. (H) *SLC7A11*. HR, hazard ratio; CI, confidence interval; OS, overall survival.

**Table S1** Clinical information of 883 patients with RCC

Variables	TCGA-RCC (n=883)
Status, n	
Alive	656
Dead	227
Age (years)	
Mean (SD)	60.2 (12.4)
Median [min, max]	60 [17, 90]
Gender, n	
Female	288
Male	595
Race, n	
American Indian	2
Asian	16
Black	120
White	721
pT stage, n	
T1	79
T1a	245
T1b	166
T2	95
T2a	17
T2b	18
T3	13
T3a	169
T3b	59
T3c	3
T4	15
TX	4

**Table S1** (continued)**Table S1** (continued)

Variables	TCGA-RCC (n=883)
pN stage, n	
N0	421
N1	43
N2	5
NX	414
pM stage, n	
M0	695
M1	91
MX	97
pTNM stage, n	
I	464
II	107
III	188
IV	103
Grade, n	
G1	14
G2	227
G3	206
G4	75
GX	5

RCC, renal cell carcinoma; TCGA, The Cancer Genome Atlas; SD, standard deviation; pT, pathological tumor; pN, pathological node; pM, pathological metastasis; pTNM, pathological tumor-node-metastasis.

**Table S2** Twelve of 18 FRGs are significantly associated with prognosis

Genes	P value	HR	Low 95% CI	High 95% CI
<i>LPCAT3</i>	0.000279	0.611296	0.468778	0.797142
<i>HSPA5</i>	0.282848	1.154061	0.888506	1.498984
<i>CARS</i>	0.000216	1.654772	1.267175	2.160926
<i>CDKN1A</i>	0.000228	0.599453	0.456624	0.78696
<i>ACSL4</i>	0.503597	1.093133	0.842066	1.419058
<i>GLS2</i>	0.000229	0.599534	0.456683	0.787069
<i>ALOX15</i>	0.069483	1.274838	0.98083	1.656976
<i>RPL8</i>	0.056248	1.29031	0.993234	1.676241
<i>FANCD2</i>	0.000565	1.593932	1.222838	2.077642
<i>GPX4</i>	0.009255	0.702277	0.538162	0.91644
<i>FDFT1</i>	0.000163	0.59631	0.455797	0.78014
<i>MT1G</i>	8.83E-06	1.840019	1.406128	2.407795
<i>NCOA4</i>	0.015428	0.721661	0.554244	0.93965
<i>SLC7A11</i>	0.007644	1.436118	1.100752	1.87366
<i>HSPB1</i>	0.134944	0.818282	0.629085	1.06438
<i>CISD1</i>	0.356558	0.884367	0.68105	1.148382
<i>SLC1A5</i>	7.42E-05	1.723584	1.316703	2.256198
<i>DPP4</i>	9.82E-06	0.539542	0.410416	0.709294

FRG, ferroptosis-related gene; HR, hazard ratio; CI, confidence interval.

**Table S3** Clinical features of RCC patients in the training set and testing set

Features	Total	Test	Train	P value
Age, n (%)				0.0497
≤65 years	576 (65.53)	302 (68.79)	274 (62.27)	
>65 years	303 (34.47)	137 (31.21)	166 (37.73)	
Gender, n (%)				0.7916
Female	287 (32.65)	141 (32.12)	146 (33.18)	
Male	592 (67.35)	298 (67.88)	294 (66.82)	
Grade, n (%)				0.481
G1	14 (1.59)	8 (1.82)	6 (1.36)	
G2	227 (25.82)	114 (25.97)	113 (25.68)	
G3	206 (23.44)	118 (26.88)	88 (20.00)	
G4	75 (8.53)	38 (8.66)	37 (8.41)	
Unknown	357 (40.61)	161 (36.67)	196 (44.55)	
Stage, n (%)				0.5242
Stage I	455 (51.76)	218 (49.66)	237 (53.86)	
Stage II	102 (11.60)	54 (12.30)	48 (10.91)	
Stage III	187 (21.27)	99 (22.55)	88 (20.00)	
Stage IV	103 (11.72)	55 (12.53)	48 (10.91)	
Unknown	32 (3.64)	13 (2.96)	19 (4.32)	
T, n (%)				0.3715
T1	482 (54.84)	230 (52.39)	252 (57.27)	
T2	125 (14.22)	67 (15.26)	58 (13.18)	
T3	255 (29.01)	135 (30.75)	120 (27.27)	
T4	15 (1.71)	6 (1.37)	9 (2.05)	
Unknown	2 (0.23)	1 (0.23)	1 (0.23)	
M, n (%)				0.5955
M0	547 (62.23)	281 (64.01)	266 (60.45)	
M1	89 (10.13)	49 (11.16)	40 (9.09)	
Unknown	243 (27.65)	109 (24.83)	134 (30.45)	
N, n (%)				0.419
N0	326 (37.09)	163 (37.13)	163 (37.05)	
N1	43 (4.89)	25 (5.69)	18 (4.09)	
N2	6 (0.68)	2 (0.46)	4 (0.91)	
Unknown	504 (57.34)	249 (56.72)	255 (57.95)	

RCC, renal cell carcinoma; T, tumor; N, node; M, metastasis.

**Table S4** List of drug sensitivities for high- and low-risk groups

Groups	List of drug sensitivities
High-risk	A-443654, AS605240, AZ628, BMS-754807, Bortezomib, CP466722, CP724714, Crizotinib, Doxorubicin, Erlotinib, Etoposide, FH535, GSK429286A, GW-2580, JNK-9L, JQ12, JW-7-24-1, KIN001-135, LAQ824, Lisitinib, MS-275, NG-25, NSC-207895, OSU-03012, Phenformin, Pyrimethamine, Salubrinal, Sorafenib, TAK-715, TL-1-85, TL-2-105, Tubastatin A, Vinorelbine, WZ3105, YM155
Low-risk	A-770041, LY317615, AKT inhibitor VIII, Midostaurin, AP-24534, NPK76-II-72-1, AS601245, NSC-87877, AT-7519, Obatoclox Mesylate, AUY922, PAC-1, BAY 61-3606, Paclitaxel, Bexarotene, Parthenolide, BI-2536, Pazopanib, Bleomycin, PF-562271, BMS345541, QL-XII-47, BMS-509744, QS11, Bryostatin 1, Rapamycin, BX-912, Roscovitine, CAL-101, Ruxolitinib, CGP-082996, Shikonin, CMK, STF-62247, Cyclopamine, S-Trityl-L-cysteine, Dasatinib, Sunitinib, DMOG, TAE684, Epothilone B, TGX221, FMK, Thapsigargin, FR-180204, Tipifarnib, Gemcitabine, VX-11e, Genentech Cpd 10, WH-4-023, GSK-650394, WZ-1-84, GSK1070916, XL-184, HG-6-64-1, XMD8-85, Imatinib, XMD14-99, IPA-3, Z-LLNle-CHO, Ispinesib Mesylate, ZSTK474, JW-7-52-1, Lapatinib, KIN001-102, LFM-A13