

## Supplementary

**Table S1** Basic information of datasets included in this study downloaded from GEO database

GEO series	GEO platform	Sample type	Total samples	Region	Publication
GSE10927	GPL570	10 normal + 22 adenomas + 33 ACC	65	USA	2009
GSE19750	GPL570	4 normal + 44 ACC	48	USA	2013
GSE76019	GPL13158	34 ACC	34	USA	2016
GSE76021	GPL96	29 ACC	29	USA	2016

GEO, Gene Expression Omnibus; ACC, adrenocortical carcinoma.

**Table S2** The list of ferroptosis regulators involved in this study

Symbol	Type	Confidence
ACSL3	Suppressor	Validated
AIFM2	Suppressor	Validated
AKR1C1	Suppressor	Validated
AKR1C2	Suppressor	Validated
AKR1C3	Suppressor	Validated
ARNTL	Suppressor	Validated
ATF4	Suppressor	Validated
BRD4	Suppressor	Validated
CA9	Suppressor	Validated
CAV1	Suppressor	Validated
CBS	Suppressor	Validated
CD44	Suppressor	Validated
CDKN1A	Suppressor	Validated
CHMP5	Suppressor	Validated
CHMP6	Suppressor	Validated
CISD1	Suppressor	Validated
CISD2	Suppressor	Validated
FADS2	Suppressor	Validated
FH	Suppressor	Validated
GCH1	Suppressor	Validated
GPX4	Suppressor	Validated
HELLS	Suppressor	Validated
HIF1A	Suppressor	Validated
HSF1	Suppressor	Validated
HSPA5	Suppressor	Validated
HSPB1	Suppressor	Validated
ISCU	Suppressor	Validated
LAMP2	Suppressor	Validated
MT1G	Suppressor	Validated
MUC1	Suppressor	Validated
NF2	Suppressor	Validated
NFE2L2	Suppressor	Validated
NFS1	Suppressor	Validated
NQO1	Suppressor	Validated
OTUB1	Suppressor	Validated
PML	Suppressor	Validated
PRDX6	Suppressor	Validated
PROM2	Suppressor	Validated
RB1	Suppressor	Validated
SCD	Suppressor	Validated
SESN2	Suppressor	Validated
SLC40A1	Suppressor	Validated
SLC7A11	Suppressor	Validated
SQSTM1	Suppressor	Validated
SRC	Suppressor	Validated
STAT3	Suppressor	Validated
TMBIM4	Suppressor	Validated
TP63	Suppressor	Validated
ZFP36	Suppressor	Validated
CHAC1	Marker	Validated
FTH1	Marker	Validated
PTGS2	Marker	Validated
ABCC1	Driver	Validated
ACSF2	Driver	Validated
ACSL4	Driver	Validated
ACVR1B	Driver	Validated

**Table S2** (continued)**Table S2** (continued)

Symbol	Type	Confidence
ALOX12	Driver	Validated
ALOX12B	Driver	Validated
ALOX15	Driver	Validated
ALOX15B	Driver	Validated
ALOX5	Driver	Validated
ALOXE3	Driver	Validated
ANO6	Driver	Validated
ATF3	Driver	Validated
ATG5	Driver	Validated
ATG7	Driver	Validated
ATM	Driver	Validated
ATP5G3	Driver	Validated
BAP1	Driver	Validated
BECN1	Driver	Validated
CARS	Driver	Validated
CDKN2A	Driver	Validated
CDO1	Driver	Validated
CS	Driver	Validated
DPP4	Driver	Validated
EGFR	Driver	Validated
EGLN2	Driver	Validated
ELAVL1	Driver	Validated
EMC2	Driver	Validated
G6PD	Driver	Validated
GOT1	Driver	Validated
HMGB1	Driver	Validated
HMOX1	Driver	Validated
IDH1	Driver	Validated
IFNG	Driver	Validated
IREB2	Driver	Validated
KEAP1	Driver	Validated
LONP1	Driver	Validated
MAPK1	Driver	Validated
MAPK3	Driver	Validated
MIOX	Driver	Validated
MTDH	Driver	Validated
MYB	Driver	Validated
NCOA4	Driver	Validated
NOX4	Driver	Validated
PANX1	Driver	Validated
PEBP1	Driver	Validated
PGD	Driver	Validated
PHKG2	Driver	Validated
PRKAA1	Driver	Validated
PRKAA2	Driver	Validated
RPL8	Driver	Validated
SAT1	Driver	Validated
SLC1A5	Driver	Validated
SOCS1	Driver	Validated
TAZ	Driver	Validated
TF	Driver	Validated
TGFBR1	Driver	Validated
TNFAIP3	Driver	Validated
TP53	Driver	Validated
VDAC2	Driver	Validated
YY1AP1	Driver	Validated
ZEB1	Driver	Validated

**Table S3** Details for primary antibodies

Antibodies	IHC	Sources	Number
HELLS	1:100	ZenBio	823182
KI-67	1:300	HuaBio	HA721115
PCNA	1:300	Proteintech	10205-2-AP
CD20	1:50	ABCAM	ab7817
CD3	1:200	Novus	NB600-144
PD1	1:50	CST	D4W2J
PDL1	1:50	CST	E1L3N

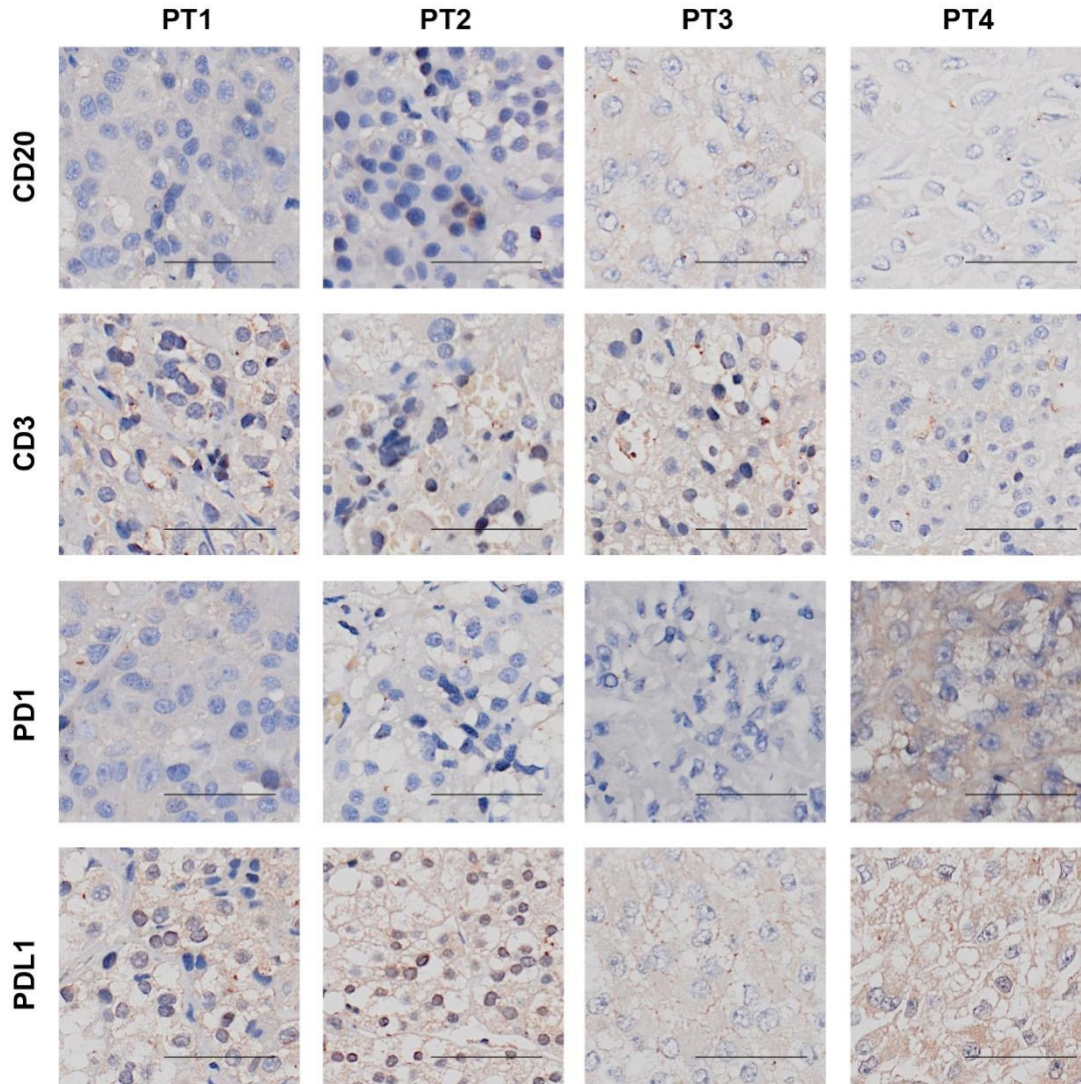
IHC, immunohistochemistry.

**Table S4** The survival analysis results of ferroptosis regulators with a P value <0.05

Gene	P value	HR	Lower	Upper
<i>ACSF2</i>	5.80E-07	0.162716309	0.071881951	0.3683344
<i>ISCU</i>	7.96E-07	0.114549113	0.053900915	0.2434374
<i>ACSL4</i>	4.58E-06	0.127218389	0.060240395	0.2686655
<i>SQSTM1</i>	3.13E-05	0.208431118	0.09549895	0.4549111
<i>TNFAIP3</i>	5.33E-05	5.107481846	2.410213082	10.823263
<i>MUC1</i>	6.42E-05	4.790714412	2.237821083	10.255934
<i>SLC7A11</i>	7.35E-05	4.482108963	2.069923934	9.7053329
<i>ATF4</i>	8.06E-05	4.258459342	1.938757921	9.3536567
<i>TGFBR1</i>	9.39E-05	4.300364879	1.99469711	9.271151
<i>MAPK3</i>	0.000294408	0.178130297	0.084885964	0.3738003
<i>CDKN2A</i>	0.000605543	3.593101595	1.668418252	7.7380951
<i>ATG7</i>	0.000943357	0.299875114	0.137976497	0.651742
<i>ATG5</i>	0.002130802	0.32553831	0.148495315	0.7136602
<i>HELLS</i>	1.27E-07	9.528565328	4.453090506	20.388887
<i>SLC40A1</i>	3.47E-05	0.219676098	0.099088078	0.4870171
<i>PRKAA2</i>	3.64E-05	0.221978799	0.100278038	0.4913797
<i>YY1AP1</i>	8.42E-05	5.472668689	2.601722311	11.511645
<i>PGD</i>	0.003117289	3.554067891	1.694192104	7.4557062
<i>IDH1</i>	0.003212508	3.550319346	1.692394716	7.4478887
<i>GPX4</i>	0.003539546	0.346902864	0.159488191	0.7545486
<i>HSPB1</i>	0.004158044	0.333322507	0.157094565	0.7072421
<i>RPL8</i>	0.004294331	2.907372505	1.3567113	6.2303711
<i>TMBIM4</i>	0.004726163	0.337492522	0.159187	0.7155182
<i>EMC2</i>	0.004755133	0.327387791	0.155497506	0.6892893
<i>NQO1</i>	0.006536479	3.033700351	1.446251161	6.363582
<i>ATF3</i>	0.007852464	2.668108774	1.237125495	5.7543107
<i>SAT1</i>	0.008191952	0.369425764	0.173414312	0.7869904
<i>MYB</i>	0.011528218	2.522672708	1.157836273	5.4963536
<i>PRKAA1</i>	0.013994666	0.400065878	0.186666265	0.8574271
<i>STAT3</i>	0.015042552	0.40830755	0.188052797	0.8865332
<i>ALOX5</i>	0.016051787	0.382320103	0.182230473	0.8021088
<i>HMGB1</i>	0.017648921	2.57144706	1.225805917	5.3942797
<i>LAMP2</i>	0.022904708	0.427404563	0.200527567	0.9109703
<i>AIFM2</i>	0.023570552	2.71169675	1.281886268	5.7363118
<i>VDAC2</i>	0.023612529	2.310018175	1.070701755	4.9838192
<i>SRC</i>	0.026417962	0.375783231	0.177448618	0.7957968
<i>CDKN1A</i>	0.026615837	0.435176859	0.204452685	0.9262725
<i>CISD2</i>	0.027261334	0.449385017	0.205774301	0.9814
<i>MT1G</i>	0.027973091	2.51005236	1.193106964	5.2806354
<i>TP63</i>	0.0285229	0.449688662	0.209222368	0.9665309
<i>ANO6</i>	0.029236323	0.445355238	0.207012276	0.9581137
<i>AKR1C1</i>	0.029657923	0.400429783	0.190304421	0.8425659
<i>AKR1C3</i>	0.033366389	0.454260381	0.211552174	0.9754213
<i>ACVR1B</i>	0.03490801	0.45995686	0.211211358	1.0016522
<i>NF2</i>	0.035624471	2.280918115	1.086788481	4.7871205
<i>HSPA5</i>	0.037083434	2.316052271	1.103543573	4.8607941
<i>PML</i>	0.043200141	0.474127605	0.218488566	1.028873
<i>MAPK1</i>	0.043551322	2.258325176	1.075590028	4.7416139
<i>CHMP6</i>	0.046734369	0.480979466	0.222002591	1.0420655
<i>ARNTL</i>	0.048807774	2.127162622	1.011473473	4.4734943

**Table S5** Multivariate Cox regression analysis

Id	Coef	Exp(coef)	Se(coef)	Z	Pr(> Z )
ATF4	0.68225752	1.978338834	0.287481006	2.3732264	0.01763345
HELLS	1.60576828	4.981685464	0.275238128	5.8341055	5.41E-09
MT1G	0.186927886	1.205540346	0.093334841	2.0027664	0.045202366



**Figure S1** Representative immunohistochemistry images of CD3, CD20, PD1, and PDL1 staining in adrenocortical carcinoma tissues. The scale bar denotes 50  $\mu$ m.