Supplementary Table 1 List of 259 ferroptosis-related genes

Symbol	Name
RPL8	Ribosomal protein L8
IREB2	Iron response element binding protein 2
ATP5MC3	ATP synthase membrane subunit c locus 3
CS	Citrate synthase
EMC2	ER membrane protein complex subunit 2
ACSF2	Acyl-CoA synthetase family member 2
NOX1	Nicotinamide adenine dinucleotide phosphate (NADPH) oxidase (NOX) 1
CYBB	Cytochrome b-245 beta chain
NOX3	Nicotinamide adenine dinucleotide phosphate (NADPH) oxidase (NOX) 3
NOX4	Nicotinamide adenine dinucleotide phosphate (NADPH) oxidase (NOX) 4
NOX5	Nicotinamide adenine dinucleotide phosphate (NADPH) oxidase (NOX) 5
DUOX1	Dual oxidase 1
DUOX2	Dual oxidase 2
G6PD	Glucose-6-phosphate dehydrogenase
PGD	Phosphoglycerate dehydrogenase
VDAC2	Valtage-dependent anion channels 2
PIK3CA	Phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha
FLT3	Fms related tyrosine kinase 3
SCP2	Sterol carrier protein 2
TP53	Tumor protein p53
ACSL4	Acyl-CoA synthetase long chain family member 4
LPCAT3	Lysophosphatidylcholine acyltransferase 3

NRAS	NRAS proto-oncogene, GTPase
KRAS	KRAS proto-oncogene, GTPase
HRAS	HRas proto-oncogene, GTPase
TF	Transferrin
TFRC	Transferrin receptor
TFR2	Transferrin receptor 2
SLC38A1	Solute carrier family 38 member 1
SLC1A5	Solute carrier family 1 member 5
GLS2	Glutaminase 2
GOT1	Glutamic-oxaloacetic transaminase 1
CARS1	Cysteinyl-tRNA synthetase 1
ALOX5	Arachidonate 5-lipoxygenase
KEAP1	Kelch like ECH associated protein 1
HMOX1	Heme oxygenase 1
ATG5	Autophagy related 5
ATG7	Autophagy related 7
NCOA4	Nuclear receptor coactivator 4
ALOX12	Arachidonate 12-lipoxygenase, 12S type
ALOX12B	Arachidonate 12-lipoxygenase, 12R type
ALOX15	Arachidonate 15-lipoxygenase
ALOX15B	Arachidonate 15-lipoxygenase type B
ALOXE3	Arachidonate lipoxygenase 3
PHKG2	Phosphorylase kinase catalytic subunit gamma 2
ACO1	Aconitase 1
G6PDX	_NA_
ULK1	Unc-51 like autophagy activating kinase 1
ATG3	Autophagy related 3
ATG4D	Autophagy related 4D cysteine peptidase
BECN1	Beclin 1

MAP1LC3A	Microtubule associated protein 1 light chain 3 alpha
GABARAPL2	GABA type A receptor associated protein like 2
GABARAPL1	GABA type A receptor associated protein like 1
ATG16L1	Autophagy related 16 like 1
WIPI1	WD repeat domain, phosphoinositide interacting 1
WIPI2	WD repeat domain, phosphoinositide interacting 2
SNX4	Sorting nexin 4
ATG13	Autophagy related 13
ULK2	Unc-51 like autophagy activating kinase 2
SAT1	Spermidine/spermine N1-acetyltransferase 1
EGFR	Epidermal growth factor receptor
MAPK3	Mitogen-activated protein kinase 3
MAPK1	Mitogen-activated protein kinase 1
BID	BH3 interacting domain death agonist
ZEB1	Zinc finger E-box binding homeobox 1
DPP4	Dipeptidyl peptidase 4
CDKN2A	Cyclin dependent kinase inhibitor 2A
PEBP1	Phosphatidylethanolamine binding protein 1
SOCS1	Suppressor of cytokine signaling 1
CDO1	Cysteine dioxygenase type 1
MYB	MYB proto-oncogene, transcription factor
MAPK8	Mitogen-activated protein kinase 8
MAPK9	Mitogen-activated protein kinase 9
CHAC1	ChaC glutathione specific gamma-glutamylcyclotransferase 1
MAPK14	Mitogen-activated protein kinase 14
LINC00472	Long intergenic non-protein coding RNA 472
PRKAA2	Protein kinase AMP-activated catalytic subunit alpha 2
PRKAA1	Protein kinase AMP-activated catalytic subunit alpha 1
ELAVL1	ELAV like RNA binding protein 1

BAP1	BRCA1 associated protein 1
ABCC1	ATP binding cassette subfamily C member 1
MIR6852	microRNA 6852
ACVR1B	Activin A receptor type 1B
TGFBR1	Transforming growth factor beta receptor 1
EPAS1	Endothelial PAS domain protein 1
HILPDA	Hypoxia inducible lipid droplet associated
HIF1A	Hypoxia inducible factor 1 subunit alpha
IFNG	Interferon gamma
ANO6	Anoctamin 6
LPIN1	Lipin 1
HMGB1	High mobility group box 1
TNFAIP3	TNF alpha induced protein 3
TLR4	Toll like receptor 4
ATF3	Activating transcription factor 3
ATM	ATM serine/threonine kinase
YY1AP1	YY1 associated protein 1
EGLN2	Egl-9 family hypoxia inducible factor 2
MIOX	Myo-inositol oxygenase
TAZ	Tafazzin
MTDH	Metadherin
IDH1	Isocitrate dehydrogenase (NADP(+)) 1
SIRT1	Sirtuin 1
FBXW7	F-box and WD repeat domain containing 7
PANX1	Pannexin 1
DNAJB6	DnaJ heat shock protein family (Hsp40) member B6
BACH1	BTB domain and CNC homolog 1
LONP1	Lon peptidase 1, mitochondrial
SLC7A11	Solute carrier family 7 member 11

GPX4	Glutathione peroxidase 4
AKR1C1	Aldo-keto reductase family 1 member C1
AKR1C2	Aldo-keto reductase family 1 member C2
AKR1C3	Aldo-keto reductase family 1 member C3
RB1	RB transcriptional corepressor 1
HSPB1	Heat shock protein family B (small) member 1
HSF1	Heat shock transcription factor 1
GCLC	Glutamate-cysteine ligase catalytic subunit
NFE2L2	Nuclear factor, erythroid 2 like 2
SQSTM1	Sequestosome 1
NQO1	NAD(P)H quinone dehydrogenase 1
FTH1	Ferritin heavy chain 1
MUC1	Mucin 1, cell surface associated
SLC3A2	Solute carrier family 3 member 2
MT1G	Metallothionein 1G
SLC40A1	Solute carrier family 40 member 1
CISD1	CDGSH iron sulfur domain 1
FANCD2	FA complementation group D2
FTMT	Ferritin mitochondrial
HSPA5	Heat shock protein family A (Hsp70) member 5
ATF4	Activating transcription factor 4
HELLS	Helicase, lymphoid specific
SCD	Stearoyl-CoA desaturase
FADS2	Fatty acid desaturase 2
SRC	SRC proto-oncogene, non-receptor tyrosine kinase
STAT3	Signal transducer and activator of transcription 3
PML	Promyelocytic leukemia
MTOR	Mechanistic target of rapamycin kinase
NFS1	NFS1 cysteine desulfurase

TP63	Tumor protein p63
CDKN1A	Cyclin dependent kinase inhibitor 1A
MIR137	microRNA 137
ENPP2	Ectonucleotide pyrophosphatase/phosphodiesterase 2
FH	Fumarate hydratase
CISD2	CDGSH iron sulfur domain 2
MIR9-1	microRNA 9-1
MIR9-2	microRNA 9-2
MIR9-3	microRNA 9-3
CBS	Cystathionine beta-synthase
ISCU	Iron-sulfur cluster assembly enzyme
ACSL3	Acyl-CoA synthetase long chain family member 3
OTUB1	OTU deubiquitinase, ubiquitin aldehyde binding 1
CD44	CD44 molecule (Indian blood group)
LINC00336	Long intergenic non-protein coding RNA 336
BRD4	Bromodomain containing 4
PRDX6	Peroxiredoxin 6
MIR17	microRNA 17
SESN2	Sestrin 2
NF2	Neurofibromin 2
ARNTL	Aryl hydrocarbon receptor nuclear translocator like
JUN	Jun proto-oncogene, AP-1 transcription factor subunit
CA9	Carbonic anhydrase 9
TMBIM4	Transmembrane BAX inhibitor motif containing 4
PLIN2	Perilipin 2
MIR212	microRNA 212
Fer1HCH	Ferritin 1 Heavy Chain Homolog
AIFM2	Apoptosis inducing factor mitochondria associated 2
LAMP2	Lysosomal associated membrane protein 2

ZFP36	ZFP36 ring finger protein
PROM2	Prominin 2
CHMP5	Charged multivesicular body protein 5
CHMP6	Charged multivesicular body protein 6
CAV1	Caveolin 1
GCH1	GTP cyclohydrolase 1
PTGS2	Prostaglandin-endoperoxide synthase 2
DUSP1	Dual specificity phosphatase 1
NOS2	Nitric oxide synthase 2
NCF2	Neutrophil cytosolic factor 2
MT3	Metallothionein 3
UBC	Ubiquitin C
ALB	Albumin
TXNRD1	Thioredoxin reductase 1
SRXN1	Sulfiredoxin 1
GPX2	Glutathione peroxidase 2
BNIP3	BCL2 interacting protein 3
OXSR1	Oxidative stress responsive kinase 1
SELENOS	Selenoprotein S
ANGPTL7	Angiopoietin like 7
DDIT4	DNA damage inducible transcript 4
LOC284561	_NA_
ASNS	Asparagine synthetase (glutamine-hydrolyzing)
TSC22D3	TSC22 domain family member 3
DDIT3	DNA damage inducible transcript 3
JDP2	Jun dimerization protein 2
SLC1A4	Solute carrier family 1 member 4
PCK2	Phosphoenolpyruvate carboxykinase 2, mitochondrial
TXNIP	Thioredoxin interacting protein

VLDLR	Very low density lipoprotein receptor
GPT2	Glutamic--pyruvic transaminase 2
PSAT1	Phosphoserine aminotransferase 1
LURAP1L	Leucine rich adaptor protein 1 like
SLC7A5	Solute carrier family 7 member 5
HERPUD1	Homocysteine inducible ER protein with ubiquitin like domain 1
XBP1	X-box binding protein 1
ZNF419	Zinc finger protein 419
KLHL24	Kelch like family member 24
TRIB3	Tribbles pseudokinase 3
ZFP69B	ZFP69 zinc finger protein B
ATP6V1G2	ATPase H+ transporting V1 subunit G2
VEGFA	Vascular endothelial growth factor A
GDF15	Growth differentiation factor 15
TUBE1	Tubulin epsilon 1
ARRDC3	Arrestin domain containing 3
CEBPG	CCAAT enhancer binding protein gamma
SNORA16A	Small nucleolar RNA, H/ACA box 16A
RGS4	Regulator of G protein signaling 4
BLOC1S5-TXND C5	BLOC1S5-TXNDC5 readthrough (NMD candidate)
LOC390705	_NA_
EIF2S1	Eukaryotic translation initiation factor 2 subunit 1
KIM-1	Kidney injury molecule-1
IL6	Interleukin 6
CXCL2	C-X-C motif chemokine ligand 2
RELA	RELA proto-oncogene, NF-kB subunit
HSD17B11	Hydroxysteroid 17-beta dehydrogenase 11

AGPAT3	1-acylglycerol-3-phosphate O-acyltransferase 3
SETD1B	SET domain containing 1B, histone lysine methyltransferase
FTL	Ferritin light chain
MAFG	MAF bZIP transcription factor G
IL33	Interleukin 33
HAMP	Hepcidin antimicrobial peptide
STEAP3	STEAP3 metalloreductase
DRD5	Dopamine receptor D5
DRD4	Dopamine receptor D4
MAP3K5	Mitogen-activated protein kinase kinase kinase 5
SLC2A1	Solute carrier family 2 member 1
SLC2A3	Solute carrier family 2 member 3
SLC2A6	Solute carrier family 2 member 6
SLC2A8	Solute carrier family 2 member 8
SLC2A12	Solute carrier family 2 member 12
GLUT13	_NA_
SLC2A14	Solute carrier family 2 member 14
EIF2AK4	Eukaryotic translation initiation factor 2 alpha kinase 4
TFAP2C	Transcription factor AP-2 gamma
SP1	Sp1 transcription factor
HBA1	Hemoglobin subunit alpha 1
NNMT	Nicotinamide N-methyltransferase
PLIN4	Perilipin 4
HIC1	HIC ZBTB transcriptional repressor 1
STMN1	Stathmin 1
RRM2	Ribonucleotide reductase regulatory subunit M2
CAPG	Capping actin protein, gelsolin like
HNF4A	Hepatocyte nuclear factor 4 alpha
NGB	Neuroglobin

	Tyrosine 3-monooxygenase/tryptophan 5-monooxygenase
YWHAE	activation protein epsilon
GABPB1	GA binding protein transcription factor subunit beta 1
AURKA	Aurora kinase A
MIR4715	microRNA 4715
RIPK1	Receptor interacting serine/threonine kinase 1
PRDX1	Peroxiredoxin 1
MIR30B	microRNA 30b

Supplementary Table 2 Clinical characteristics of samples from TCGA and METABRIC cohorts

	Training set	Validation set
	TCGA	Metabric
	N=168	N=126
Age(%)		
≤60	82(0.49)	76(0.62)
>60	86(0.51)	50(0.38)
T(%)		
T1	33(0.20)	-
T2	108(0.64)	-
T3	18(0.11)	-
T4	9(0.05)	-
N(%)		
N0	66(0.49)	-
N1	66(0.39)	-
N2	23(0.14)	-
N3	13(0.08)	-
M(%)		
M0	164(0.98)	-
M1	4(0.02)	-
Stage(%)		
Ⅰ	18(0.11)	26(0.27)
Ⅱ	99(0.59)	74(0.56)
Ⅲ	47(0.28)	25(0.16)
Ⅳ	4(0.02)	1(0.01)
OS(%)		
0	144(0.85)	29(0.37)
1	25(0.15)	97(0.63)

Radio therapy(%)		
Yes	8(0.05)	90(0.70)
No	13(0.08)	36(0.30)
Unknown	147(0.87)	0
OS.year[Median]	2.48	4.66

Supplementary Table 3 Marker genes of distinct cell types for manually annotated in single cell datasets

cell_type	cell_marker
epithelial cell	"*VWF*" "*CLDN5*"
endothelial cells	"*EPCAM*"
perithelial cell	"*MCAM*" "*RGS5*"
myeloid cells	"*CD68*"
T cells	"*CD3D*" "*CD3E*" "*CD3G*"
B cells	"*CD79A*" "*CD19*"
mastocyte	"*MS4A2*"
NK cells	"*NKG7*"
fibroblast	"*COL1A1*" "*PDGFRA*" "*PDPN*"

Supplementary Table 4 **The final manually annotated outcomes of different cell clusters**

cluster	cell_type

0	Epithelial
1	Epithelial
2	Stromal
3	Epithelial
4	Epithelial
5	Immune
6	Stromal
7	Immune
8	Stromal
9	Immune
10	Stromal
11	Stromal
12	Epithelial
13	Stromal
14	Stromal
15	Epithelial
16	Immune
17	Stromal
18	Stromal
19	Stromal
20	Epithelial
21	Epithelial
22	Stromal
23	Epithelial
24	Stromal
25	Stromal
26	Epithelial
27	Stromal
28	Immune

29	Immune
30	Epithelial
31	Stromal
32	Epithelial
33	Immune
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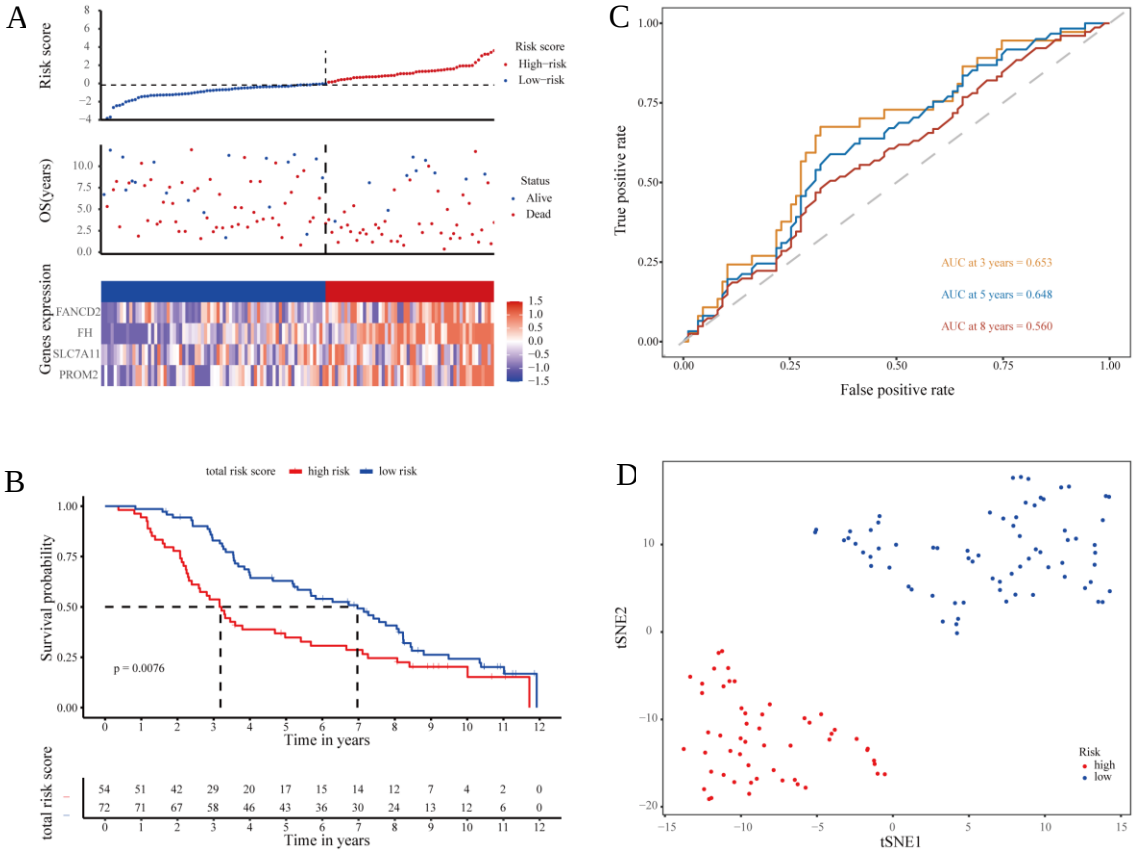
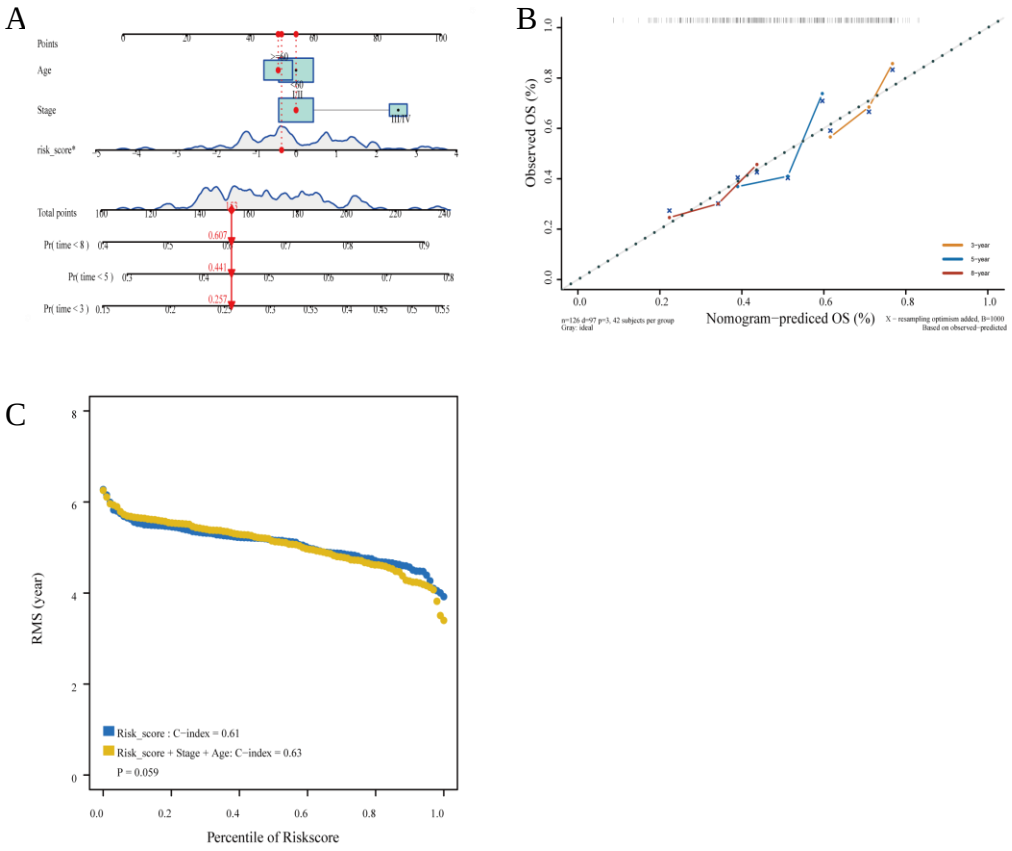
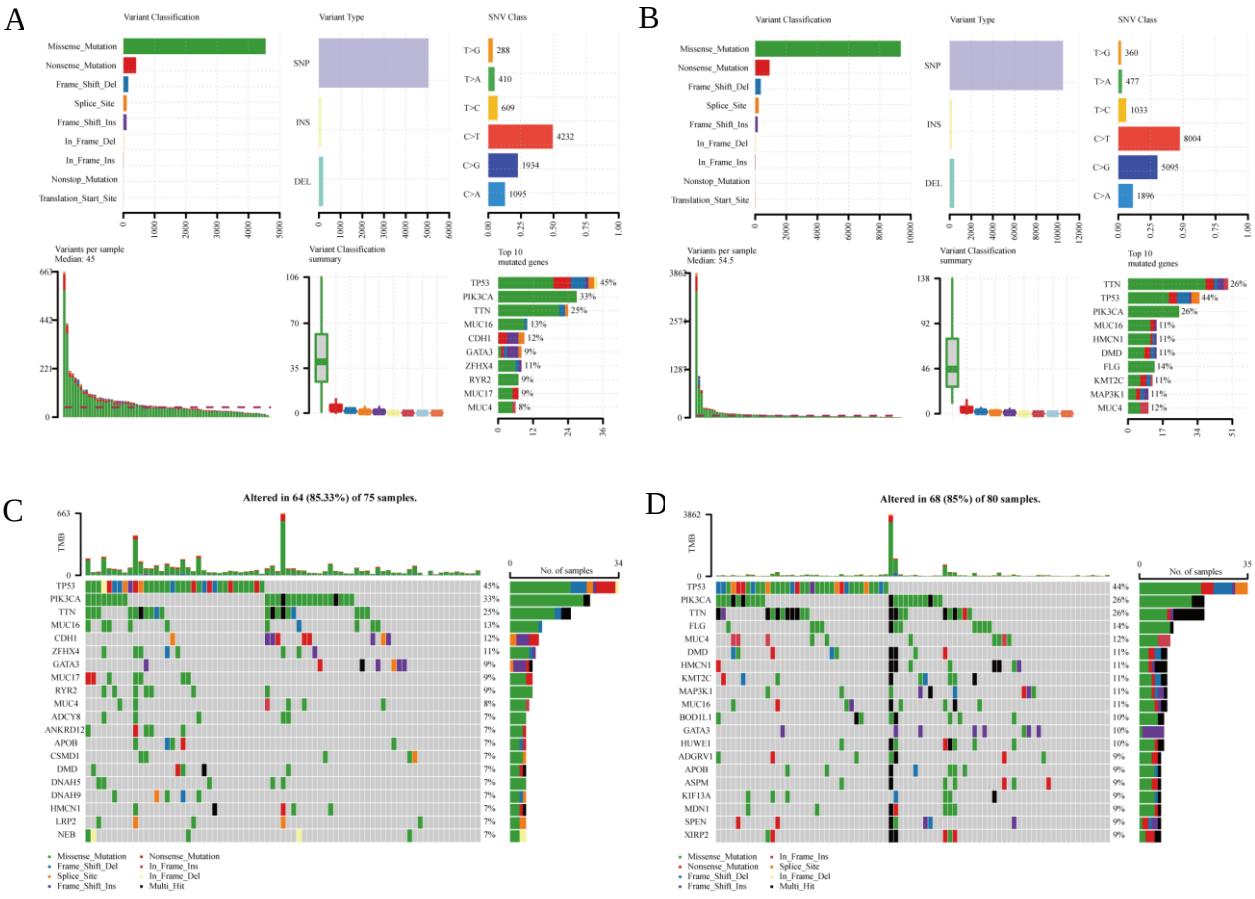
37	Immune
38	Epithelial
39	Stromal
40	Epithelial
41	Immune
42	Stromal



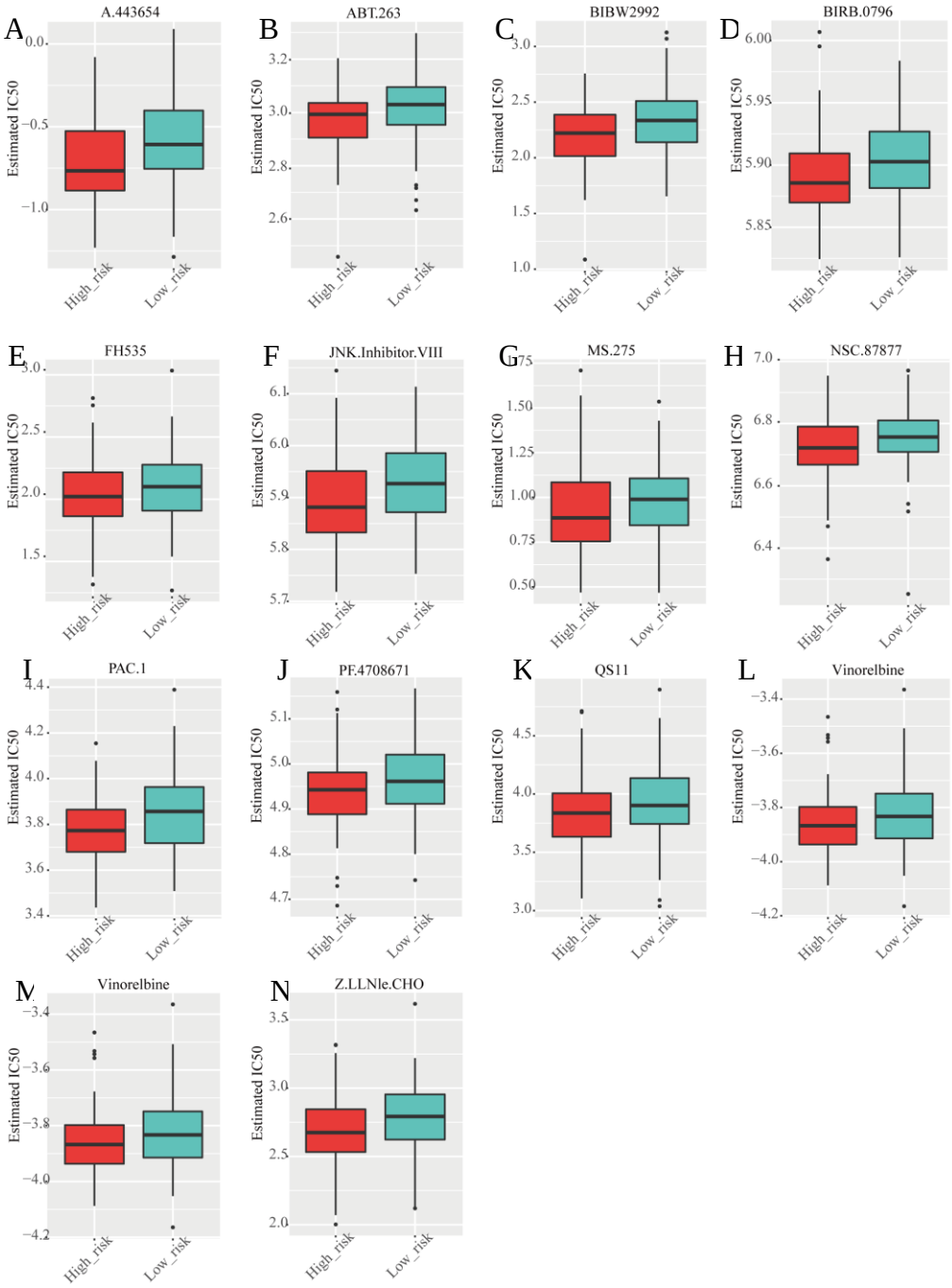
Supplementary Figure 1 Prognostic analysis of four ferroptosis-related gene signature models in the MRTABRIC cohort. (A) Risk curves were plotted in the METABRIC cohort. (B) Kaplan–Meier curves for the OS of patients in the high-risk and low-risk groups in the MRTABRIC cohort. (C) The AUCs of time-dependent ROC curves verified the prognostic performance of the risk score in the MRTABRIC cohort. (D) t-SNE analysis of the MRTABRIC cohort.



Supplementary Figure 2 The four ferroptosis-related prognostic gene signature models for predicting 3-, 5-, and 8-year OS in the METABRIC cohort. (A) Independent risk factors were used to build a risk estimation nomogram to predict the probability of OS in Her2-positive BRCA patients. (B) Calibration plots for 3-, 5-, and 8-year survival probabilities in the METABRIC cohort. (C)RMS time Curve in the METABRIC cohort.



Supplementary Figure 3 The mutation profile of different subgroups in the TCGA cohort. (A, B) Visualizations of variants, base mutations, and mutated genes between high- and low-risk groups. (C, D) Waterfall plot in high- and low-risk groups.



Supplementary Figure 4 Drug prediction and tumor neoantigen therapy drug sensitivity. (A-N). Visualized box diagram about IC50 sensitivity difference of 13 drugs between high-risk and low-risk groups