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REVIEW

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Ferroptosis-related LncRNAs in diseases

Wu Zhou[1*] and Jean Paul Thiery[2*]

Abstract

Ferroptosis is a form of regulated cell death (RCD) caused by the accumulation of intracellular iron and lipids and is involved in many pathological processes, including neurodegenerative and cardiovascular diseases, and cancer. Long non-coding RNAs (lncRNAs), RNA molecules exceeding 200 nt in length that do not possess protein coding function can interfere with ferroptosis by binding ferroptosis-related miRNAs or proteins. Recently, ferroptosis-related lncRNAs (FRlncRNAs) have been identified in cancer and non-malignant disease models, including inprediction of drug resistance, intra-tumoral immune infiltration, metabolic reprogramming and mutation landscape. Here, we review FRlncRNAs in cancer and non-malignant diseases, from prognosis to treatment.

Keywords Ferroptosis, LncRNAs, Cancer, Non-malignant diseases

Introduction

Iron is a vital trace element for almost all living organisms, including humans. Iron metabolism operates through a highly controlled system that maintains a balance between iron absorption and excretion [1]. Due to its importance, iron levels in organisms are finely regulated, and excessive iron can damage the organism through various mechanisms, inducing a unique form of cell death known as ferroptosis.

Ferroptosis is a type of regulated cell death (RCD) that is iron dependent and driving by lipid peroxidation. This is different to other forms of RCD such as apoptosis, autophagy, necroptosis, and pyroptosis, and as such ferroptosis is associated with different cell morphology, biochemistry, and genetics [2–4]. Under normal circumstances, ferroptosis primarily manifests as morphological changes in mitochondria, including reduced or absent mitochondrial cristae, increased membrane density, rupture of mitochondrial outer membrane, and significantly smaller mitochondria [5–7]. Ferroptosis is a novel type of programmed cell death that is iron dependent and driven by lipid peroxidation [8]. However, ferroptosis and other forms of RCD are not independent of each other. Studies have shown that cell apoptosis can be transformed into ferroptosis under certain conditions, and ferroptosis promotes cell sensitivity to apoptosis [9, 10]. It was found that activation of autophagy could degrade ferritin and induce ferroptosis in cancer cells [11] and ferroptosis coexisted with necroptosis to work as two complementary forms of cell death [12].

The primary biochemical characteristics of ferroptosis include the aggregation of intracellular lipid peroxide and reduced glutathione (GSH) levels [8]. In addition, ferroptosis is considered a form of inflammatory cell death in immunology, characterized by the release of damage-associated molecular patterns (DAMPs) and lipid oxidation products [2, 8]. Since its discovery, increasing evidence has shown that ferroptosis is associated with many diseases such as neurodegenerative and cardiovascular diseases, ischemia/reperfusion (I/R) injury, and cancer [13–17].

Following the completion of the Encyclopedia of DNA Elements (ENCODE) [18], it has been revealed that nearly 90% of genes in eukaryotic genomes can be transcribed into RNA. Still, only 1–2% of transcribed genes are translated into proteins, and most genes are transcribed as noncoding RNAs (ncRNAs) [19, 20], including

*Correspondence:
Wu Zhou
wzhou@zjxu.edu.cn
Jean Paul Thiery
jpthiery@biosg.com
[1] Medical College, Jiaxing University, Jiaxing 314001, China
[2] Biosyngen Pte Ltd, Singapore 536671, Singapore

long noncoding RNAs (lncRNAs) which are ncRNAs with a transcript length of more than 200 nt. Unlike messenger RNAs (mRNAs), which encode proteins, lncRNAs play a crucial role in the epigenetic regulation of gene expression at both the transcriptional and post-transcriptional levels [21], serving as scaffolds, guides, decoys, and miRNA sponges [22] (Fig. 1).

An increasing number of lncRNAs have been identified as regulators of ferroptosis. The role of LncRNA in ferroptosis [23] and ferroptosis-related lncRNAs (FRlncRNAs) in cancer therapy have been reviewed elsewhere [24–26]. However, the unique role of FRlncRNAs in cancer prognosis, the close association between FRlncRNAs and non-malignant diseases, and the promising application for targeted interventions on FRlncRNAs have not yet been summarized. Here, we provide a brief review of the discovery of ferroptosis and describe the crucial mechanisms driving this process, as well as recent advances in identifying the role of FRlncRNAs in diseases, particularly in cancer prognosis, mechanisms associated with malignancy, drug resistance, and other conditions.

Discovery and critical mechanisms of ferroptosis

The discovery of ferroptosis originated from the identification of system xc- which was first reported in 1980 [27]. System xc- was identified as an antiporter that exchanges intracellular glutamate for extracellular cystine on the cell membrane, consisting of solute carrier family 7 member 11 (SLC7 A11) and solute carrier family 3 member 2 (SLC3 A2). Under the transport of system xc-, glutamate and cysteine are exchanged in and out of cells, leading to synthesize GSH through the catalysis of glutathione synthetase (GS) and glutamate cysteine ligase (GCL) [28].

In 2003, the Stockwell laboratory identified a cell death pattern distinct from apoptosis using erastin, which targets cancer cells harboring RAS gene mutations [29]. However, the authors did not name this mode of cell death at that time. Five years later, their laboratory [30]

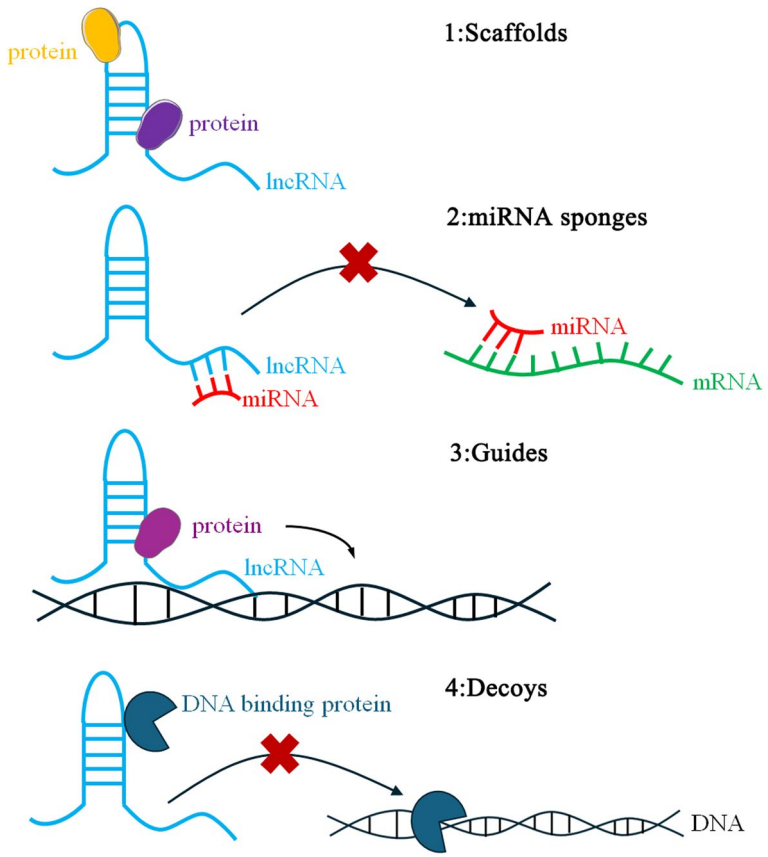

Fig. 1 Schematic diagram of the four main regulatory mechanisms of lncRNAs. 1: As scaffolds, lncRNAs can bring together multiple proteins to form ribonucleoprotein complexes, enabling information exchange and integration between different signaling pathways. 2: As miRNA sponges, lncRNAs can sponge specific miRNAs to block the interaction between miRNA and mRNA. 3: As guides, lncRNAs can bind with proteins and then locate protein complexes to specific DNA sequences to regulate gene expression. 4: As decoys, lncRNAs can bind to DNA-binding proteins (such as transcription factors), thereby blocking the action of the protein molecule and regulating the expression of downstream genes

reported that a compound Ras selective lethal 3 (RSL3) could induce cell death like erastin and demonstrated that this cell death pathway can be inhibited by iron chelators and antioxidants, suggesting its association with iron and reactive oxygen species (ROS). Based on the foundational understanding of the mechanisms of the control of ROS and the regulation of iron [8], this type of cell death was termed "ferroptosis" in 2012: an iron-dependent form of nonapoptotic cell death [6].

Studies conducted over the next decade demonstrated that ferroptosis is ultimately driven by specific lipid peroxidation, primarily determined by lipid metabolism, ROS, and iron regulation [8]. The main components of ferroptosis are shown in Fig. 2, core lipid peroxidation regulated by three interrelated factors: lipid metabolism, ROS antioxidant defense, and iron regulation.

Polyunsaturated fatty acids (PUFAs) are highly prone to peroxidation due to the presence of extremely weak C-H bonds between adjacent C = C double bonds [31]. Under the catalysis of lysophosphatidylcholine acyltransferase 3 (LPCAT3) [32] and acyl CoA synthase long-chain family member 4 (ACSL4) [33], free PUFA combines with phosphatidyl ethanolamine (PE) to generate polyunsaturated fatty acid phospholipids (PUFA-PL) [34, 35]. PUFA-PL is sensitive to ROS and converts to peroxidized PUFA-PL-OOH, which induces ferroptosis [36].

ROS-mediated PUFA-PL peroxidation is associated with iron regulation, including labile iron pool and iron-dependent enzymes. In the Fenton reaction, 1 mol of H_2O_2 reacts with 1 mol of Fe^{2+} to generate 1 mol of Fe^{3+}, 1 mol of OH^- plus 1 mol of hydroxyl radical. After Fe^{3+} reduction to Fe^{2+} in cells, iron-binding complexes will be preferentially formed to participate in diverse physiological and biochemical reactions. Excess Fe^{2+} will accumulate in the cell, creating an unstable iron ion pool that engages in the Fenton reaction to generate free radicals and induce ROS. Iron-dependent enzymes, including lipoxygenases (ALOXs) [31] and cytochrome P450 reductase (POR) [37], are recruited to generate hydrogen peroxide, the substrate of the Fenton reaction.

PUFA-PL-OOH-driven ferroptosis is monitored by two systems, one mediated by glutathione peroxidase 4 (GPX4), which catalyzes the reduction of phospholipid peroxides. It was found that selenoprotein GPX4 converts PUFA-PL-OOH to PUFA-PL-OH, and inhibition of this activity will lead to the accumulation of PUFA-PL-OOH in the cell membrane and promote ferroptosis [38]. The other surveillance system is GPX4-independent and mediated

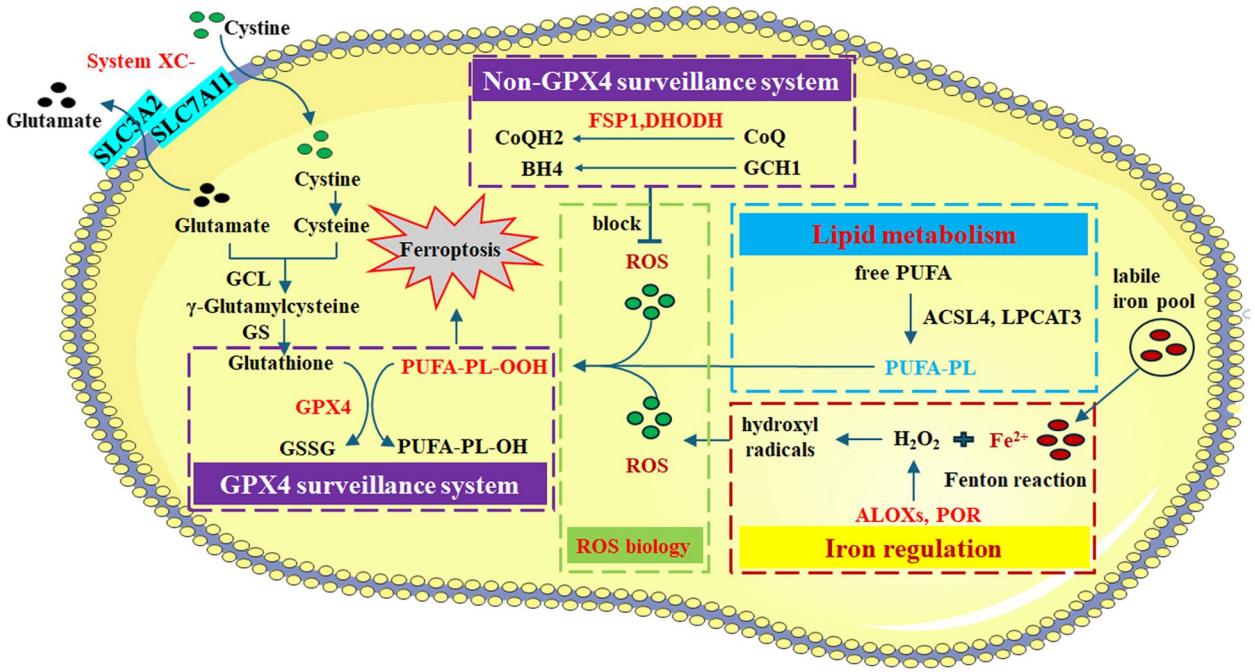

Fig. 2 Critical features of ferroptosis. The core incentive of ferroptosis is lipid peroxidation, typically involving polyunsaturated fatty acids (PUFAs), which are regulated by three related factors: lipid metabolism, ROS antioxidant defense, and iron regulation. Ferroptosis is monitored by two systems, one mediated by GPX4 and primarily catalyzing the reduction of lipid peroxides. The other set is dominated by non-GPX4 enzymes, mainly by scavenging free radicals to inhibit ferroptosis through antioxidant pathways. PUFA, polyunsaturated fatty acid; ROS, reaction oxygen species; ACSL4, acyl-CoA synthetase long-chain family member 4; LPCAT3, lysophosphatidylcholine acyltransferase 3; POR, p450 oxidoreductase; ALOXs, lipoxygenases; FSP1, ferroptosis suppressor protein; GCH1, GTP cyclohydrolase 1; DHODH, dihydroorotate dehydrogenase; BH4, tetrahydrobiopterin; GPX4, glutathione peroxidase 4; GS, glutathione synthetase; GCL, glutamate cysteine ligase

by enzymes that produce metabolites with free radical-trapping antioxidant activity (non-GPX4 surveillance system). Currently, three non-GPX4 surveillance systems have been identified, namely FSP1/CoQ10, DHODH/CoQ10, and GCH1/BH4. Ferroptosis suppressor protein 1 (FSP1), formerly known as apoptosis-inducing factor mitochondrial 2 (AIFM2) [39], and dihydrolactate dehydrogenase (DHODH) [40] are a class of coenzyme Q (CoQ) oxidoreductases that can reduce CoQ to CoQH2, directly reducing the generation of free radicals and halting the propagation of lipid peroxides. GTP cyclohydrolase 1 (GCH1) scavenges free radicals and inhibits ferroptosis by producing the lipophilic antioxidant tetrahydropterin (BH4) [41, 42].

FRlncRNAs in cancer

FRlncRNAs in cancer prognosis

For cancer patients, it is a matter of vital importance to predict long-term outcomes accurately. A good prognosis prediction model can guide oncologists in prescribing the most appropriate treatment to maximize benefits for patients. In recent years, cancer prognosis prediction models of cell aging (senescence [43, 44]) and cell death (pyroptosis [45, 46], cuproptosis [47, 48], and ferroptosis) related lncRNAs have been developed.

The general strategy for establishing a cancer prognosis model of ferroptosis based on LncRNAs involves leveraging clinical data and transcriptome expression data from patients in public databases, such as The Cancer Genome Atlas (TCGA), to construct expression signatures.

Combined with FerrDb (http://zhounan.org/ferrdb) data, differentially expressed ferroptosis-related genes are then identified by comparing the differences of ferroptosis-related genes between cancer and normal or peritumoral tissues. Differentially expressed FRlncRNAs may then be acquired by Pearson or Spearman correlation analysis and differentially expressed FRlncRNAs associated with overall survival identified using univariate Cox regression, followed by least absolute shrinkage and selection operator (LASSO) regression. Multivariate Cox analysis can then be used to further select differentially expressed FRlncRNAs, to construct a prognostic model based on the ferroptosis-related lncRNA score (FL score) in training cohorts. The FL scores calculated by the regression coefficient of each lncRNA and the expression level of the corresponding lncRNA determine the prognostic model including two groups: low-risk group and high-risk group. High-risk group lncRNAs can be marked as FRlncRNA signatures after being assessed for predictive accuracy by time-dependent receiver operating characteristic curves in the validation cohorts. Some studies performed cyclical single pairing of differentially expressed FRlncRNAs before Cox regression analysis and selected effective FRlncRNA pairs for cancer prognosis.

Recently, FRlncRNA signatures (Table 1) [49–95] and FRlncRNA pairs (Table 2) [96–102] prognostic models have been established in various type of cancers and these models have been applied to predict drug resistance, intra-tumoral immune infiltration, metabolic reprogramming, mutation landscape, and other features. Although there is currently no universal FRlncRNA model for cancer prognosis, several lncRNAs are repeatedly found in FRlncRNA signatures or FRlncRNA pairs proposed by different research groups, indicating that these lncRNAs have specific predictive value.

AP003555.1

AP003555.1, also known as long intergenic non-protein-coding RNA 2753 (LINC02753) or oncogenic lncRNA 626 (oncRNA-626), was mainly reported as a prognostic FRlncRNA for colorectal cancer (CRC) [49, 52, 53, 103–105]. A 4- FRlncRNA signature including AP003555.1 was observed to exhibit better predictive performance than traditional clinicopathological features in CRC patients [49]. A model with a five-FRlncRNAs signature consisting of AP001469.3, ITGB1-DT, AC129492.1, AC010973.2, and AP003555.1 showed a powerful capacity for survival prediction in patients with colon adenocarcinoma [103]. A prognostic signature composed of eight FRlncRNAs with AP003555.1 was reported as closely related to the theoretical evaluation of recurrence and metastasis in CRC patients [52]. Other groups found that AP003555.1-included FRlncRNAs signatures were significantly correlated with the survival of CRC patients, which can serve as potential therapeutic targets for CRC prognosis [53, 103–105]. AP003555.1 was also identified as one of the disulfidptosis-related lncRNAs [106, 107], oxidative stress-related lncRNAs [108], and genomic instability-related lncRNAs [105] in the prognosis model of colorectal cancer.

ZFPM2-AS1

ZFPM2-AS1 is an antisense RNA for zinc finger protein multitype 2 (ZFPM2) and has been associated with tumor size and stage, as well as poor survival in various solid tumors [109, 110]. ZFPM2-AS1 was verified as a prognostic lncRNA in FRlncRNA signature of hepatocellular carcinoma (HCC) patients [54, 58, 111, 112]. ZFPM2-AS1 was identified in a nine FRlncRNA-based signature, as the ferroptosis-related prognostic model for HCC using the LASSO algorithm and Cox regression from the TCGA and gene expression omnibus (GEO) dataset [54]. It was demonstrated that a prognostic model consisting of two ferroptosis-related mRNAs (SLC7 A11 and SLC1 A5) and eight ferroptosis-related lncRNAs (NRAV,

Table 1 Ferroptosis-related LncRNA signatures in cancer prognosis

LncRNA signatures	Samples
AP003555.1, AC000584.1, LINC02381, AC104819.3	TCGA, CRC (*n* = 437)
XXbac-B476 C20.9, TP73-AS1, SNHG15	TCGA, CRC (*n* = 499)
AC016027.1, AC099850.3, ELFN1-AS1, VPS9D1-AS1	TCGA, CRC (*n* = 673)
AL161729.4,AC010973.2,CCDC144 NL-AS1,AC009549.1,LINC01857,AP003555.1,AC099850.3, AC008494.3	TCGA, CRC (N.A)
AP003555.1, AC010973.2, LINC01857, AP001469.3, ITGB1-DT and AC129492.1	TCGA, CRC (*n* = 514)
CTD-2033 A16.3, CTD-2116 N20.1, CTD-2510 F5.4, DDX11-AS1, LINC00942, LINC01224, LINC01231, LINC01508, ZFPM2-AS1	TCGA, HCC (*n* = 424)
PCAT6, MKLN1-AS, POLH-AS1, LINC00942, AL031985.3, LINC00942	TCGA, HCC (N.A)
DANCR, MKLN1-AS1, ZFPM2-AS1, NRAV, LNCSRLR, AL137186.2	TCGA, HCC (*n* = 422); ICGC (*n* = 445)
ZFPM2-AS1, LUCAT1, GDNF-AS1, AC099850.3, AC092119.2, AL356234.2, AC009005.1, LINC01224	TCGA, HCC (*n* = 421)
KDM4 A-AS1, ZFPM2-AS1, AC099850.3, MKLN1-AS, and BACE1-AS	TCGA,HCC (*n* = 377)
LINC01572, LINC01224, ZFPM2-AS1, LINC01353, SLC2 A1-AS1, SNHG4, CTB-147 N14.6, CTC-297 N7.9, RP11-818 F20.5, RP11-479G22.8, ST3GAL4-AS1, FOXD2-AS1	HCC (N.A)
MKLN1-AS, LINC01224, LNCSRLR, LINC01063, PRRT3-AS1, POLH-AS1	TCGA,HCC (*n* = 342)
AC009779.2, ZFPM2-AS1, AC009005.1, AC074117.1, AC012467.2, AL031985.3, AC009403.1, LUCAT1, AC026369.2, AC068580.3, LINC01871, AL139384.1, TMEM220-AS1, NRAV, AL365203.2, MIR210HG	TCGA-LIHC (*n* = 714)
AATBC, AC145423.2, LINC01871, AC125807.2, AC245041.1	TCGA, CM (*n* = 461); GTEx (*n* = 233)
ZNF790-AS1, LINC01239, LINC00452, HLA-DQB-AS1, JARID2-AS1, LINC00592, KCTD21-AS1, SEMA6 A-AS1, LRP4-AS1, MIAT, PLA2G4E-AS1	TCGA, CM (*n* = 471), GTEx (*n* = 812)
LINC00861, PIK3 CD-AS1, FAM30 A, LINC02642, LINC01482, LINC02481, LINC01281, LINC00996, LINC02132, LINC02273, MDS2, LINC00402, AC006369.2, LINC01727, LINC02285, LINC02812	TCGA, CM (*n* = 471); GTEx (*n* = 1000)
AC104129.1, AC136475.3, LINC00963, PPP1R14B-AS1, ZNF667-AS1	TCGA, CM (*n* = 80)
USP30-AS1, LINC01871, AC026369.3, AL606807.1, AC021078.1, AC093297.2, AC004865.2, AC010245.2, AC018645.3, AC011511.5, AL021368.2, AC024909.1, KANSL1L-AS1, PPP1R26-AS1, AC100778.3, AC069222.1, AL592211.1, MALINC1	TCGA, CM (*n* = 471)
SNHG29, RB1-DT, MEG3, LOC100507144, LINC02269, LINC01970, FAM13 A-AS1, EBLN3P, CAHM, APOA1-AS	TCGA, ESCC (*n* = 398)
AC083862.2, CYTOR, AC114296.1, LINC02768, GATA2-AS1, CTB-178M22.2	TCGA, LSCC (*n* = 123)
AC055720.2, DPP4-DT, AC012038.2, LINC02454, LINC00900	TCGA, THCA (*n* = 502)
ARHGEF26-AS1, LINC01137, C20orf197, MGC32805, TMPO-AS1, LINC00324, LINC01116	TCGA, LUAD (*n* = 477)
RP11-386M24.3, LINC00592, FENDRR, AC104699.1, AC091132.1, LANCL1-AS1, LINC-PINT, IFNG-AS1, LINC00968, AC006129.2	TCGA, LUAD (*n* = 535)
AL606489.1, AC106047.1, LINC02081, AC090559.1, AC026355.1, FAM83 A-AS1, AL034397.3, AC092171.5, AC010980.2, AC123595.1	TCGA, LUAD (*n* = 535)
C5orf64, LINC01800, LINC00968, LINC01352, PGM5-AS1, LINC02097, DEPDC1-AS1, WWC2-AS2, SATB2-AS1, LINC00628, LINC01537, LMO7DN	TCGA, LUAD (*n* = 594)
CYTOR, AP005131.2, LMNTD2-AS1, LYPLAL1-AS1, USP30-AS1, AC004988.1, RHPN1-AS1, AC079298.3, HSD11B1-AS1, LINC01655	TCGA, BRCA (*n* = 1208)
LINC02298, AP000851.2, SNHG6, RPARP-AS1, AL162274.1	TCGA, OS (*n* = 484)
AC138904.1, AP005205.2, AC007114.1, LINC00665, UBXN10-AS1, AC083880.1, LINC01558,AL023583.1	TCGA, OC (*n* = 374)
AC007848.1, AC010336.5, AL157871.2, AP001033.1, AC009403.1, AC068792.1, AC011445.1, AC093895.1, LINC01857, LINC00239, AL513550.1	TCGA, OC (*n* = 365)
AC007796.1, TLR8-AS1, RP11-713M15.2, CTB-171 A8.1, LBX2-AS1, CTD-2130 F23.2, RP11-88G17.6, RP11-388M20.1, RP11-678G14.3, RP4-650 F12.2, RP11-701H24.7, RP11-1018 N14.5, LINC01281, RP11-301G19.1, CTD-2330 K9.3, AP000344.3, CTD-2506 J14.1, AC078842.3	TCGA, OC (*n* = 515)
AC009299.2, AC012020.1, AC092723.2, AC093642.1, AC243829.4, AL121748.1, FLNB-AS1, LINC01614, LINC02485, LINC02728	TCGA, STAD (*n* = 337)
AP003392.1, AC245041.2, AP001271.1, BOLA3-AS1	TCGA, STAD (*n* = 407)
LINC02716, AL356489.2, AC115619.1, AC023511.1, AC005165.1, AC006942.1, GHICG, AC027682.6, BNC2-AS1, AL049838.1, NR2 F1-AS1, AC007541.1, LINC01579, AC002451.1, AP001528.1, AL590226.1, SENCR, MIR99 AHG, MAGI2.AS3, LINC00519, MIR100HG, BOLA3-AS1, LINC01614, LINC01705	TCGA, STAD (*n* = 407)
AL031775.1, AL162586.1, AC034236.2, LINC01004, OCIAD1-AS1, AL136084.3, AP003352.1, Z84484.1, AC022150.2	TCGA, BC (*n* = 406) cBioPortal (*n* = 319)
AC245060.5, AC024060.2, Z98200.1, AC021321.1, AC073046.1, LINC02762, BX322562.1, AL031775.1, LINC00649, AC009690.2, STAG3L5P-PVRIG2P-PILRB, ZNF436-AS1, AL136084.2, AC096921.2	TCGA, BC (*n* = 425)
AL133415.1, LINC01426, AC009227.1	TCGA, Glioma (*n* = 698); GTEx (*n* = 1152)

Table 1 (continued)

LncRNA signatures	Samples
LINC00844, FAM66 C, TUBA3 FP, SNHG8, CRNDE, HAR1 A, LINC00641, MYCNOS	TCGA, Glioma (*n* = 408)
APCDD1L-AS1, H19, LINC00205, LINC00346, LINC00475, LINC00484, LINC00601, LINC00664, LINC00886, LUCAT1, MIR155HG, NEAT1, PVT1, SNHG18	TCGA, Glioma (*n* = 698), CGGA (*n* = 1018)
LINC01133, CASC8, AL356740.3, LINC02535, LINC01091, AC068580.2, LINC02004, AC092171.3, AC015660.1	Frozen PAAD and adjacent tissues (*n* = 30)
LINC00460, AC124854.1, AC084876.1, IGFL2-AS1, LINC00551, AC083967.1, AC073487.1, LINC02446	TCGA, ccRCC (*n* = 513)
LINC00894, DUXAP8, LINC01426, PVT1, PELATON, LINC02609, MYG1-AS1	TCGA, ccRCC (*n* = 526)
PVT1, CYTOR, MIAT, SNHG17, LINC00265, LINC00894	TCGA, ccRCC (N.A)
SCN1 A_AS1, MNX1_AS1, LINC01016, FAM230 C, ZNF710_AS1, MIR100HG, SIRLNT, LINC01108, LINC00896	TCGA, KIRP (*n* = 321)
AC103563.2, DM1-AS, AC080013.4, LINC01629, AC009237.15, BOLA3-AS1, RAB11B-AS1, AC244517.7, CFAP58-DT	TCGA, UCEC (*n* = 549)
LINC02084, AC004540.2, AC026979.2, AC099568.2, SOX21-AS1, ATP2 A1-AS1, AC005332.4	TCGA, CC (*n* = 309)
ZFAS1, AC010624.2, AL031710.1, AL355102.4, MNX1-AS1, AC109460.1, AC127537.1, AC099850.4, LINC02154, AC024022.1, AC026401.3, LINC02535, ADAMTS9-AS1, AC107464.2, MIR4435-2HG	TCGA, PRCC (*n* = 321)
AC007406.1, AC005208.1, LINC01770, DLGAP1-AS2, AP002761.4, STPG3-AS1, AC129507.1, AC234772.2, LINC02447, AC009570.1, ZBTB20-AS1, LINC01179	TCGA, Wilms tumor (*n* = 30)

CRC Colorectal cancer, *HCC* Hepatocellular carcinoma, *CM* Cutaneous melanoma, *ESCC* Esophageal squamous cell carcinoma, *LSCC* Laryngeal squamous carcinoma, *THCA* Thyroid carcinoma, *LUAD* Lung adenocarcinoma, *BRCA* Breast cancer, *OS* Osteosarcoma, *OC* Ovarian cancer, *STAD* Stomach cancer, *BC* Bladder cancer, *PAAD* Pancreatic adenocarcinoma, *ccRCC* Clear cell renal cell carcinoma, *UCEC* Uterine corpus endometrial carcinoma, *CC* Cervical cancer, *KIRP* Kidney renal papillary cell carcinoma, *PRCC* Papillary renal cell carcinoma, *ICGC* International Cancer Genome Consortium, *TCGA* The Cancer Genome Atlas, *TCGA-LIHC* The Cancer Genome Atlas-Liver HCC dataset, *GTE* Genotype-Tissue Expression, *CGGA* Chinese Glioma Genome Atlas, *N.A* No data available

Table 2 Ferroptosis-related LncRNA pairs in cancer prognosis

LncRNA pairs	Samples
LMO7-AS1:LINC00513, LINC01614:AC145423.2, LINC01703:FENDRR, LINC02487:AC010973.2, LINC02195:AC048344.4, AC020907.4:AC010973.2, MHENCR:AC025857.2, AL031716.1:AL117379.1, MIR17HG:AL161729.4, AC127024.4:AL355802.3, AC0 10973.2:AL031673.1,AL021578.1:AL133243.2, AC016831.4:AC011676.1, AC090116.1:AL353804.2, AP002336.2:AC093732.1, AC011676.1:AC092168.2, AP005899.1:GK-AS1, LINC-PINT:LINC00513, AF117829.1:SNHG22, AC245100.7:LINC01811, AL354836.1:SNHG4, SCARNA9:AC104695.4, AL137782.1:AP001469.3. AP001469.3:ABALON, ABALON:CD44-AS1	TCGA, CRC (*n* = 521)
NRAV:CTBP1-DT, LINC00342:AL049840.5, LINC00342:AC016394.2, AC102953.2:C2orf27 A, LINC NC00205:NCK1-DT, AC124045.1:AC026356.1, PTOV1-AS2:ZEB1-AS1, AL031985.3:NRSN2-AS1, AC232271.1:C2orf27 A, AC004908.1:AC073842.2, LINC01521:AL606489.1, AC099850.4:SNHG12, AC145207.5:AC022150.2, SNHG4:AC024075.1, AC091057.1:AC005253.1, AC099850.4:OTUD6B-AS1	TCGA, HCC (*n* = 415)
TCERG1L-AS1:ITPR1-AS1, LINC01510:LINC01140, MIR646HG:NEXN-AS1, LINC01354:MEOX2-AS1, LINC01224:FOXP1-AS1, VLDLR-AS1:LINC00473, LINC00475:LINC01474, CYP1B1-AS1:SOX9-AS1, LINC00511:LINC00973	TCGA, PTC (*n* = 549)
AL356299.3:AF124730.2, AC007128.2:AL354928.1, KCNMB2-AS1:AL117382.2, AL354928.1:MIR1-1HG-AS1, HHLA3-AS1:LINC01614, C5orf66-AS1:AC112484.3, LNCAROD:AC007277.1, AL161729.4:CFAP61-AS1, HAND2-AS1:TSPEAR-AS2, LINC00941:AC120498.4	TCGA, STAD (*n* = 407)
LINC02195:AP003071.4, LINC02195:NR4 A1 AS, LINC02154:AC112721.1, AC007128.1:AC010331.1, AC091182.2:AC010789.1, LINC01767:AC106875.1, LINC01767:AC114489.2, AP005432.2:AL161772.1, AC012645.4:AC010331.1, MYOSLID:AC010331.1, AL513218.1:ZNF710-AS1, AC073195.2:AATBC	TCGA, BC (*n* = 430)
AC1350123:AP003071.4, ADAMTS9-AS1:AC015923.1, AC002398.2:AC005180.2, AP001189.1:ACTA2-AS1, AP001189.1:AL023755.1, AP003071.4:LINC02195, MIR100HG:AATBC, JAZ:F1-AS1:AP005432.2, AC099850.3:U623172, AC099850.3:LINC01833, AL161772.1:AATBC, AC090673.1:FP325330.3, LINC00460:PICSAR, AL161431.1:AC104984.6, AC090825.1:MAG12-AS3, RMRP: MAG12-AS3, AC053503.4:LINC01778, AC087521.1:AC079313.1, AP003071.3:FENDRR, LINC00402:FENDRR, RMRP:CDKN2B-AS1, LINC01615:LINC02195	TCGA, BC (*n* = 427)
AC022211.3:AC005920.2, AL158166.1:AC004264.1, GK-AS1:AP002907.1, AL033384.1:U62317.4, HOXC13:-AS:AC091182.2, EXOC3-AS1:AC040169.1, LINC01503:AL590617.2, LINC02195:Z95115.1, SCAT2:C2orf27 A,CASC8:AC007785.1, AC005041.3:Z95115.1, AC022144.1:AC108673.2, AC245100.7:AC136475.3, AL391056.1:AL022316.1, AL109615.3:AC023043.1, DLG5-AS1:AC008669.1, AC007128.1:MUC12-AS1	TCGA, EC (*n* = 171)
AC079336.5:AC011676.1, MNX1-AS1:AC068473.3, LINC02195:LINC02454, AC011676.1:AC114730.3, AC015878.1:AL499627.1, C5orf66-AS1:LINC01711, STARD4-AS1:HOTAIR, MIR9-3HG:TYMSOS, AC053503.3:AL031600.1, AC019171.1:AC089983.1, AC016773.2:LINC01063	TCGA, HNSCC (*n* = 545)

TCGA The Cancer Genome Atlas, *CRC* Colorectal cancer, *HCC* hepatocellular carcinoma, *PTC* Papillary thyroid carcinoma, *STAD* Stomach adenocarcinoma, *BC* Bladder cancer, *EC* Esophageal cancer, *HNSCC* Head and neck squamous cell carcinoma

ZFPM2-AS1, AL031985.3, AC015908.3, SREBF2-AS1, MYLK-AS1, MSC-AS1, and AC245297.3) was significantly associated with the immune functional enrichment for HCC patients [111]. The risk-score model by seventeen differentially expressed FRlncRNAs including ZFPM2-AS1 can be applied to predict the function of immune cell subpopulation, the expression of immune checkpoint and carcinogenic N6-methyladenosine (m6 A)-related mRNAs [112]. ZFPM2-AS1 was also correlated to various type of immune cells infiltrated in the tumor microenvironment [113] and to be one member of cuproptosis-related lncRNAs [114], necroptosis-related lncRNAs [58, 115], genomic instability-related lncRNAs [116, 117], pyroptosis-related lncRNAs [118], N7-methylguanosine-related lncRNAs [119], and autophagy-related lncRNAs [120] in HCC patients.

MKLN1-AS

MKLN1-AS is an antisense RNA for muskelin 1 (MKLN1) and a potential diagnostic biomarker and therapeutic target for HCC [121–123]. The currently reported prognostic models containing MKLN1-AS were mainly established in HCC patients. MKLN1-AS was included in the six FRlncRNAs models showing a promising clinical prediction of prognosis and immunotherapeutic responses in patients with HCC [55]. Another six FRlncRNAs prognostic signatures also proved the capability of the MKLN1-AS included FRlncRNA signature to predict the effects of immunotherapy and targeted therapy, and contribute to precise and individualized treatment for HCC patients [60]. A risk signature composed of seven FRLncRNAs with MKLN1-AS was constructed and showed prognostic value in HBV-HCC patients [124]. In addition to being a FRlncRNA [55, 58, 60, 112, 124], MKLN1-AS was also used in a risk prognosis model associated with disulfidptosis lncRNAs [125, 126], cuproptosis-related lncRNAs [127–130], 5-Methyladenosine (m5 C)-related lncRNAs [131], pyroptosis-related lncRNAs [118], autophagy-related lncRNAs [132], and hypoxia-related lncRNAs [133].

AC099850.3

AC099850.3, also known as proline-rich 11 antisense RNA 1(PRR11-AS1), has been reported to be a FRlncRNA in different types of cancers. It was found that five ferroptosis and necroptosis-related lncRNAs including AC099850.3 were associated with prognosis and the prediction of immune function and immunotherapy responses in HCC patients [58]. A prognostic model was constructed in kidney renal papillary cell carcinoma patients using LASSO regression and found that AC099850.3 was included in one FRlncRNAs model [134]. AC099850.3 was identified among the eight differentially expressed FRlncRNAs prognosis models and was associated with poor cancer prognosis and T cell function in non-small cell lung cancer (NSCLC) patients [135]. A prognostic risk model, of six lncRNAs, including AC099850.3 was constructed and was validated as a new independent prognostic factor for pancreatic adenocarcinoma [136].

Moreover, AC099850.3 was identified as one FRlncRNA in CRC [51, 52, 104], one acetylation-related lncRNA in NSCLC [137], one necroptosis-related lncRNA [138], and hypoxia-related lncRNA [139] in lung adenocarcinoma, cuproptosis-related lncRNA in pancreatic adenocarcinoma [140], N6-methylandenosine-related lncRNA [141], and cuproptosis-related lncRNA [142] in CRC. For patients with HCC, AC099850.3 was found to be one component of costimulatory molecule-related lncRNAs [143], immune-related lncRNAs [144], pyroptosis-related lncRNAs [118, 145], cuproptosis-associated LncRNAs [146], autophagy-related LncRNAs [120, 147, 148], epithelial-mesenchymal transition (EMT)-related LncRNAs [149, 150], exosome-related LncRNAs [151], and stemness-associated LncRNAs [152].

AC010973.2

AC010973.2 lncRNA was found to be a diagnostic biomarker and significantly related to the survival of CRC patients [153] and one of six stemness-related genes that predict overall survival of renal clear cell carcinoma patients [154]. As an FRlncRNA, AC010973.2 was detected as one of the members of the FRlncRNA signature in CRC patients, either with [52, 53, 103, 104] or without AP003555.1 [155]. Additionally, AC010973.2 was not only associated with ferroptosis predict prognosis signature [52, 53, 103, 104, 155] but also with prognosis FRlncRNA pairs in CRC [96]. The paired DEfrlncRNAs were selected by analyzing the data from TGCA. AC010973.2 coupled with LINC02487, AC020907.4, or AL031673.1 were identified as novel prognostic FRlncRNA pair in colon adenocarcinoma [96].

LINC02195

Long intergenic non-protein coding RNA 2195 (LINC02195) has been reported to be an immune-related lncRNA [156], a hypoxia-related lncRNA [157], and a regulator of MHC I molecules and a favorable prognostic marker for head and neck squamous cell carcinoma [158]. LINC02195 together with AC048344.4 was one of the novel FRlncRNA prognostic pairs in colon adenocarcinoma.[96], LINC02195 with AP003071.4 [100, 101], or LINC01615[101] provided a prognostic signature to predict the immune landscape of human bladder cancer [100], and LINC02195 with LINC02454 was one promising prognostic FRlncRNA pair to predict immune function and immunotherapy response in esophageal cancer patients [102].

FRlncRNAs in cancer progression

In living organisms, programmed cell death such as apoptosis is essential for maintaining the normal function of tissues and organs. However, in cancer, programmed cell death is often be inhibited, leading to higher tumor growth. FRlncRNAs indirectly act on ferroptosis-related key genes by targeting miRNAs or proteins (Table 3) [56, 159–187], promoting or inhibiting ferroptosis and mediating the progression of cancer.

Targeting miRNA

FRlncRNAs can act as a molecular sponge for ferroptosis-related miRNA, competitively binding tomiRNA to reduce its inhibitory effect on its target. SLC7 A11 is a key component of the System Xc—located on the cell membrane, mainly exerting an inhibitory effect on ferroptosis by regulating the metabolism of cysteine, glutamate, and glutathione [15]. Studies have shown that several lncRNAs of antisense RNAs can competitively sponge SLC7 A11-targeted miRNAs in cancer. Li Y Z et al. revealed that antisense RNA for solute carrier family 16 member 1 (SLC16 A1-AS1) served as a sponge of miR-143-3p, and SLC7 A11 was found as the target protein of miR-143-3p in renal cell carcinoma [162]. Li J et al. determined that antisense RNA for protein tyrosine phosphatase receptor type G (PTPRG-AS1) was increased in triple-negative breast cancer tissues and carcinoma cells and PTPRG-AS1 targeted miR-376c-3p to upregulate SLC7 A11 [163]. Zhang Y et al. identified that antisense RNA for opa interacting protein 5 (OIP5-AS1) sponged miR-128-3p to promote the expression of SLC7 A11 and mediated cadmium-induced ferroptosis and in prostate cancer [164]. Pan C et al. showed that miR-513a-3p was a target of antisense RNA for gamma-butyrobetaine hydroxylase 1 (BBOX1-AS1) and SLC7 A11 regulated by miR-513a-3p in esophageal squamous cell cancer [169]. Moreover, Zong K et al. verified that lncRNA negative regulator of antiviral response (NRAV) can increase ferroptosis resistance by competitively sponging to miR-375-3P and blocking the inhibitory effect of miR-375-3P on SLC7 A11 in HCC [56]. Zhang N et al. identified that lncRNA T-UCR Uc.339 mediated the interaction with miR-339 and regulated the expression of SLC7 A11 to participate in lung adenocarcinoma tumor metastasis [167].

GPX4, an enzyme to catalyze the reduction of hydrogen peroxide and protect cells from oxidative damage [188], is another regulated protein of FRlncRNA. He GN et al. demonstrated that lncRNA PVT1 directly bind with miR-214-3p to attenuate its role as a sponge of GPX4 in liver cancer [159]. Li SQ et al. determined that overexpression of small nucleolar RNA host gene 4 (SNHG4) sponged the miR-150-5p and promoted GPX4 expression in CRC cells [165].

FRlncRNAs can also regulate other ferroptosis-related genes by targeting miRNAs, mediating cancer progression. Knockdown of LncRNA SNHG1 increased erastin-mediated ferroptosis by sponging miR-199a and upregulating FA complementation group D2 (FANCD2) and glucose-6-phosphate dehydrogenase (G6PD) in HCC [160]. LncRNA RP11-89 enhanced tumorigenesis

Table 3 FRlncRNAs regulate cancer progression

FRlncRNA	Target	Regulator	Disease	FRlncRNA	Target	Regulator	Disease
PVT1	miR-214-3p	GPX4	HCC	SNHG1	miR-199a-5p/3p	FANCD2/G6PD	HCC
RP11-89	miR-129-5p	PROM2	BC	SLC16 A1-AS1	miR-143-3p	SLC7 A11	RCC
NRAV	miR-375-3P	SLC7 A11	HCC	PTPRG-AS1	miR-376c-3p	SLC7 A11	TNBC
OIP5-AS1	miR-128-3p	SLC7 A11	PCa	SNHG4	miR-150-5p	c-Myb/CDO1/GPX4	CRC
GSEC	miR-101-3p	CISD1	LUAD	T-UCR Uc.339	miR-339	SLC7 A11	LUAD
LINC00324	miR-200c-3p	TFAP2 A	LUAD	BBOX1-AS1	miR-513a-3p	SLC7 A11	ESCC
NEAT1	miR-362-3p	MIOX	HCC	DSCAM-AS1	IGF2BP1	SLC7 A11	BRCA
P53RRA	G3BP1	p53	BRCA	DLEU1	ZFP36	ATF3/SLC7 A11	Glioma
A2M-AS1	PCBP3	p38	PC	LINC02936	SIX1	Ceruloplasmin	EC
ROR1-AS1	IGF2BP1	SLC7 A11	LUAD	RGMB-AS1	HMOX1/NAA10	TRC8/acetyl-CoA	NSCLC
SNAI3-AS1	SND1	Nrf2	glioma	OTUD6B-AS1	HuR	TRIM16/GPX4	CRC
FTX	FEN1	ACSL4	OSCC	CBSLR	YTHDF2	CBS/ACSL4	GC
PMAN	ELAVL1	SLC7 A11	GC	CASC2	FMR1	SOCS2/SLC7 A11	GC
HOXC-AS3	EP300	GPX4	NSCLC	BDNF-AS	WDR5	FBXW7/VDAC3	GC
HEPFAL	mTORC1	SLC7 A11	HCC	ABHD11-AS1	IGF2BP2	FOXM1	CRC

HCC Hepatocellular carcinoma, *BC* Bladder cancer, *RCC* Renal cell carcinoma, *PCa* Prostate cancer, *TNBC* Triple-negative breast cancer, *LUAD* Lung adenocarcinoma, *ESCC* Esophageal squamous cell cancer, *CRC* Colorectal cancer, *OSCC* Oral squamous cell carcinoma, *NSCLC* Non-small cell lung cancer, *EC* Endometrial cancer, *BRCA* Breast cancer, *GC* Gastric cancer, *PC* Pancreatic cancer

and ferroptosis resistance through sponging miR-129-5p and thus upregulating the expression of the target protein prominin 2 (PROM2) in bladder cancer [161]. The FRLncRNA GSEC targeted miRNA-101-3p and then regulated CDGSH iron sulfur domain 1 (CISD1) in lung adenocarcinoma [166]. The cuproptosis-related ferroptosis lncRNA LINC00324 targeted miR-200c-3p and then regulated transcription tactor AP-2 alpha (TFAP2 A), facilitating the progression of lung adenocarcinoma by [168]. The overexpression of lncRNA NEAT1 modulated the miR-362-3p/MIOX axis as a competing endogenous RNA and enhanced ferroptosis, increasing the antitumor activity of erastin [170].

Targeting proteins

Besides targeting miRNA, FRlncRNA can also directly bind to target proteins to regulate ferroptosis in cancer. FRlncRNAs can direct bind to the target protein and regulates the ferroptosis of cancer cells through SLC7 A11 signaling. The transcription factor POU6 F1 was found to bind directly to lncRNA CASC2 and increase suppressor of cytokine signaling 2 (SOCS2) stability by targeting fragile X messenger ribonucleoprotein 1 (FMR1), thereby blocking SLC7 A11 signaling to induce ferroptosis in gastric cancer cells thus preventing gastric cancer progression [183]. LncRNA DLEU1 was found to bind with the zinc finger protein 36 (ZFP36) and facilitates ZFP36 to degrade activating transcription factor 3 (ATF3) mRNA, thus increasing the expression of SLC7 A11 to downregulate erastin-induced ferroptosis in glioblastoma [173].

Other proteins directly interacting with FRlncRNA and their mediated mechanisms of ferroptosis in cancer cells have also been reported. LncRNA LINC02936 was reported to bind with sine oculis homeobox homolog 1 (SIX1) and upregulated the expression of ceruloplasmin, leading the inhibition of ferroptosis and promotion of endometrial cancer progression [175]. LncRNA A2M-AS1 directly interacted with the poly (rC) binding protein 3 (PCBP3) and regulated the process of iron metabolism, thereby promoting ferroptosis in pancreatic cancer [174].

Methylation, one of the most prevalent epigenetic modifications of RNA [189], is involved in the regulatory mechanism of FRlncRNA directly binding to target proteins and mediating ferroptosis in cancer cells. LncRNA SNAI3-AS1 could competitively bind to staphylococcal nuclease domain containing 1 (SND1) and damage the m6 A-dependent recognition for nuclear factor erythroid 2-related factor 2 (NRF2), thereby promoting ferroptosis in glioma [178]. SETD1 A-mediated H3 K4 me3 methylation upregulated lncRNA HOXC-AS3 and the binding of HOXC-AS3 to EP300 to suppress the ferroptosis of NSCLC cells [184].

Furthermore, studies have demonstrated that FRlncRNA secreted by cancer-associated fibroblasts (CAFs) can directly bind to proteins, thereby mediating the ferroptosis of cancer cells. Li Y et al. identified that podoplanin (PDPN) positive expressed CAFs transferred exosomal lncRNA FTX to cancer cells and promoted FTX bound to flap endonuclease-1 (FEN1), inhibiting the ferroptosis in oral squamous cell carcinoma [180]. Yao F et al. revealed that CAFs secreted exosomal lncRNA ROR1-AS1, which interacted with insulin-like growth factor 2 binding protein 1 (IGF2BP1), thereby promoting the expression of SLC7 A11and inhibiting ferroptosis of lung cancer cells [176].

FRLncRNAs can also regulate ferroptosis in cancer cells through mechanisms different from directly binding to target proteins, such as affecting the stability of ferroptosis-related genes. It was demonstrated that lncRNA BDNF-AS could recruit WD repeat domain 5 (WDR5), thus affecting the protein expression of voltage-dependent anion channel 3 (VDAC3) through ubiquitination, which regulated ferroptosis in gastric cancer [185]. Li H et al. showed that lncRNA LINC00578 recruited ubiquitin-conjugating enzyme E2 K (UBE2 K) to inhibit the ubiquitination of SLC7 A11, thereby suppressing ferroptosis and promoting pancreatic cancer cell progression [190]. Lin Z et al. elucidated that hypoxia-inducible factor 1 subunit alpha (HIF-1α) upregulated lncRNA PMAN and enhanced the stability of SLC7 A11, thereby inhibiting ferroptosis and inducing the peritoneal metastasis of gastric cancer [182]. Zhang B et al. found that lncRNA HEPFAL improved the ubiquitination of SLC7 A11 and promoted the ferroptosis in HCC [186]. The overexpression of lncRNA OTUD6B-AS1 stabilizes the tripartite motif containing 16 (TRIM16) via binding to human antigen R (HuR) and increases GPX4-mediated ferroptosis, thus attenuating CRC radioresistance [179]. The methylation modification was also included in the regulatory mechanism by which FRlncRNA affected the stability of ferroptosis-related genes. Yan Z et al. found that methyltransferase 3 (METTL3)-modified lncRNA DSCAM-AS1 enhanced SLC7 A11 stability and promoted breast cancer progression by inhibiting ferroptosis [171]. lncRNA CBSLR could be induced by hypoxia and interact with YTH N6-methyladenosine RNA binding protein F2 (YTHDF2) to decrease the stability of cystathionine beta-synthase (CBS) mRNA and then protect gastric cancer cells from ferroptosis [181]. The m6 A modification of lncRNA ABHD11-AS1 induced ABHD11-AS1 to bind with insulin-like growing factor 2 mRNA-binding protein 2 (IGF2BP2) and enhance forkhead box M1 (FOXM1) stability, promoting CRC progression and inhibiting ferroptosis [187].

FRlncRNAs can encode micropeptides that regulate ferroptosis in cancer cells. By definition, non-coding RNAs (ncRNAs) have not been considered to code for proteins. However, thanks to the development of technologies such as deep ribosome sequencing (Ribo-Seq) and mass spectrometry, it has recently been proposed that ncRNAs may retain small open reading frames (smORFs) and potentially encode micropeptides, which may exhibit regulatory functions such as the development of tumors [191–193]. For example, a conserved small peptide with 53-amino acid that was encoded by lncRNA HOXB cluster antisense RNA 3 (HOXB-AS3) blocked pyruvate kinase 2 (PKM2) formation, miR-18a processing, and subsequent metabolic reprogramming, inhibiting tumorigenesis in CRC cells [194]. The dwarf open reading frame (DWORF), which was previously annotated as a lncRNA gene, encoded a peptide of 34 amino acids and enhanced sarcoplasmic/endoplasmic reticulum calcium ATPase (SERCA) activity in muscle [195]. HCP5-132aa, a peptide of 132 amino acids being encoded by the open reading frame in lncRNA HCP5, regulated GPX4 expression and lipid ROS level through the ferroptosis pathway, promoting triple-negative breast cancer growth [196].

FRlncRNAs in cancer drug resistance

Although significant breakthroughs has been made in oncological therapy, the development of cancer drug resistance remains a considerable challenge, with numerous preclinical and clinical studies focused on overcoming drug resistance [197]. FRlncRNAs have recently been proven to correlate with cancer drug resistance by targeting miRNAs or proteins.

Glioma is the most common primary intracranial malignant tumor in the brain. Dihydroartemisinin (DHA), a semisynthetic derivative of artemisinin, has been shown to exhibit antitumor activity to glioma. Gong H et al. found that DHA could induce ferroptosis in glioma cells, but lncRNA TUG1 attenuated the anti-glioma effect of DHA because TUG1 could directly bind with MYC-associated zinc finger (MAZ) and MAZ-regulated ferritin heavy chain 1 (FTH1) and thus inhibiting ferroptosis [198]. From the perspective of epigenetics, Luo J et al. explored the mechanism of temozolomide (TMZ)-resistance of glioma and found that lncRNA ATXN8OS acted on adenosine deaminase ADAR and stabilizes glutaminase 2 (GLS2), restraining TMZ-resistance of glioma both in vitro and in vivo [199].

Sorafenib is a first-line molecular targeted drug for the treatment of advanced HCC patients, but the development of drug resistance limits its efficacy. Gao Y et al. uncovered that lncRNA URB1-AS1 induced phase separation of ferritin and reduced the cellular free iron content, thus repressing the ferroptosis in sorafenib-resistant HCC samples [200]. Shi Z et al. revealed that lncRNA DUXAP8 facilitated SLC7 A11 palmitoylation, thereby enhancing SLC7 A11 action and reducing the sensitivity of HCC to sorafenib-induced ferroptosis [201].

Gefitinib is the first tyrosine kinase inhibitor approved by the US Food and Drug Administration (FDA), which inhibits the growth and spread of tumor cells by blocking the tyrosine kinase of the epidermal growth factor receptor (EGFR). Osimertinib is a highly selective third-generation EGFR inhibitor that can simultaneously target EGFR T790M and EGFR self-mutations [202]. Zhen S et al. identified that lncRNA NEAT1_1 sponged miR-338-3p to neutralize its suppression on aldo–keto reductase family 1 member C1 (AKR1 C1) and the significant upregulation AKR1 C1 stimulated ferroptosis protection, resulting in gefitinib resistance on EGFR-mutated lung adenocarcinoma cells [203]. More significantly, Wang L et al. designed a nanocatalytic sensitizer (VF/S/A@CaP) to deliver vitamin C-Fe(II), otubain-2 siRNA and antisense oligonucleotide for lncRNA MALAT1 and proved that VF/S/A@CaP could overcome Osimertinib resistance and metastasis of NSCLC via ferroptosis and multitarget interference [204].

FRlncRNAs are also involved in the regulation of drug resistance in CRC, breast cancer, and osteosarcoma. Li SQ et al. revealed that lncRNA SNHG4 promoted the instability of phosphatase and tensin homolog (PTEN), thereby suppressing ferroptosis and mediating the resistance to oxaliplatin in CRC [205]. Saatci O et al. elucidated that lncRNA LINC00152 destabilized phosphodiesterase 4D (PDE4D) and restored tamoxifen-dependent ferroptosis by increasing cAMP and Ca^{2+} levels [206]. The lncRNA SNHG14 was found to competitively sponge miR-206 and affect the expression of SLC7 A11, further preventing nutlin3a-resistant osteosarcoma cell line NR-SJSA1 cells undergoing ferroptosis [207].

FRlncRNAs in non-malignant diseases

FRlncRNAs are not only associated with the progression and prognostic prediction of cancer, but also with that of neurodegenerative diseases, cardiovascular diseases, ischemia/reperfusion injury, and other diseases (Table 4) [61, 208–236].

Neurodegenerative diseases

Neurodegenerative disorders are characterized by progressive loss of selectively vulnerable populations of neurons and result from neuronal degeneration or demyelination in the brain or spinal cord, such as Alzheimer's disease, Parkinson's disease, Huntington's disease, and amyotrophic lateral sclerosis [237]. An emerging number of evidence supports FRlncRNAs as key players for driving ferroptosis of neurodegenerative diseases. Zhao J.

Table 4 FRlncRNAs regulate other diseases

FRlncRNA	Target	Regulator	Disease	FRlncRNA	Target	Regulator	Disease
NEAT1	miR-150-5p	SLC7 A11	PD	FTX	miR-142-5p	GABPB1	Epilepsy
GM47283	miR-706	PTGS2	MI	SNHG7	TBX5	GLS2	CH
AC005332.7	miR-331-3p	CCND2	MI	PVT1	miR-214	SLC7 A11	I/R injury
NEAT1	miR-9-5p	GPX4	SAE	TUG1	SRSF1	ASCL4	I/R injury
SNHG1	miR-324-3p	GPX4	Sepsis	Mir9-3 hg	PUM2	PRDX6	I/R injury
MALAT1	miR-145-5p	MUC1	Endometriosis	ROR	miR-769-5p	CBX7	I/R injury
FRMD6-AS1	miR-491-5p	USP13	Fibrosis	Lnc-HMOX1	miR-3587	HMOX1	I/R injury
ZFAS1	miR-150-5p	SLC38 A1	Fibrosis	AABR07025387.1	miR-205	ACSL4	I/R injury
ADAMTS9-AS1	miR-6516-5p	GPX4	Endometriosis	WAC-AS1	BACH2	GPX4	I/R injury
lnc-HZ06	HIF1α-SUMO	NCOA4	Miscarriage	ZFAS1	miR-7-5p	ACSL4	DR
LINC00616	miR-370	TFRC	Periodontitis	SNHG1	miR-16-5p	ACSL4	DN
NORAD	HuR	GPX4	Aortic dissection	MEG3	PTBP1	GPX4	ARC
PVT1	miR-106b-5p	ACSL4	Atherosclerosis	Mir22 hg	YTHDC1	ANGPTL4	Sepsis
MEG3	miR-885-5p	SLC7 A11	Osteoarthritis	LINC00472	FOXO1	GPX4	AD
H19	miR-106b-5p	ACSL4	IH	HOTAIR	UPF1	ACSL4	IH

PD Parkinson's disease, *MI* Myocardial infarction, *CH* Cardiac hypertrophy, *I/R* Ischemia–reperfusion, *SAE* sepsis-associated encephalopathy, *DR* Diabetic retinopathy, *DN* Diabetic nephropathy, *ARC* Age-related cataract, *AD* Alzheimer's disease, aortic dissection, *IH* Intracerebral hemorrhage

et al. reported that lncRNA NEAT1 sponged miR-150-5p and regulated BRCA1-associated protein 1 (BAP1)/SLC7 A11 axis and the knockdown of NEAT1 inhibited 1-methyl-4-phenylpyridinium (MPP +)-induced ferroptosis in Parkinson's disease [208]. Zhang G et al. found that lncRNA FTX targeted miR-142-5p, regulated GABPB1 expression, and thus mitigated ferroptosis in magnesium-free (MGF)-induced rat hippocampal neurons displaying epileptiform discharges [209]. Lin P et al. screened the GEO database for FRlncRNAs and found that the inhibition of lncRNA LINC00472 upregulated tau protein phosphorylation and decreased the level of GPX4 via forkhead box O1 (FOXO1) in Alzheimer's disease cells or mouse model [234]. Wang M et al. identified that lncRNA NEAT1 acted on phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha (PIK3 CA), driving α-synuclein (α-syn) induced ferroptosis in Parkinson's disease [238].

Cardiovascular diseases

Cardiovascular diseases are a leading cause of morbidity with a high rate of hospitalization. Ferroptosis broadly participates in cardiovascular diseases involving iron regulation, metabolic mechanism, and lipid peroxidation [239]. Ferroptosis of vascular smooth muscle cells is related to the incidence of aortic dissection. Liao M et al. identified that the m6 A methylation of lncRNA NORAD was induced by methyltransferase-like 3 (METTL3) and induced the interaction between NORAD and HuR, which elevated GPX4 levels and inhibited the ferroptosis of vascular smooth muscle cells to attenuate the aortic dissection progression [229]. Myocardial infarction is the leading cause of sudden death. Gao F et al. identified that lncRNA Gm47283 sponged miR-706 and mediated the myocardial infarction via ferroptosis [210]. Dai R et al. identified that miR-331-3p was a target of lnc RNA AC005332.7 and AC005332.7 regulated cyclin D2 (CCND2), and thus blocks ferroptosis to alleviate acute myocardial infarction [212].

Coronary atherosclerotic disease exhibits an increasing incidence with high mortality and disability rates, which has prompted much research recently [240]. You Z et al. detected that the newly discovered lncRNA lnc-MRG-PRF-6:1 promotes macrophage ferroptosis induced by oxidized low-density lipoprotein (ox-LDL) through suppressing GPX4 in patients with coronary atherosclerotic disease [241]. Zhang M et al. showed that lncRNA PVT1 bind with miR-106b-5p and thus regulate ACSL4 to play a crucial role in atherosclerosis progression [231]. Tang F et al. revealed that lncRNA H19 exacerbated ox-LDL-induced arterial endothelial cell damage via enhancing ferroptosis in atherosclerosis [242].

Virus/bacterial infection

FRlncRNAs have also been shown to have roles in viral or bacterial infection. Viral infection often leads to significant changes in the host transcriptome including lncRNA, affecting the survival of the virus in host cells. Banerjee S et al. revealed that rotavirus induced the expression of lncRNA SLC7 A11-AS1 and thus decreased the gene SLC7 A11/xCT that encodes the light chain subunit of the system XC- to facilitate virus infection via

ferroptosis pathway [243]. Streptococcus pneumoniae (SP) is a major cause of community-acquired pneumonia which can involve ferroptosis. Xu L et al. explored the mechanism of lncRNA NEAT1 on SP-induced ferroptosis. They found that the loss of lncRNA NEAT1 activated GPX4 pathway to suppress SP-induced ferroptosis of human pulmonary alveolar epithelial cells, thereby alleviating cell injury and inflammatory response [244]. Sepsis is a kind of systemic inflammatory response syndrome caused by infection, which has high morbidity and mortality. Yang Y et al. demonstrated that lncRNA SNGH11 could sponge miR-324-3p and regulated the expression of GPX4, mediating the sepsis induced ferroptosis of liver injury cells [216]. Wei XB et al. revealed that sepsis induced high expression of serous exosome-derived lncRNA NEAT1, and its interaction with miR-9-5p regulated the expression of transferrin receptor (TFRC) and glutamic-oxaloacetic transaminase 1 (GOT1), promoting ferroptosis and exacerbating sepsis-associated encephalopathy (SAE) [214]. Huang Y et al. found that lncRNA Lcn2-204 promoted the expression of lipocalin-2 (Lcn2) and ferroptosis in a sepsis -induced myocardial injury mouse model [245]. Ferritinophagy-mediated ferroptosis plays a crucial role in fighting pathogen aggression. Deng W et al. showed that lncRNA Mir22 hg recruited the m6 A reader YTH domain-containing protein 1 (YTHDC1), stabilized angiopoietin-like 4 (ANGPTL4) and thereby lightened the expression of GPX4, upregulating ferroptosis and ferritinophagy in a sepsis mouse model [232].

Ischemia–reperfusion (I/R) injury

Organ ischemia can have serious consequences, leading to irreversible tissue damage, while tissue reperfusion is employed to prevent further ischemia. However, in some cases, ischemia and reperfusion may worsen the injury through a process called ischemia/reperfusion injury (IRI), leading to disease, disability, and even death [246, 247]. Ferroptosis is emerging as a critical pathway in I/R injury and the role of FRlncRNAs in I/R injury was investigated by several groups. Lu J et al. found that lncRNA PVT1 sponged miR-214 upregulating transferrin receptor 1 (TFR1) and tumor protein P53 (TP53) expression, thus protecting ferroptosis in brain I/R injury mouse models and PC12 cell models [213]. Lai G et al. uncovered that lncRNA regulator of reprogramming (ROR) regulated ferroptosis through miR-769-5p mediated CBX7 expression, inhibiting hypoxia induced cardiomyocyte ferroptosis in I/R injury model [218]. Tao W et al. demonstrated that lncRNA Lnc-HMOX1 interacts with miR-3587, which promotes the protein expression of heme oxygenase 1 (HMOX1) and alleviated renal I/R-induced ferroptotic injury [220]. Sun W et al. revealed that a novel lncRNA lncAABR07025387.1, as a competing endogenous RNA (ceRNA), upregulated the ACSL4 level by sponging miR-205 and thus promoting ferroptosis and enhancing myocardial I/R injury [222].

Ferroptosis is the leading cause of renal I/R injury after kidney transplantation, which can lead to delayed graft function and poor long-term prognosis. A "ferroptosis wave" [248] can lead to larger areas of tubular necrosis, thereby exacerbating renal transplant I/R injury [224]. Li X et al. deciphered that lncRNA WAC-AS1 was delivered by Renal I/R injury cell-secreted small extracellular vesicles (IRI-sEVs), consequently enhancing O-GlcNAcylation and facilitating ferroptosis [224].

Other diseases

Worldwide, the incidence of diabetes and its complications has increased rapidly, posing a serious threat to human health. Emerging studies have shown that the occurrence and development of diabetes and its complications are affected by lncRNAs-regulating ferroptosis [249]. Diabetic nephropathy, diabetic retinopathy, and diabetic cardiomyopathy are complications of diabetes [250]. Liu Y et al. validated that lncRNA ZFAS1 may act as a ceRNA to sponge miR-7-5p and downregulates its downstream molecule ACSL4 to inhibit the ferroptosis process in diabetic retinopathy [226]. Fang X et al. observed that lncRNA SNHG1 knockdown inhibited ferroptosis via the miR-16-5p/ACSL4 axis to alleviate diabetic nephropathy [228]. Ni T et al. investigated the important role of lncRNA ZFAS1 in the pathological process of diabetic cardiomyopathy and found that ZFAS1 acted as a ceRNA by competitively binding with miR-150-5p, modulating the expression of cyclin D2 (CCND2) to promote cardiomyocyte ferroptosis and diabetic cardiomyopathy [251].

Endometriosis is one of the most frequent diseases of reproductive-age women and a chronic disorder characterized by the implantation of endometrial glands and stroma outside the uterus [252]. Liang Z et al. demonstrated that lncRNA MALAT1 functioned as a ceRNA by sponging miR-145-5p to repress erastin-induced ferroptosis in ectopic endometrial stromal cells [61]. Wan Y et al. showed that lncRNA ADAMTS9-AS1 derepressed the expression of GPX4 through miR-6516-5p and repressed ferroptosis of endometrial stromal cells [223].

Osteoarthritis is one of the most common chronic diseases in the 60–69 age group after hypertension, obesity, hypercholesterolemia, and various soft tissue diseases [253]. FRlncRNAs have been described to be closely related to the pathogenesis of osteoarthritis. Qiu Y et al. screened ferroptosis-related genes using two machine-learning methods from GEO database and identified some lncRNAs by ceRNA network analysis, which could regulate the ferroptosis-related genes in osteoarthritis

[254]. Zhu C et al. showed that silencing of lncRNA MEG3 increased miR-885-5p and further downregulated SLC7 A11, inducing chondrocytes to erastin-induced ferroptosis in patients with osteoarthritis [233].

Fibrosis is an unregulated form of tissue repair, characterized by its main pathological changes of increased fibrous connective tissue and decreased parenchymal cells in organ tissues [255]. Li Z et al. found that lncRNA FRMD6-AS1 could interact with miR-491-5p, negatively modulating ubiquitin-specific peptidase 13 (USP13) and thus repressing ferroptosis, which promotes extracellular matrix (ECM) deposition and facilitating liver fibrosis [219]. Yang Y et al. demonstrated that lncRNA ZFAS1 acted as a ceRNA and sponged miR-150-5p to reduce solute carrier family 38 member 1 (SLC38 A1) expression, thus accelerating ferroptosis and pulmonary fibrosis progression [221].

Age-related cataract (ARC) is regarded as the principal cause of vision impairment among the aged [256]. Zhang X et al. found that the silencing of lncRNA MEG3 accelerates cell viability and attenuates ferroptosis by interaction with polypyrimidine tract binding protein 1 (PTBP1) for GPX4 messenger RNA decay in ARC [230]. Wang Y et al. revealed that m6 A modification of lncRNA ENST00000586817 regulated the expression of GPX4 and implicated in ferroptosis in ARCs [257].

FRlncRNAs have been reported as having regulatory roles in development and physiology, such as bronchopulmonary dysplasia, premature delivery, and andmiscarriage. Zhang Z et al. established a prediction model based on FRlncRNAs, which provides a non-invasive approach and is expected to improve the early detection and management of this challenging chronic lung disease in premature infants [258]. Qiu L et al. collected fetal membranes from a hundred premature newborns and hundred term newborns and found that lncRNA PSMA3-AS1 sponged miR-224-3p and upregulated NRF2, thereby activating GPX4 and suppressing ferroptosis of human trophoblast cells [259]. Tian P et al. identified for the first time that a novel lncRNA lnc-HZ06 regulated hypoxia, resulting in ferroptosis and then inducing miscarriage by suppressing SENP1-mediated deSUMOylation in hypoxic trophoblast cells [225]. Wang H et al. explored the role of lncRNA LINC00616 in the regulation of periodontitis and found that LINC00616 acted as a ceRNA to promote ferroptosis of periodontal ligament stem cells via the miR-370/transferrin receptor (TFRC) axis [227]. Chen B et al. evidenced that lncRNA H19 sponged miR-106b-5p and upregulated ACSL4, promoting ferroptosis of brain microvascular endothelial cells in intracerebral hemorrhage patients [235]. Jin ZL et al. found that lncRNA HOTAIR reversed paeonol-induced inhibition of ferroptosis by mediating the activation of UPF1/ACSL4 axis in neurons [236].

FRlncRNAs in the treatment of diseases

The therapeutic potential of FRlncRNAs lies in its specific targeting of miRNAs or proteins, influencing ferroptosis gene expression and potentially offering novel treatments for diseases. While these studies are still in the early stages and face challenges, they hold promise for future clinical applications.

The most promising avenue for targeted interventions is ferroptosis-related stem cell-derived exosomal lncRNAs. Sun Z et al. described that lncRNA TUG1 from human urine-derived stem cells (USCs)-derived exosomes (USC-Exo) regulated the stability of ACSL4 and the treatment of USC-Exo ameliorated kidney injury in I/R injury-induced acute kidney injury mouse models [215]. Zhang JK et al. showed that lncRNA Mir9-3 hg from bone marrow mesenchymal stem cells (BMSCs)-derived exosomes (BMSCs-Exo) suppressed cardiomyocyte ferroptosis in ischemia–reperfusion mice and the treatment of BMSCs-Exo attenuates I/R-induced cardiac injury [217]. Zhang L et al. found that lncRNA TUBB6/NRF2 pathways were activated by human umbilical cord mesenchymal stem cell-derived exosomes (HUCMSC-Exo) and the administration of HUCMSC-Exo suppressed traumatic brain injury-induced inflammation and ferroptosis after traumatic brain injury [260]. Shao C et al. investigated the exosomes derived from mesenchymal stem cells (MSC-Exo) for cell therapy of acute spinal cord injury. They showed that lncRNA lncGm36569 was enriched in the MSCs-Exo and acted as a competitive RNA of miR-5627-5p to induce FSP1 upregulation, enhancing repair of neurological function in the acute spinal cord injury mouse model [261].

Aside from stem cell-derived exosomal lncRNAs, other FRlncRNA strategies are developed for therapeutic intervention. Based on the previous findings that lncRNA metallothionein 1D pseudogene (MT1DP) aggravates oxidative stress by repressing antioxidation, Gai C et al. assembled nanoparticles combined with folate (FA)-modified liposome (FA-LP), erastin, and lncRNA MT1DP (E/M@FA-LPs) and proved that E/M@FA-LPs had a favorable therapeutic effect on NSCLC xenografts by MT1DP competitively sponging miR-365a-3p and thus regulating the expression of NRF2 protein [262].

Conclusions and perspectives

Recently, FRlncRNAs have been extensively investigated as they could play a major role in the control of cancer progression (Fig. 3) and non-malignant diseases (Fig. 4). The mechanism by which FRlncRNAs regulate the progression of cancer through targeted proteins or miRNAs is gradually being elucidated. An increasing number of reports have established signatures of FRlncRNAs for cancer prognosis through bioinformatics analysis from

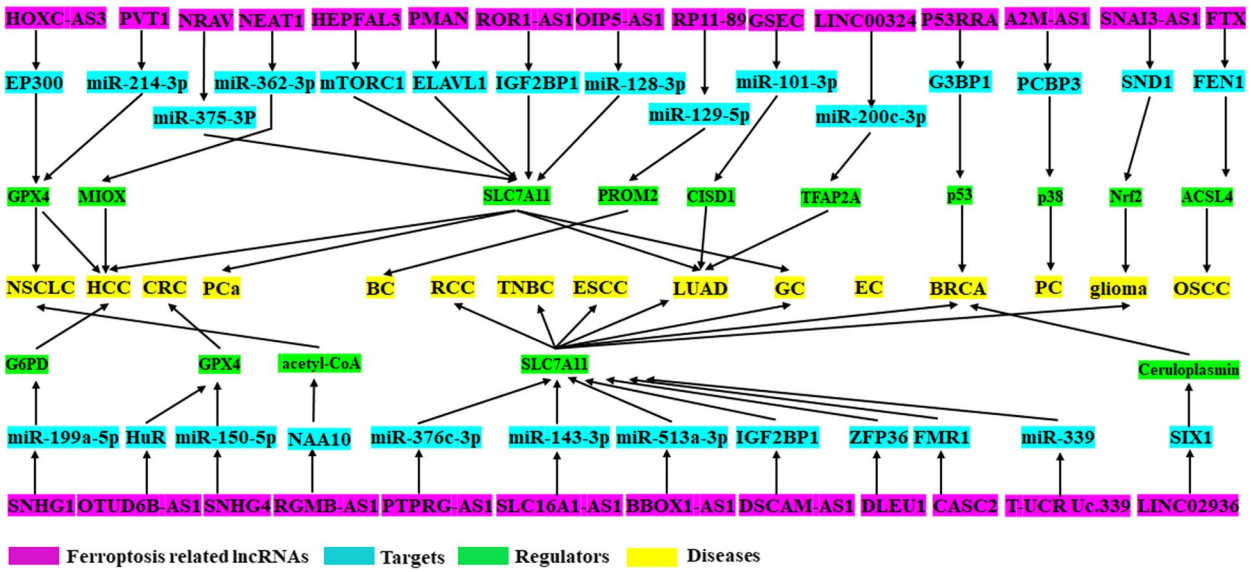

Fig. 3 FRlncRNAs that regulate cancer progression. HCC, hepatocellular carcinoma; BC, bladder cancer; RCC, renal cell carcinoma; PCa, prostate cancer; TNBC, Triple-negative breast cancer; LUAD, Lung adenocarcinoma; ESCC, esophageal squamous cell cancer; CRC, colorectal cancer; OSCC, oral squamous cell carcinoma; NSCLC, non-small cell lung cancer; EC, endometrial cancer; BRCA, breast cancer; GC, gastric cancer; PC, pancreatic cancer

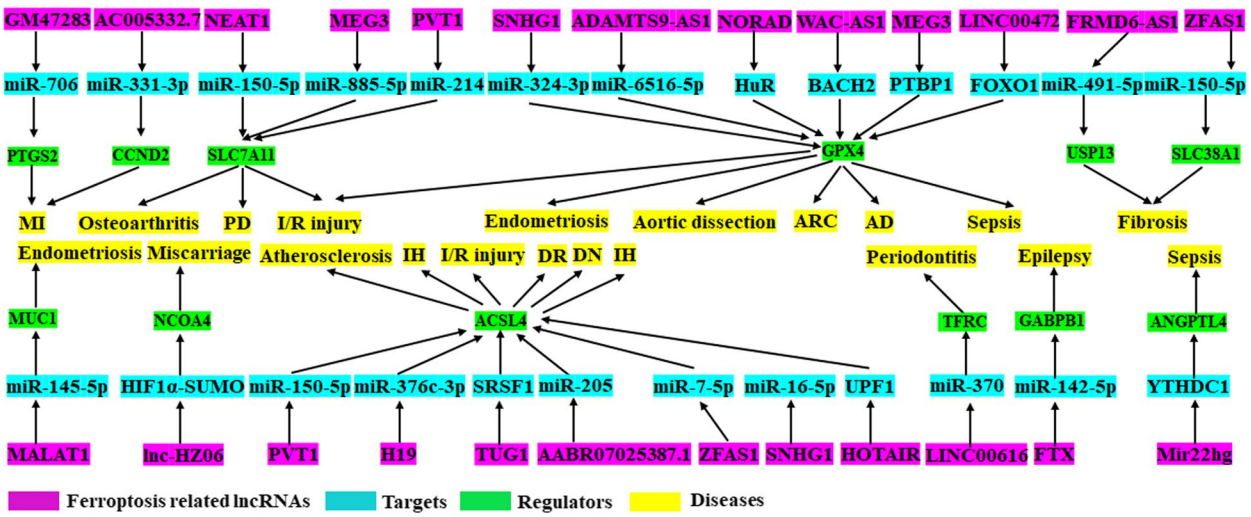

Fig. 4 FRlncRNAs that regulate non-malignant diseases. PD, Parkinson's disease; MI, myocardial infarction; CH, cardiac hypertrophy; I/R, ischemia–reperfusion; SAE, sepsis-associated encephalopathy; DR, diabetic retinopathy; DN, diabetic nephropathy; ARC, age-related cataract; AD, Alzheimer's disease; aortic dissection; IH, intracerebral hemorrhage

online databases. The mechanisms by which FRlncRNAs mediate tumor drug resistance have now been documented. The functions of FRlncRNAs in non-malignant diseases can now be therapeutically addressed. In sum, lipid metabolism, ROS, and iron regulation mediated by FRlncRNAs are critically involved in the occurrence and development of diseases.

These findings provide the basis for future exploiting the diagnostic and therapeutic potential of FRlncRNAs. One goal is to establish more robust FRlncRNA cancer prognostic signatures. So far, some lncRNAs, such as AP003555.1, ZFPM2-AS1, MKLN1-AS, and AC099850.3, have been identified as key players in multiple predictive models. FRlncRNAs may exhibit organ-specificity,

for example, AP003555.1 and AC010973.2 for prognosis of CRC [49, 52, 53, 103–105], and ZFPM2-AS1 and MKLN1-AS for HCC [54, 58, 111, 112]. It is thus anticipated that more reliable FRlncRNA prognostic signatures will be established for different types of cancer.

The second goal could be focused on monitoring FRlncRNA activities in vivo. Fluorescent probes can be used to monitor various biologically related molecules and microenvironments during ferroptosis at the cellular, tissue, and in vivo levels [263]. However, due to the lack of specific probes, imaging ferroptosis in patients remains a critical unresolved issue. A distinct, ferroptotic-like, necrotic cell death has recently been reported occurring in vivo during wounding of the Drosophila embryo using live imaging [264]. Unfortunately, this real-time imaging technology, which does not require probes, is not yet suitable for clinical application in patients. Thus, the development of future technologies may enable the in vivo detection of ferroptosis and facilitate further investigation into the roles of FRlncRNAs in diseases.

Another direction is to apply FRlncRNAs in clinical development. Although research reports from the past 3 years have shown that FRlncRNAs can interfere with drug resistance and that FRlncRNAs in stem cell-derived exosomes could potentially treat diseases such as ischemia–reperfusion, the enormous potential of FRlncRNAs in treating diseases remains largely unexplored. Nonetheless, it is worth reiterating that targeting lncRNAs is a promising method for treating various diseases [265]. A better understanding of the mechanisms associated with FRlncRNA-mediated diseases, improvements in delivering FRlncRNAs to target cells, reducing the immunogenicity of lncRNA drugs, and ensuring a significant clinical response will significantly promote the application of FRlncRNAs in therapeutic applications.

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References

1. Estevao D, da Cruz-Ribeiro M, Cardoso AP, Costa AM, Oliveira MJ, Duarte TL, da Cruz TB. Iron metabolism in colorectal cancer: a balancing act. Cell Oncol (Dordr). 2023;46(6):1545–58.
2. Stockwell BR, Friedmann Angeli JP, Bayir H, Bush AI, Conrad M, Dixon SJ, Fulda S, Gascon S, Hatzios SK, Kagan VE, et al. Ferroptosis: A Regulated Cell Death Nexus Linking Metabolism, Redox Biology, and Disease. Cell. 2017;171(2):273–85.
3. You HM, Wang L, Meng HW, Huang C, Fang GY, Li J. Pyroptosis: shedding light on the mechanisms and links with cancers. Front Immunol. 2023;14:1290885.
4. Tang D, Kang R, Berghe TV, Vandenabeele P, Kroemer G. The molecular machinery of regulated cell death. Cell Res. 2019;29(5):347–64.
5. Tang D, Chen X, Kang R, Kroemer G. Ferroptosis: molecular mechanisms and health implications. Cell Res. 2021;31(2):107–25.
6. Dixon SJ, Lemberg KM, Lamprecht MR, Skouta R, Zaitsev EM, Gleason CE, Patel DN, Bauer AJ, Cantley AM, Yang WS, et al. Ferroptosis: an iron-dependent form of nonapoptotic cell death. Cell. 2012;149(5):1060–72.
7. Li J, Cao F, Yin HL, Huang ZJ, Lin ZT, Mao N, Sun B, Wang G. Ferroptosis: past, present and future. Cell Death Dis. 2020;11(2):88.
8. Stockwell BR. Ferroptosis turns 10: Emerging mechanisms, physiological functions, and therapeutic applications. Cell. 2022;185(14):2401–21.
9. Mou Y, Wang J, Wu J, He D, Zhang C, Duan C, Li B. Ferroptosis, a new form of cell death: opportunities and challenges in cancer. J Hematol Oncol. 2019;12(1):34.
10. Zheng DW, Lei Q, Zhu JY, Fan JX, Li CX, Li C, Xu Z, Cheng SX, Zhang XZ. Switching Apoptosis to Ferroptosis: Metal-Organic Network for High-Efficiency Anticancer Therapy. Nano Lett. 2017;17(1):284–91.
11. Ma S, Dielschneider RF, Henson ES, Xiao W, Choquette TR, Blankstein AR, Chen Y, Gibson SB. Ferroptosis and autophagy induced cell death occur independently after siramesine and lapatinib treatment in breast cancer cells. PLoS ONE. 2017;12(8): e0182921.
12. Muller T, Dewitz C, Schmitz J, Schroder AS, Brasen JH, Stockwell BR, Murphy JM, Kunzendorf U, Krautwald S. Necroptosis and ferroptosis are alternative cell death pathways that operate in acute kidney failure. Cell Mol Life Sci. 2017;74(19):3631–45.
13. Lei G, Zhuang L, Gan B. Targeting ferroptosis as a vulnerability in cancer. Nat Rev Cancer. 2022;22(7):381–96.
14. Jiang X, Stockwell BR, Conrad M. Ferroptosis: mechanisms, biology and role in disease. Nat Rev Mol Cell Biol. 2021;22(4):266–82.
15. Wang C, Liu H, Xu S, Deng Y, Xu B, Yang T, Liu W. Ferroptosis and Neurodegenerative Diseases: Insights into the Regulatory Roles of SLC7A11. Cell Mol Neurobiol. 2023;43(6):2627–42.
16. Zhang Q, Luo Y, Peng L, Rong X, Liu Y, Li J, Luo J. Ferroptosis in cardiovascular diseases: role and mechanism. Cell Biosci. 2023;13(1):226.
17. Laukaitiene J, Gujyte G, Kadusevicius E. Cardiomyocyte damage: ferroptosis relation to ischemia-reperfusion injury and future treatment options. Int J Mol Sci. 2023;24(16):12846.
18. Consortium EP, Birney E, Stamatoyannopoulos JA, Dutta A, Guigo R, Gingeras TR, Margulies EH, Weng Z, Snyder M, Dermitzakis ET, et al. Identification and analysis of functional elements in 1% of the human genome by the ENCODE pilot project. Nature. 2007;447(7146):799–816.
19. Consortium EP. An integrated encyclopedia of DNA elements in the human genome. Nature. 2012;489(7414):57–74.
20. Djebali S, Davis CA, Merkel A, Dobin A, Lassmann T, Mortazavi A, Tanzer A, Lagarde J, Lin W, Schlesinger F, et al. Landscape of transcription in human cells. Nature. 2012;489(7414):101–8.
21. Quinn JJ, Chang HY. Unique features of long non-coding RNA biogenesis and function. Nat Rev Genet. 2016;17(1):47–62.
22. Aurilia C, Donati S, Palmini G, Miglietta F, Iantomasi T, Brandi ML. The involvement of long non-coding rnas in bone. Int J Mol Sci. 2021;22(8):3909.

23. Wen Y, Lei W, Zhang J, Liu Q, Li Z. Advances in understanding the role of lncRNA in ferroptosis. PeerJ. 2024;12: e17933.
24. Huang K, Yu L, Lu D, Zhu Z, Shu M, Ma Z. Long non-coding RNAs in ferroptosis, pyroptosis and necroptosis: from functions to clinical implications in cancer therapy. Front Oncol. 2024;14:1437698.
25. Shi W, Sethi G. Long noncoding RNAs induced control of ferroptosis: Implications in cancer progression and treatment. J Cell Physiol. 2023;238(5):880–95.
26. Balihodzic A, Prinz F, Dengler MA, Calin GA, Jost PJ, Pichler M. Non-coding RNAs and ferroptosis: potential implications for cancer therapy. Cell Death Differ. 2022;29(6):1094–106.
27. Bannai S, Kitamura E. Transport interaction of L-cystine and L-glutamate in human diploid fibroblasts in culture. J Biol Chem. 1980;255(6):2372–6.
28. Tu H, Tang LJ, Luo XJ, Ai KL, Peng J. Insights into the novel function of system Xc- in regulated cell death. Eur Rev Med Pharmacol Sci. 2021;25(3):1650–62.
29. Dolma S, Lessnick SL, Hahn WC, Stockwell BR. Identification of genotype-selective antitumor agents using synthetic lethal chemical screening in engineered human tumor cells. Cancer Cell. 2003;3(3):285–96.
30. Yang WS, Stockwell BR. Synthetic lethal screening identifies compounds activating iron-dependent, nonapoptotic cell death in oncogenic-RAS-harboring cancer cells. Chem Biol. 2008;15(3):234–45.
31. Yang WS, Kim KJ, Gaschler MM, Patel M, Shchepinov MS, Stockwell BR. Peroxidation of polyunsaturated fatty acids by lipoxygenases drives ferroptosis. Proc Natl Acad Sci U S A. 2016;113(34):E4966-4975.
32. Dixon SJ, Winter GE, Musavi LS, Lee ED, Snijder B, Rebsamen M, Superti-Furga G, Stockwell BR. Human Haploid Cell Genetics Reveals Roles for Lipid Metabolism Genes in Nonapoptotic Cell Death. ACS Chem Biol. 2015;10(7):1604–9.
33. Doll S, Proneth B, Tyurina YY, Panzilius E, Kobayashi S, Ingold I, Irmler M, Beckers J, Aichler M, Walch A, et al. ACSL4 dictates ferroptosis sensitivity by shaping cellular lipid composition. Nat Chem Biol. 2017;13(1):91–8.
34. Kagan VE, Mao G, Qu F, Angeli JP, Doll S, Croix CS, Dar HH, Liu B, Tyurin VA, Ritov VB, et al. Oxidized arachidonic and adrenic PEs navigate cells to ferroptosis. Nat Chem Biol. 2017;13(1):81–90.
35. Wenzel SE, Tyurina YY, Zhao J, St Croix CM, Dar HH, Mao G, Tyurin VA, Anthonymuthu TS, Kapralov AA, Amoscato AA, et al. PEBP1 Wardens Ferroptosis by Enabling Lipoxygenase Generation of Lipid Death Signals. Cell. 2017;171(3):628-641 e626.
36. Feng S, Tang D, Wang Y, Li X, Bao H, Tang C, Dong X, Li X, Yang Q, Yan Y, et al. The mechanism of ferroptosis and its related diseases. Mol Biomed. 2023;4(1):33.
37. Koppula P, Zhuang L, Gan B. Cytochrome P450 reductase (POR) as a ferroptosis fuel. Protein Cell. 2021;12(9):675–9.
38. Yang WS, SriRamaratnam R, Welsch ME, Shimada K, Skouta R, Viswanathan VS, Cheah JH, Clemons PA, Shamji AF, Clish CB, et al. Regulation of ferroptotic cancer cell death by GPX4. Cell. 2014;156(1–2):317–31.
39. Bersuker K, Hendricks JM, Li Z, Magtanong L, Ford B, Tang PH, Roberts MA, Tong B, Maimone TJ, Zoncu R, et al. The CoQ oxidoreductase FSP1 acts parallel to GPX4 to inhibit ferroptosis. Nature. 2019;575(7784):688–92.
40. Mao C, Liu X, Zhang Y, Lei G, Yan Y, Lee H, Koppula P, Wu S, Zhuang L, Fang B, et al. DHODH-mediated ferroptosis defence is a targetable vulnerability in cancer. Nature. 2021;593(7860):586–90.
41. Kraft VAN, Bezjian CT, Pfeiffer S, Ringelstetter L, Muller C, Zandkarimi F, Merl-Pham J, Bao X, Anastasov N, Kossl J, et al. GTP Cyclohydrolase 1/Tetrahydrobiopterin Counteract Ferroptosis through Lipid Remodeling. ACS Cent Sci. 2020;6(1):41–53.
42. Hu Q, Wei W, Wu D, Huang F, Li M, Li W, Yin J, Peng Y, Lu Y, Zhao Q, et al. Blockade of GCH1/BH4 Axis Activates Ferritinophagy to Mitigate the Resistance of Colorectal Cancer to Erastin-Induced Ferroptosis. Front Cell Dev Biol. 2022;10: 810327.
43. He Y, Huang X, Ma Y, Yang G, Cui Y, Lv X, Zhao R, Jin H, Tong Y, Zhang X, et al. A novel aging-associated lncRNA signature for predicting prognosis in osteosarcoma. Sci Rep. 2024;14(1):1386.
44. Feng D, Li L, Shi X, Zhu W, Wang J, Wu R, Li D, Wei W, Han P. Identification of senescence-related lncRNA prognostic index correlating with prognosis and radiosensitivity in prostate cancer patients. Aging (Albany NY). 2023;15(18):9358–76.
45. Wu Y, Liang L, Li Q, Shu L, Wang P, Huang S. The role of pyroptosis-related lncRNA risk signature in ovarian cancer prognosis and immune system. Discov Oncol. 2023;14(1):149.
46. Zeng T, Ye J, Wang H, Tian W. Identification of pyroptosis-related lncRNA subtype and signature predicts the prognosis in bladder cancer. Medicine (Baltimore). 2023;102(42): e35195.
47. Li D, Qu G, Ling S, Sun Y, Cui Y, Yang Y, Cao X. A cuproptosis-related lncRNA signature to predict prognosis and immune microenvironment of colon adenocarcinoma. Sci Rep. 2023;13(1):6284.
48. Di H, Zhao J, Zhu X, Zhou X, Hu Y, Wang M, Qiu Z, Zhang W, Chen X. A novel prognostic signature for lung adenocarcinoma based on cuproptosis-related lncRNAs: A Review. Medicine (Baltimore). 2022;101(49): e31924.
49. Wu Z, Lu Z, Li L, Ma M, Long F, Wu R, Huang L, Chou J, Yang K, Zhang Y, et al. Identification and Validation of Ferroptosis-Related LncRNA Signatures as a Novel Prognostic Model for Colon Cancer. Front Immunol. 2021;12: 783362.
50. Lu J, Tan J, Yu X. A Prognostic Ferroptosis-Related lncRNA Model Associated With Immune Infiltration in Colon Cancer. Front Genet. 2022;13: 934196.
51. Zhang W, Fang D, Li S, Bao X, Jiang L, Sun X. Construction and Validation of a Novel Ferroptosis-Related lncRNA Signature to Predict Prognosis in Colorectal Cancer Patients. Front Genet. 2021;12: 709329.
52. Xu S, Zhou Y, Luo J, Chen S, Xie J, Liu H, Wang Y, Li Z. Integrated analysis of a ferroptosis-related LncRNA signature for evaluating the prognosis of patients with colorectal cancer. Genes (Basel). 2022;13(6):1094.
53. Chen W, Deng J, Zhou Y. The construction of a novel ferroptosis-related lncRNA model to predict prognosis in colorectal cancer patients. Medicine (Baltimore). 2023;102(10): e33114.
54. Xu Z, Peng B, Liang Q, Chen X, Cai Y, Zeng S, Gao K, Wang X, Yi Q, Gong Z, et al. Construction of a Ferroptosis-Related Nine-lncRNA Signature for Predicting Prognosis and Immune Response in Hepatocellular Carcinoma. Front Immunol. 2021;12: 719175.
55. Fang C, Liu S, Feng K, Huang C, Zhang Y, Wang J, Lin H, Wang J, Zhong C. Ferroptosis-related lncRNA signature predicts the prognosis and immune microenvironment of hepatocellular carcinoma. Sci Rep. 2022;12(1):6642.
56. Zong K, Lin C, Luo K, Deng Y, Wang H, Hu J, Chen S, Li R. Ferroptosis-related lncRNA NRAV affects the prognosis of hepatocellular carcinoma via the miR-375-3P/SLC7A11 axis. BMC Cancer. 2024;24(1):496.
57. Huang A, Li T, Xie X, Xia J. Computational Identification of Immune- and Ferroptosis-Related LncRNA Signature for Prognosis of Hepatocellular Carcinoma. Front Mol Biosci. 2021;8: 759173.
58. Zhao L, You Z, Bai Z, Xie J. Machine learning-based construction of a ferroptosis and necroptosis associated lncRNA signature for predicting prognosis and immunotherapy response in hepatocellular cancer. Front Oncol. 2023;13:1171878.
59. Xuan Z, Liu L, Huang P, Ye Q. Establishment of a novel ferroptosis-correlative lncRNA signature and validation of ST3GAL4-AS1 for predicting overall survival of hepatocellular carcinoma. Asian J Surg. 2024;47(5):2524–6.
60. Zhang Z, Zhang W, Wang Y, Wan T, Hu B, Li C, Ge X, Lu S. Construction and Validation of a Ferroptosis-Related lncRNA Signature as a Novel Biomarker for Prognosis, Immunotherapy and Targeted Therapy in Hepatocellular Carcinoma. Front Cell Dev Biol. 2022;10: 792676.
61. Liang Z, Wu Q, Wang H, Tan J, Wang H, Gou Y, Cao Y, Li Z, Zhang Z. Silencing of lncRNA MALAT1 facilitates erastin-induced ferroptosis in endometriosis through miR-145-5p/MUC1 signaling. Cell Death Discov. 2022;8(1):190.
62. Xu Y, Chen Y, Niu Z, Yang Z, Xing J, Yin X, Guo L, Zhang Q, Yang Y, Han Y. Ferroptosis-related lncRNA signature predicts prognosis and immunotherapy efficacy in cutaneous melanoma. Front Surg. 2022;9: 860806.
63. Xiong K, Wang Z, Hounye AH, Peng L, Zhang J, Qi M. Development and validation of ferroptosis-related lncRNA signature and immune-related gene signature for predicting the prognosis of cutaneous melanoma patients. Apoptosis. 2023;28(5–6):840–59.
64. Guo S, Chen J, Yi X, Lu Z, Guo W. Identification and validation of ferroptosis-related lncRNA signature as a prognostic model for skin cutaneous melanoma. Front Immunol. 2022;13: 985051.
65. Ma X, Yu S, Zhao B, Bai W, Cui Y, Ni J, Lyu Q, Zhao J. Development and Validation of a Novel Ferroptosis-Related LncRNA Signature for

Predicting Prognosis and the Immune Landscape Features in Uveal Melanoma. Front Immunol. 2022;13: 922315.
66. Sun S, Zhang G, Zhang L. A Novel Ferroptosis-Related lncRNA Prognostic Model and Immune Infiltration Features in Skin Cutaneous Melanoma. Front Cell Dev Biol. 2021;9: 790047.
67. Zhu J, Zhao Y, Wu G, Zhang X, Chen Q, Yang B, Guo X, Ji S, Gu K. Ferroptosis-Related lncRNA Signature Correlates with the Prognosis, Tumor Microenvironment, and Therapeutic Sensitivity of Esophageal Squamous Cell Carcinoma. Oxid Med Cell Longev. 2022;2022:7465880.
68. Dong Y, Zhao K, Qiu Q, Zheng S, Zhang X, Liu J, Xu H, Pan X, Liu M. Ferroptosis-associated lncRNA prognostic signature predicts prognosis and immune response in laryngeal squamous carcinoma. Cell Mol Biol (Noisy-le-grand). 2023;69(12):223–31.
69. Qin Y, Zhang D, Zhang H, Hou L, Wang Z, Yang L, Zhang M, Zhao G, Yao Q, Ling R, et al. Construction of a ferroptosis-related five-lncRNA signature for predicting prognosis and immune response in thyroid carcinoma. Cancer Cell Int. 2022;22(1):296.
70. Yao J, Chen X, Liu X, Li R, Zhou X, Qu Y. Characterization of a ferroptosis and iron-metabolism related lncRNA signature in lung adenocarcinoma. Cancer Cell Int. 2021;21(1):340.
71. Wang Y, Lu G, Xue X, Xie M, Wang Z, Ma Z, Feng Y, Shao C, Duan H, Pan M, et al. Characterization and validation of a ferroptosis-related LncRNA signature as a novel prognostic model for lung adenocarcinoma in tumor microenvironment. Front Immunol. 2022;13: 903758.
72. Guo Y, Qu Z, Li D, Bai F, Xing J, Ding Q, Zhou J, Yao L, Xu Q. Identification of a prognostic ferroptosis-related lncRNA signature in the tumor microenvironment of lung adenocarcinoma. Cell Death Discov. 2021;7(1):190.
73. Lu L, Liu LP, Zhao QQ, Gui R, Zhao QY. Identification of a Ferroptosis-Related LncRNA Signature as a Novel Prognosis Model for Lung Adenocarcinoma. Front Oncol. 2021;11: 675545.
74. Shen S, Yang D, Yang Y, Chen Y, Xiong J, Hu X. A Novel Prognostic Ferroptosis-Related lncRNA Signature Associated with Immune Landscape in Invasive Breast Cancer. Dis Markers. 2022;2022:9168556.
75. Zhang Y, He R, Lei X, Mao L, Yin Z, Zhong X, Cao W, Zheng Q, Li D. Comprehensive Analysis of a Ferroptosis-Related lncRNA Signature for Predicting Prognosis and Immune Landscape in Osteosarcoma. Front Oncol. 2022;12: 880459.
76. Feng S, Yin H, Zhang K, Shan M, Ji X, Luo S, Shen Y. Integrated clinical characteristics and omics analysis identifies a ferroptosis and iron-metabolism-related lncRNA signature for predicting prognosis and therapeutic responses in ovarian cancer. J Ovarian Res. 2022;15(1):10.
77. Peng J, Hao Y, Rao B, Zhang Z. A ferroptosis-related lncRNA signature predicts prognosis in ovarian cancer patients. Transl Cancer Res. 2021;10(11):4802–16.
78. Yang S, Ji J, Wang M, Nie J, Wang S. Construction of ovarian cancer prognostic model based on the investigation of ferroptosis-related lncRNA. Biomolecules. 2023;13(2):306.
79. Lai D, Tan L, Zuo X, Liu D, Jiao D, Wan G, Lu C, Shen D, Gu X. Prognostic Ferroptosis-Related lncRNA Signatures Associated With Immunotherapy and Chemotherapy Responses in Patients With Stomach Cancer. Front Genet. 2021;12: 798612.
80. Wei J, Zeng Y, Gao X, Liu T. A novel ferroptosis-related lncRNA signature for prognosis prediction in gastric cancer. BMC Cancer. 2021;21(1):1221.
81. Cai Y, Wu S, Jia Y, Pan X, Li C. Potential Key Markers for Predicting the Prognosis of Gastric Adenocarcinoma Based on the Expression of Ferroptosis-Related lncRNA. J Immunol Res. 2022;2022:1249290.
82. Chen M, Nie Z, Li Y, Gao Y, Wen X, Cao H, Zhang S. A New Ferroptosis-Related lncRNA Signature Predicts the Prognosis of Bladder Cancer Patients. Front Cell Dev Biol. 2021;9: 699804.
83. Wang Y, Zhang S, Bai Y, Li G, Wang S, Chen J, Liu X, Yin H. Development and Validation of Ferroptosis-Related LncRNA Biomarker in Bladder Carcinoma. Front Cell Dev Biol. 2022;10: 809747.
84. Huang L, Zhang J, Gong F, Han Y, Huang X, Luo W, Cai H, Zhang F. Identification and validation of ferroptosis-related lncRNA signatures as a novel prognostic model for glioma. Front Genet. 2022;13: 927142.
85. Huang QR, Li JW, Yan P, Jiang Q, Guo FZ, Zhao YN, Mo LG. Establishment and Validation of a Ferroptosis-Related lncRNA Signature for Prognosis Prediction in Lower-Grade Glioma. Front Neurol. 2022;13: 861438.
86. He Y, Ye Y, Tian W, Qiu H. A Novel lncRNA Panel Related to Ferroptosis, Tumor Progression, and Microenvironment is a Robust Prognostic Indicator for Glioma Patients. Front Cell Dev Biol. 2021;9: 788451.
87. Li J, Li W, Wang H, Ni B, Liu Y. Development and validation of a novel ferroptosis-related lncRNA prognostic signature for pancreatic adenocarcinoma. Mol Med Rep. 2023;27(2):56.
88. Lai J, Miao S, Ran L. Ferroptosis-associated lncRNA prognostic signature predicts prognosis and immune response in clear cell renal cell carcinoma. Sci Rep. 2023;13(1):2114.
89. Ju L, Shi Y, Liu G. Identification and validation of a ferroptosis-related lncRNA signature to robustly predict the prognosis, immune microenvironment, and immunotherapy efficiency in patients with clear cell renal cell carcinoma. PeerJ. 2022;10: e14506.
90. Zheng Q, Gong Z, Lin S, Ou D, Lin W, Shen P. Integrated analysis of a competing endogenous RNA network reveals a ferroptosis-related 6-lncRNA prognostic signature in clear cell renal cell carcinoma. Adv Clin Exp Med. 2024;12:1391–1407.
91. Gong Y, Zhang C, Li H, Yu X, Li Y, Liu Z, He R. Ferroptosis-Related lncRNA to Predict the Clinical Outcomes and Molecular Characteristics of Kidney Renal Papillary Cell Carcinoma. Curr Issues Mol Biol. 2024;46(3):1886–903.
92. Qin A, Qian Q, Cui X, Bai W. Ferroptosis-related lncRNA model based on CFAP58-DT for predicting prognosis and immunocytes infiltration in endometrial cancer. Ann Transl Med. 2023;11(3):151.
93. Jiang Z, Li J, Feng W, Sun Y, Bu J. A Ferroptosis-Related lncRNA Model to Enhance the Predicted Value of Cervical Cancer. J Oncol. 2022;2022:6080049.
94. Dang R, Jin M, Nan J, Jiang X, He Z, Su F, Li D. A Novel Ferroptosis-Related lncRNA Signature for Prognosis Prediction in Patients with Papillary Renal Cell Carcinoma. Int J Gen Med. 2022;15:207–22.
95. Liu H, Zhang M, Zhang T, Shi M, Lu W, Yang S, Cui Q, Li Z. Identification of a ferroptosis-related lncRNA signature with prognosis for Wilms tumor. Transl Pediatr. 2021;10(10):2418–31.
96. Li H, Liu L, Huang T, Jin M, Zheng Z, Zhang H, Ye M, Liu K. Establishment of a novel ferroptosis-related lncRNA pair prognostic model in colon adenocarcinoma. Aging (Albany NY). 2021;13(19):23072–95.
97. Xie H, Shi M, Liu Y, Cheng C, Song L, Ding Z, Jin H, Cui X, Wang Y, Yao D, et al. Identification of m6A- and ferroptosis-related lncRNA signature for predicting immune efficacy in hepatocellular carcinoma. Front Immunol. 2022;13: 914977.
98. Xiao W, Lai Y, Yang H, Que H. Predictive Role of a Novel Ferroptosis-Related lncRNA Pairs Model in the Prognosis of Papillary Thyroid Carcinoma. Biochem Genet. 2024;62(2):775–97.
99. Li J, Xiang R, Song W, Wu J, Kong C, Fu T. A Novel Ferroptosis-Related LncRNA Pair Prognostic Signature Predicts Immune Landscapes and Treatment Responses for Gastric Cancer Patients. Front Genet. 2022;13: 899419.
100. Li X, Zhou L, Lu T, Zhang L, Li Y, Xu J, Yin M, Long H. Constructing an immune- and ferroptosis-related lncRNA signature to predict the immune landscape of human bladder cancer. J Clin Lab Anal. 2022;36(5): e24389.
101. Zhou R, Liang J, Tian H, Chen Q, Yang C, Liu C. Development of a Ferroptosis-Related lncRNA Signature to Predict the Prognosis and Immune Landscape of Bladder Cancer. Dis Markers. 2021;2021:1031906.
102. Liu X, Shi X, Guo W, Ke Y, Li Y, Pan S, Li X, Liu M, Liu M, Wang Y, et al. A Promising Esophageal Cancer Prognostic Signature of Ferroptosis-Related LncRNA to Predict Immune Scenery and Immunotherapy Response. Int J Gen Med. 2021;14:5845–62.
103. Guo Y, Wang Z, Tian Y, Li L, Dong J. A Ferroptosis-related lncRNAs signature predicts prognosis of colon adenocarcinoma. Life (Basel). 2023;13(7):1557.
104. Li N, Shen J, Qiao X, Gao Y, Su HB, Zhang S. Long Non-Coding RNA Signatures Associated with Ferroptosis Predict Prognosis in Colorectal Cancer. Int J Gen Med. 2022;15:33–43.
105. Liang Y, Sun HX, Ma B, Meng QK. Identification of a Genomic Instability-Related Long Noncoding RNA Prognostic Model in Colorectal Cancer Based on Bioinformatic Analysis. Dis Markers. 2022;2022:4556585.
106. Dong X, Liao P, Liu X, Yang Z, Wang Y, Zhong W, Wang B. Construction and validation of a reliable disulfidptosis-related LncRNAs signature of the subtype, prognostic, and immune landscape in colon cancer. Int J Mol Sci. 2023;24(16):12915.

107. Chen P, Yu J, Luo Q, Li J, Wang W. Construction of disulfidptosis-related lncRNA signature for predicting the prognosis and immune escape in colon adenocarcinoma. BMC Gastroenterol. 2023;23(1):382.
108. Chen R, Wei JM. Integrated analysis identifies oxidative stress-related lncRNAs associated with progression and prognosis in colorectal cancer. BMC Bioinformatics. 2023;24(1):76.
109. Sasa GBK, Xuan C, Lyu G, Ding X, Meiyu F. Long Non-coding RNA ZFPM2-AS1: A Novel Biomarker in the Pathogenesis of Human Cancers. Mol Biotechnol. 2022;64(7):725–42.
110. Tan F. ZFPM2-AS1: An Oncogenic Long Non-coding RNA in Multiple Cancer Types. Mini Rev Med Chem. 2023;23(1):88–98.
111. Chen ZA, Tian H, Yao DM, Zhang Y, Feng ZJ, Yang CJ. Identification of a Ferroptosis-Related Signature Model Including mRNAs and lncRNAs for Predicting Prognosis and Immune Activity in Hepatocellular Carcinoma. Front Oncol. 2021;11: 738477.
112. Lin X, Yang S. A prognostic signature based on the expression profile of the ferroptosis-related long non-coding RNAs in hepatocellular carcinoma. Adv Clin Exp Med. 2022;31(10):1099–109.
113. Chen D, Wang M, Jiang X, Xiong Z. Comprehensive analysis of ZFPM2-AS1 prognostic value, immune microenvironment, drug sensitivity, and co-expression network: from gastric adenocarcinoma to pan-cancers. Discov Oncol. 2022;13(1):24.
114. Wang S, Bai H, Fei S, Miao B. A Cuproptosis-Related LncRNA Risk Model for Predicting Prognosis and Immunotherapeutic Efficacy in Patients with Hepatocellular Carcinoma. Biochem Genet. 2024;62(3):2332–51.
115. Chen M, Wu GB, Hua S, Zhao ZF, Li HJ, Luo M. Identification and validation of a prognostic model of necroptosis-related lncRNAs in hepatocellular carcinoma. Front Genet. 2022;13: 907859.
116. Xun Z, Wang Y, Long J, Li Y, Yang X, Sun H, Zhao H. Development and validation of a genomic instability-related lncRNA prognostic model for hepatocellular carcinoma. Front Genet. 2022;13:1034979.
117. Wu J, Ren X, Wang N, Zhou R, Chen M, Cai Y, Lin S, Zhang H, Xie X, Dang C, et al. A Mutation-Related Long Noncoding RNA Signature of Genome Instability Predicts Immune Infiltration and Hepatocellular Carcinoma Prognosis. Front Genet. 2021;12: 779554.
118. Wang T, Yang Y, Sun T, Qiu H, Wang J, Ding C, Lan R, He Q, Wang W. The Pyroptosis-Related Long Noncoding RNA Signature Predicts Prognosis and Indicates Immunotherapeutic Efficiency in Hepatocellular Carcinoma. Front Cell Dev Biol. 2022;10: 779269.
119. Yang C, Zhang L, Hao X, Tang M, Zhou B, Hou J. Identification of a Novel N7-Methylguanosine-Related LncRNA Signature Predicts the Prognosis of Hepatocellular Carcinoma and Experiment Verification. Curr Oncol. 2022;30(1):430–48.
120. Wu H, Liu T, Qi J, Qin C, Zhu Q. Four Autophagy-Related lncRNAs Predict the Prognosis of HCC through Coexpression and ceRNA Mechanism. Biomed Res Int. 2020;2020:3801748.
121. Guo C, Zhou S, Yi W, Yang P, Li O, Liu J, Peng C. Long non-coding RNA muskelin 1 antisense RNA (MKLN1-AS) is a potential diagnostic and prognostic biomarker and therapeutic target for hepatocellular carcinoma. Exp Mol Pathol. 2021;120: 104638.
122. Chen X, Ye Q, Chen Z, Lin Q, Chen W, Xie C, Wang X. Long non-coding RNA muskelin 1 antisense RNA as a potential therapeutic target in hepatocellular carcinoma treatment. Bioengineered. 2022;13(5):12237–47.
123. Qu J, Tao D, Huang W, Lu L, Fan J, Zhang S, Huang F. Assessment of prognostic role of a novel 7-lncRNA signature in HCC patients. Heliyon. 2023;9(8): e18493.
124. Wang W, Wang L, Song C, Mu T, Hu J, Feng H. Prognostic Signature Constructed of Seven Ferroptosis-Related lncRNAs Predicts the Prognosis of HBV-Related HCC. J Gastrointest Cancer. 2024;55(1):444–56.
125. Jia X, Wang Y, Yang Y, Fu Y, Liu Y. Constructed risk prognosis model associated with disulfidptosis lncRNAs in HCC. Int J Mol Sci. 2023;24(24):17626.
126. Liu Y, Meng J, Ruan X, Wei F, Zhang F, Qin X. A disulfidptosis-related lncRNAs signature in hepatocellular carcinoma: prognostic prediction, tumor immune microenvironment and drug susceptibility. Sci Rep. 2024;14(1):746.
127. Liangyu Z, Bochao Z, Guoquan Y, Yuan Z, Heng L, Hanyu Z. Bioinformatics prediction and experimental verification identify cuproptosis-related lncRNA as prognosis biomarkers of hepatocellular carcinoma. Biochem Biophys Rep. 2023;35: 101502.
128. Li D, Jin S, Chen P, Zhang Y, Li Y, Zhong C, Fan X, Lin H. Comprehensive analysis of cuproptosis-related lncRNAs for prognostic significance and immune microenvironment characterization in hepatocellular carcinoma. Front Immunol. 2022;13: 991604.
129. Wei M, Lu L, Luo Z, Ma J, Wang J. Prognostic analysis of hepatocellular carcinoma based on cuproptosis -associated lncRNAs. BMC Gastroenterol. 2024;24(1):142.
130. Yuan W, Xiao JH, Zhang JS, Mao BL, Wang PZ, Wang BL. Identification of a cuproptosis and copper metabolism gene-related lncRNAs prognostic signature associated with clinical and immunological characteristics of hepatocellular carcinoma. Front Oncol. 2023;13:1153353.
131. Lu Q, Liu L, Wang S, Zhang Q, Li L. Comprehensive analysis of m5C-Related lncRNAs in the prognosis and immune landscape of hepatocellular carcinoma. Front Genet. 2022;13: 990594.
132. Deng X, Bi Q, Chen S, Chen X, Li S, Zhong Z, Guo W, Li X, Deng Y, Yang Y. Identification of a Five-Autophagy-Related-lncRNA Signature as a Novel Prognostic Biomarker for Hepatocellular Carcinoma. Front Mol Biosci. 2020;7: 611626.
133. Tang P, Qu W, Wang T, Liu M, Wu D, Tan L, Zhou H. Identifying a Hypoxia-Related Long Non-Coding RNAs Signature to Improve the Prediction of Prognosis and Immunotherapy Response in Hepatocellular Carcinoma. Front Genet. 2021;12: 785185.
134. Wu Z, Huang X, Cai M, Huang P. Potential biomarkers for predicting the overall survival outcome of kidney renal papillary cell carcinoma: an analysis of ferroptosis-related LNCRNAs. BMC Urol. 2022;22(1):152.
135. Yi WW, Guo XQ, Xu Y, Liang B, Song P. A prognostic model based on ferroptosis-related long non-coding RNA signatures and immunotherapy responses for non-small cell lung cancer. Eur Rev Med Pharmacol Sci. 2023;27(6):2591–604.
136. Li J, Zhang J, Tao S, Hong J, Zhang Y, Chen W. Prognostication of Pancreatic Cancer Using The Cancer Genome Atlas Based Ferroptosis-Related Long Non-Coding RNAs. Front Genet. 2022;13: 838021.
137. Zhou J, Zhang M, Dong H, Wang M, Cheng Y, Wang S, Ma W, Xu H. Comprehensive Analysis of Acetylation-Related lncRNAs and Identified AC099850,3 as Prognostic Biomarker in Non-Small Cell Lung Cancer. J Oncol. 2021;2021:4405697.
138. Lu Y, Luo X, Wang Q, Chen J, Zhang X, Li Y, Chen Y, Li X, Han S. A Novel Necroptosis-Related lncRNA Signature Predicts the Prognosis of Lung Adenocarcinoma. Front Genet. 2022;13: 862741.
139. Liu P, Zhou L, Chen H, He Y, Li G, Hu K. Identification of a novel intermittent hypoxia-related prognostic lncRNA signature and the ceRNA of lncRNA GSEC/miR-873-3p/EGLN3 regulatory axis in lung adenocarcinoma. PeerJ. 2023;11: e16242.
140. Chen L, Zhang L, He H, Shao F, Gao Y, He J. Systemic analyses of cuproptosis-related lncRNAs in pancreatic adenocarcinoma, with a focus on the molecular mechanism of LINC00853. Int J Mol Sci. 2023;24(9):7923.
141. Wang Y, Zhang D, Li Y, Wu Y, Ma H, Jiang X, Fu L, Zhang G, Wang H, Liu X, et al. Constructing a novel signature and predicting the immune landscape of colon cancer using N6-methylandenosine-related lncRNAs. Front Genet. 2023;14: 906346.
142. Cui G, Liu J, Wang C, Gu R, Wang M, Sun Z, Wei F. Comprehensive analysis of the prognostic signature and tumor microenvironment infiltration characteristics of cuproptosis-related lncRNAs for patients with colon adenocarcinoma. Front Oncol. 2022;12:1007918.
143. Wang Q, Fang Q, Huang Y, Zhou J, Liu M. Identification of a novel prognostic signature for HCC and analysis of costimulatory molecule-related lncRNA AC099850.3. Sci Rep. 2022;12(1):9954.
144. Wu F, Wei H, Liu G, Zhang Y. Bioinformatics Profiling of Five Immune-Related lncRNAs for a Prognostic Model of Hepatocellular Carcinoma. Front Oncol. 2021;11: 667904.
145. Cheng Z, Han J, Jiang F, Chen W, Ma X. Prognostic pyroptosis-related lncRNA signature predicts the efficacy of immunotherapy in hepatocellular carcinoma. Biochem Biophys Rep. 2022;32: 101389.
146. Luo L, Hu X, Huang A, Liu X, Wang L, Du T, Liu L, Li M. A Noval Established Cuproptosis-Associated LncRNA Signature for Prognosis Prediction in Primary Hepatic Carcinoma. Evid Based Complement Alternat Med. 2022;2022:2075638.
147. Jia Y, Chen Y, Liu J. Prognosis-Predictive Signature and Nomogram Based on Autophagy-Related Long Non-coding RNAs for Hepatocellular Carcinoma. Front Genet. 2020;11: 608668.

148. Wang Y, Ge F, Sharma A, Rudan O, Setiawan MF, Gonzalez-Carmona MA, Kornek MT, Strassburg CP, Schmid M, Schmidt-Wolf IGH. Immunoautophagy-related long noncoding RNA (IAR-lncRNA) signature predicts survival in hepatocellular carcinoma. Biology (Basel). 2021;10(12):1301.
149. Xu BH, Jiang JH, Luo T, Jiang ZJ, Liu XY, Li LQ. Signature of prognostic epithelial-mesenchymal transition related long noncoding RNAs (ERLs) in hepatocellular carcinoma. Medicine (Baltimore). 2021;100(30): e26762.
150. Huang S, Li D, Zhuang L, Zhang J, Wu J. Identification of an Epithelial-Mesenchymal Transition-Related Long Non-coding RNA Prognostic Signature to Determine the Prognosis and Drug Treatment of Hepatocellular Carcinoma Patients. Front Med (Lausanne). 2022;9: 850343.
151. Su D, Zhang Z, Xu Z, Xia F, Yan Y. A prognostic exosome-related LncRNA risk model correlates with the immune microenvironment in liver cancer. Front Genet. 2022;13: 965329.
152. Zhang Q, Cheng M, Fan Z, Jin Q, Cao P, Zhou G. Identification of Cancer Cell Stemness-Associated Long Noncoding RNAs for Predicting Prognosis of Patients with Hepatocellular Carcinoma. DNA Cell Biol. 2021;40(8):1087–100.
153. Liu X, Xiao C, Tan F, Yi R, Zhao X. Discovered differentially expressed lncRNA AC010973.2 can act as a diagnostic and prognostic biomarker for colon adenocarcinoma. Transl Cancer Res. 2020;9(10):6275–86.
154. Liu Y, Wang J, Li L, Qin H, Wei Y, Zhang X, Ren X, Ding W, Shen X, Li G, et al. AC010973.2 promotes cell proliferation and is one of six stemness-related genes that predict overall survival of renal clear cell carcinoma. Sci Rep. 2022;12(1):4272.
155. Cai HJ, Zhuang ZC, Wu Y, Zhang YY, Liu X, Zhuang JF, Yang YF, Gao Y, Chen B, Guan GX. Development and validation of a ferroptosis-related lncRNAs prognosis signature in colon cancer. Bosn J Basic Med Sci. 2021;21(5):569–76.
156. Bueno-Urquiza LJ, Martinez-Barajas MG, Villegas-Mercado CE, Garcia-Bernal JR, Pereira-Suarez AL, Aguilar-Medina M, Bermudez M. The two faces of immune-related lncRNAs in head and neck squamous cell carcinoma. Cells. 2023;12(5):727.
157. Yang C, Zheng X. Identification of a Hypoxia-Related lncRNA Biomarker Signature for Head and Neck Squamous Cell Carcinoma. J Oncol. 2022;2022:6775496.
158. Li H, Xiong HG, Xiao Y, Yang QC, Yang SC, Tang HC, Zhang WF, Sun ZJ. Long Non-coding RNA LINC02195 as a Regulator of MHC I Molecules and Favorable Prognostic Marker for Head and Neck Squamous Cell Carcinoma. Front Oncol. 2020;10:615.
159. He GN, Bao NR, Wang S, Xi M, Zhang TH, Chen FS. Ketamine Induces Ferroptosis of Liver Cancer Cells by Targeting lncRNA PVT1/miR-214-3p/GPX4. Drug Des Devel Ther. 2021;15:3965–78.
160. Zhou L, Zhang Q, Cheng J, Shen X, Li J, Chen M, Zhou C, Zhou J. LncRNA SNHG1 upregulates FANCD2 and G6PD to suppress ferroptosis by sponging miR-199a-5p/3p in hepatocellular carcinoma. Drug Discov Ther. 2023;17(4):248–56.
161. Luo W, Wang J, Xu W, Ma C, Wan F, Huang Y, Yao M, Zhang H, Qu Y, Ye D, et al. LncRNA RP11-89 facilitates tumorigenesis and ferroptosis resistance through PROM2-activated iron export by sponging miR-129-5p in bladder cancer. Cell Death Dis. 2021;12(11):1043.
162. Li YZ, Zhu HC, Du Y, Zhao HC, Wang L. Silencing lncRNA SLC16A1-AS1 Induced Ferroptosis in Renal Cell Carcinoma Through miR-143-3p/SLC7A11 Signaling. Technol Cancer Res Treat. 2022;21:15330338221077804.
163. Li J, Li PT, Wu W, Ding BN, Wen YG, Cai HL, Liu SX, Hong T, Zhang JF, Zhou JD, et al. POU2F2-mediated upregulation of lncRNA PTPRG-AS1 inhibits ferroptosis in breast cancer via miR-376c-3p/SLC7A11 axis. Epigenomics. 2024;16(4):215–31.
164. Zhang Y, Guo S, Wang S, Li X, Hou D, Li H, Wang L, Xu Y, Ma B, Wang H, et al. LncRNA OIP5-AS1 inhibits ferroptosis in prostate cancer with long-term cadmium exposure through miR-128-3p/SLC7A11 signaling. Ecotoxicol Environ Saf. 2021;220: 112376.
165. Li SQ, Lv F, Xu WT, Yin YX, Wei HT, Li KZ, Hu BL. lncRNA SNHG4 inhibits ferroptosis by orchestrating miR-150-5p/c-Myb axis in colorectal cancer. Int J Biol Macromol. 2024;268(Pt 2): 131961.
166. Jiang X, Yuan Y, Tang L, Wang J, Zhang D, Duan L. Systematic Analysis and Validation of the Prognosis, Immunological Role and Biology Function of the Ferroptosis-Related lncRNA GSEC/miRNA-101-3p/CISD1 Axis in Lung Adenocarcinoma. Front Mol Biosci. 2021;8: 793732.
167. Zhang N, Huang J, Xu M, Wang Y. LncRNA T-UCR Uc.339/miR-339/SLC7A11 Axis Regulates the Metastasis of Ferroptosis-Induced Lung Adenocarcinoma. J Cancer. 2022;13(6):1945–57.
168. Wang T, Jiang X, Lu Y, Ruan Y, Wang J. Identification and integration analysis of a novel prognostic signature associated with cuproptosis-related ferroptosis genes and relevant lncRNA regulatory axis in lung adenocarcinoma. Aging (Albany NY). 2023;15(5):1543–63.
169. Pan C, Chen G, Zhao X, Xu X, Liu J. lncRNA BBOX1-AS1 silencing inhibits esophageal squamous cell cancer progression by promoting ferroptosis via miR-513a-3p/SLC7A11 axis. Eur J Pharmacol. 2022;934: 175317.
170. Zhang Y, Luo M, Cui X, O'Connell D, Yang Y. Long noncoding RNA NEAT1 promotes ferroptosis by modulating the miR-362-3p/MIOX axis as a ceRNA. Cell Death Differ. 2022;29(9):1850–63.
171. Yan Z, Liang Z, Luo K, Yu L, Chen C, Yu M, Guo X, Li M. METTL3-modified lncRNA DSCAM-AS1 promotes breast cancer progression through inhibiting ferroptosis. J Bioenerg Biomembr. 2024;56(4):451–9.
172. Mao C, Wang X, Liu Y, Wang M, Yan B, Jiang Y, Shi Y, Shen Y, Liu X, Lai W, et al. A G3BP1-Interacting lncRNA Promotes Ferroptosis and Apoptosis in Cancer via Nuclear Sequestration of p53. Cancer Res. 2018;78(13):3484–96.
173. Zhao J, Yang S, Lv C, Liu Y. Cancer-associated fibroblasts suppressed ferroptosis in glioblastoma via upregulating lncRNA DLEU1. Am J Physiol Cell Physiol. 2023;324(5):C1039–52.
174. Qiu X, Shi Q, Zhang X, Shi X, Jiang H, Qin S. LncRNA A2M-AS1 Promotes Ferroptosis in Pancreatic Cancer via Interacting With PCBP3. Mol Cancer Res. 2022;20(11):1636–45.
175. Zhang Z, Li B, Wang Z, Yang L, Peng J, Wang H, Wang Y, Hong L. Novel LncRNA LINC02936 Suppresses Ferroptosis and Promotes Tumor Progression by Interacting with SIX1/CP Axis in Endometrial Cancer. Int J Biol Sci. 2024;20(4):1356–74.
176. Yao F, Zhao Y, Wang G, Zhao M, Hong X, Ye Z, Dong F, Li W, Deng Q. Exosomal lncRNA ROR1-AS1 from cancer-associated fibroblasts inhibits ferroptosis of lung cancer cells through the IGF2BP1/SLC7A11 signal axis. Cell Signal. 2024;120: 111221.
177. Gao GB, Chen L, Pan JF, Lei T, Cai X, Hao Z, Wang Q, Shan G, Li J. LncRNA RGMB-AS1 inhibits HMOX1 ubiquitination and NAA10 activation to induce ferroptosis in non-small cell lung cancer. Cancer Lett. 2024;590: 216826.
178. Zheng J, Zhang Q, Zhao Z, Qiu Y, Zhou Y, Wu Z, Jiang C, Wang X, Jiang X. Epigenetically silenced lncRNA SNAI3-AS1 promotes ferroptosis in glioma via perturbing the m(6)A-dependent recognition of Nrf2 mRNA mediated by SND1. J Exp Clin Cancer Res. 2023;42(1):127.
179. Zhang Z, Ye B, Lin Y, Liu W, Deng J, Ji W. LncRNA OTUD6B-AS1 overexpression promoted GPX4-mediated ferroptosis to suppress radioresistance in colorectal cancer. Clin Transl Oncol. 2023;25(11):3217–29.
180. Li Y, Ma Z, Li W, Xu X, Shen P, Zhang SE, Cheng B, Xia J. PDPN(+) CAFs facilitate the motility of OSCC cells by inhibiting ferroptosis via transferring exosomal lncRNA FTX. Cell Death Dis. 2023;14(11):759.
181. Yang H, Hu Y, Weng M, Liu X, Wan P, Hu Y, Ma M, Zhang Y, Xia H, Lv K. Hypoxia inducible lncRNA-CBSLR modulates ferroptosis through m6A-YTHDF2-dependent modulation of CBS in gastric cancer. J Adv Res. 2022;37:91–106.
182. Lin Z, Song J, Gao Y, Huang S, Dou R, Zhong P, Huang G, Han L, Zheng J, Zhang X, et al. Hypoxia-induced HIF-1alpha/lncRNA-PMAN inhibits ferroptosis by promoting the cytoplasmic translocation of ELAVL1 in peritoneal dissemination from gastric cancer. Redox Biol. 2022;52: 102312.
183. Wang J, Jia Q, Jiang S, Lu W, Ning H. POU6F1 promotes ferroptosis by increasing lncRNA-CASC2 transcription to regulate SOCS2/SLC7A11 signaling in gastric cancer. Cell Biol Toxicol. 2024;40(1):3.
184. Shi Z, Zhang H, Shen Y, Zhang S, Zhang X, Xu Y, Sun D. SETD1A-mediated H3K4me3 methylation upregulates lncRNA HOXC-AS3 and the binding of HOXC-AS3 to EP300 and increases EP300 stability to suppress the ferroptosis of NSCLC cells. Thorac Cancer. 2023;14(25):2579–90.
185. Huang G, Xiang Z, Wu H, He Q, Dou R, Lin Z, Yang C, Huang S, Song J, Di Z, et al. The lncRNA BDNF-AS/WDR5/FBXW7 axis mediates ferroptosis in gastric cancer peritoneal metastasis by regulating VDAC3 ubiquitination. Int J Biol Sci. 2022;18(4):1415–33.
186. Zhang B, Bao W, Zhang S, Chen B, Zhou X, Zhao J, Shi Z, Zhang T, Chen Z, Wang L, et al. LncRNA HEPFAL accelerates ferroptosis in

hepatocellular carcinoma by regulating SLC7A11 ubiquitination. Cell Death Dis. 2022;13(8):734.
187. Bian Y, Xu S, Gao Z, Ding J, Li C, Cui Z, Sun H, Li J, Pu J, Wang K. m(6) A modification of lncRNA ABHD11-AS1 promotes colorectal cancer progression and inhibits ferroptosis through TRIM21/IGF2BP2/ FOXM1 positive feedback loop. Cancer Lett. 2024;596: 217004.
188. Zhang W, Liu Y, Liao Y, Zhu C, Zou Z. GPX4, ferroptosis, and diseases. Biomed Pharmacother. 2024;174: 116512.
189. Zhang J, Qiu T, Yao X, Sun X. Insights into the role of N6-methyladenosine in ferroptosis. Biomed Pharmacother. 2023;165: 115192.
190. Li H, Wei Y, Wang J, Yao J, Zhang C, Yu C, Tang Y, Zhu D, Yang J, Zhou J. Long Noncoding RNA LINC00578 Inhibits Ferroptosis in Pancreatic Cancer via Regulating SLC7A11 Ubiquitination. Oxid Med Cell Longev. 2023;2023:1744102.
191. Zhou H, Wu Y, Cai J, Zhang D, Lan D, Dai X, Liu S, Song T, Wang X, Kong Q, et al. Micropeptides: potential treatment strategies for cancer. Cancer Cell Int. 2024;24(1):134.
192. Xiao Y, Ren Y, Hu W, Paliouras AR, Zhang W, Zhong L, Yang K, Su L, Wang P, Li Y, et al. Long non-coding RNA-encoded micropeptides: functions, mechanisms and implications. Cell Death Discov. 2024;10(1):450.
193. Patraquim P, Magny EG, Pueyo JI, Platero AI, Couso JP. Translation and natural selection of micropeptides from long non-canonical RNAs. Nat Commun. 2022;13(1):6515.
194. Huang JZ, Chen M, Chen D, Gao XC, Zhu S, Huang H, Hu M, Zhu H, Yan GR. A Peptide Encoded by a Putative lncRNA HOXB-AS3 Suppresses Colon Cancer Growth. Mol Cell. 2017;68(1):171-184 e176.
195. Nelson BR, Makarewich CA, Anderson DM, Winders BR, Troupes CD, Wu F, Reese AL, McAnally JR, Chen X, Kavalali ET, et al. A peptide encoded by a transcript annotated as long noncoding RNA enhances SERCA activity in muscle. Science. 2016;351(6270):271–5.
196. Tong X, Yu Z, Xing J, Liu H, Zhou S, Huang Y, Lin J, Jiang W, Wang L. LncRNA HCP5-encoded protein regulates ferroptosis to promote the progression of triple-negative breast cancer. Cancers (Basel). 2023;15(6):1880.
197. Zhang C, Liu X, Jin S, Chen Y, Guo R. Ferroptosis in cancer therapy: a novel approach to reversing drug resistance. Mol Cancer. 2022;21(1):47.
198. Gong H, Gao M, Lin Y, Liu J, Hu Z, Liu J. TUG1/MAZ/FTH1 Axis Attenuates the Antiglioma Effect of Dihydroartemisinin by Inhibiting Ferroptosis. Oxid Med Cell Longev. 2022;2022:7843863.
199. Luo J, Bai R, Liu Y, Bi H, Shi X, Qu C. Long non-coding RNA ATXN8OS promotes ferroptosis and inhibits the temozolomide-resistance of gliomas through the ADAR/GLS2 pathway. Brain Res Bull. 2022;186:27–37.
200. Gao Y, Tong M, Wong TL, Ng KY, Xie YN, Wang Z, Yu H, Loh JJ, Li M, Ma S. Long Noncoding RNA URB1-Antisense RNA 1 (AS1) Suppresses Sorafenib-Induced Ferroptosis in Hepatocellular Carcinoma by Driving Ferritin Phase Separation. ACS Nano. 2023;17(22):22240–58.
201. Shi Z, Li Z, Jin B, Ye W, Wang L, Zhang S, Zheng J, Lin Z, Chen B, Liu F, et al. Loss of LncRNA DUXAP8 synergistically enhanced sorafenib induced ferroptosis in hepatocellular carcinoma via SLC7A11 depalmitoylation. Clin Transl Med. 2023;13(6): e1300.
202. Singh S, Sadhukhan S, Sonawane A. 20 years since the approval of first EGFR-TKI, gefitinib: Insight and foresight. Biochim Biophys Acta Rev Cancer. 2023;1878(6): 188967.
203. Zhen S, Jia Y, Zhao Y, Wang J, Zheng B, Liu T, Duan Y, Lv W, Wang J, Xu F, et al. NEAT1_1 confers gefitinib resistance in lung adenocarcinoma through promoting AKR1C1-mediated ferroptosis defence. Cell Death Discov. 2024;10(1):131.
204. Wang L, Fu H, Song L, Wu Z, Yu J, Guo Q, Chen C, Yang X, Zhang J, Wang Q, et al. Overcoming AZD9291 Resistance and Metastasis of NSCLC via Ferroptosis and Multitarget Interference by Nanocatalytic Sensitizer Plus AHP-DRI-12. Small. 2023;19(4): e2204133.
205. Li SQ, Xu WT, Yin YX, Wei HT, Li KZ, Xie MZ, Lv F, Xie LY, Hu BL. SNHG4-mediated PTEN destabilization confers oxaliplatin resistance in colorectal cancer cells by inhibiting ferroptosis. Apoptosis. 2024;29(5–6):835–48.
206. Saatci O, Alam R, Huynh-Dam KT, Isik A, Uner M, Belder N, Ersan PG, Tokat UM, Ulukan B, Cetin M, et al. Targeting LINC00152 activates cAMP/Ca(2+)/ferroptosis axis and overcomes tamoxifen resistance in ER+ breast cancer. Cell Death Dis. 2024;15(6):418.
207. Li L, Zhang Y, Gao Y, Hu Y, Wang R, Wang S, Li Y, He Y, Yuan C. LncSNHG14 promotes nutlin3a resistance by inhibiting ferroptosis via the miR-206 /SLC7A11 axis in osteosarcoma cells. Cancer Gene Ther. 2023;30(5):704–15.
208. Zhao J, Wan XN, Zhu JP, Liu QC, Gan L. LncRNA NEAT1 promoted MPP+-induced ferroptosis via regulating miR-150-5p/BAP1 pathway in SK-N-SH cells. Acta Neurobiol Exp (Wars). 2022;82(2):226–36.
209. Zhang G, Gao Y, Jiang L, Zhang Y. LncRNA FTX Inhibits Ferroptosis of Hippocampal Neurons Displaying Epileptiform Discharges In vitro Through the miR-142-5p/GABPB1 Axis. Neuroscience. 2023;526:48–60.
210. Gao F, Zhao Y, Zhang B, Xiao C, Sun Z, Gao Y, Dou X. Suppression of lncRNA Gm47283 attenuates myocardial infarction via miR-706/ Ptgs2/ ferroptosis axis. Bioengineered. 2022;13(4):10786–802.
211. Zhang Q, Song C, Zhang M, Liu Y, Wang L, Xie Y, Qi H, Ba L, Shi P, Cao Y, et al. Super-enhancer-driven lncRNA Snhg7 aggravates cardiac hypertrophy via Tbx5/GLS2/ferroptosis axis. Eur J Pharmacol. 2023;953: 175822.
212. Dai R, Yang X, He W, Su Q, Deng X, Li J. LncRNA AC005332.7 Inhibited Ferroptosis to Alleviate Acute Myocardial Infarction Through Regulating miR-331–3p/CCND2 Axis. Korean Circ J. 2023;53(3):151–67.
213. Lu J, Xu F, Lu H. LncRNA PVT1 regulates ferroptosis through miR-214-mediated TFR1 and p53. Life Sci. 2020;260: 118305.
214. Wei XB, Jiang WQ, Zeng JH, Huang LQ, Ding HG, Jing YW, Han YL, Li YC, Chen SL. Exosome-Derived lncRNA NEAT1 Exacerbates Sepsis-Associated Encephalopathy by Promoting Ferroptosis Through Regulating miR-9-5p/TFRC and GOT1 Axis. Mol Neurobiol. 2022;59(3):1954–69.
215. Sun Z, Wu J, Bi Q, Wang W. Exosomal lncRNA TUG1 derived from human urine-derived stem cells attenuates renal ischemia/reperfusion injury by interacting with SRSF1 to regulate ASCL4-mediated ferroptosis. Stem Cell Res Ther. 2022;13(1):297.
216. Yang Y, Wang A, Zhou J, Yang Y, Wu H. LncRNA SNHG11 induces ferroptosis in liver injury cells through miR-324–3p/GPX4 axis-mediated sepsis. Cell Mol Biol (Noisy-le-grand). 2023;69(12):163–9.
217. Zhang JK, Zhang Z, Guo ZA, Fu Y, Chen XJ, Chen WJ, Wu HF, Cui XJ. The BMSC-derived exosomal lncRNA Mir9-3hg suppresses cardiomyocyte ferroptosis in ischemia-reperfusion mice via the Pum2/PRDX6 axis. Nutr Metab Cardiovasc Dis. 2022;32(2):515–27.
218. Lai G, Shen J, Hu Y, Yang F, Zhang C, Le D, Liu Q, Liang Y. LncRNA RNA ROR Aggravates Hypoxia/Reoxygenation-Induced Cardiomyocyte Ferroptosis by Targeting miR-769–5p/CBX7 Axis. Biochem Genet. 2024;62(5):3586–3604.
219. Li Z, Zou W, Jin X, Wang Y. LncRNA FRMD6-AS1/miR-491-5p/USP13 pathway attenuated ferroptosis and contributed to liver fibrosis. Environ Toxicol. 2024;39(6):3760–71.
220. Tao W, Lu Y, Xiao R, Zhang J, Hu P, Zhao N, Peng W, Qian K, Liu F. LncRNA HMOX1 alleviates renal ischemia-reperfusion-induced ferroptotic injury via the miR-3587/HMOX1 axis. Cell Signal. 2024;119: 111165.
221. Yang Y, Tai W, Lu N, Li T, Liu Y, Wu W, Li Z, Pu L, Zhao X, Zhang T, et al. lncRNA ZFAS1 promotes lung fibroblast-to-myofibroblast transition and ferroptosis via functioning as a ceRNA through miR-150-5p/SLC38A1 axis. Aging (Albany NY). 2020;12(10):9085–102.
222. Sun W, Wu X, Yu P, Zhang Q, Shen L, Chen J, Tong H, Fan M, Shi H, Chen X. LncAABR07025387.1 Enhances Myocardial Ischemia/Reperfusion Injury Via miR-205/ACSL4-Mediated Ferroptosis. Front Cell Dev Biol. 2022;10:672391.
223. Wan Y, Gu C, Kong J, Sui J, Zuo L, Song Y, Chen J. Long noncoding RNA ADAMTS9-AS1 represses ferroptosis of endometrial stromal cells by regulating the miR-6516-5p/GPX4 axis in endometriosis. Sci Rep. 2022;12(1):2618.
224. Li X, Peng X, Zhou X, Li M, Chen G, Shi W, Yu H, Zhang C, Li Y, Feng Z, et al. Small extracellular vesicles delivering lncRNA WAC-AS1 aggravate renal allograft ischemia-reperfusion injury by inducing ferroptosis propagation. Cell Death Differ. 2023;30(9):2167–86.
225. Tian P, Xu Z, Guo J, Zhao J, Chen W, Huang W, Wang M, Mi C, Zhang Y, Yang Y, et al. Hypoxia causes trophoblast cell ferroptosis to induce miscarriage through lnc-HZ06/HIF1alpha-SUMO/NCOA4 axis. Redox Biol. 2024;70: 103073.
226. Liu Y, Zhang Z, Yang J, Wang J, Wu Y, Zhu R, Liu Q, Xie P. lncRNA ZFAS1 Positively Facilitates Endothelial Ferroptosis via miR-7-5p/ACSL4 Axis in Diabetic Retinopathy. Oxid Med Cell Longev. 2022;2022:9004738.
227. Wang H, Qiao X, Zhang C, Hou J, Qi S. Long non-coding RNA LINC00616 promotes ferroptosis of periodontal ligament stem cells

via the microRNA-370 / transferrin receptor axis. Bioengineered. 2022;13(5):13070–81.
228. Fang X, Song J, Chen Y, Zhu S, Tu W, Ke B, Wu L. LncRNA SNHG1 knockdown inhibits hyperglycemia induced ferroptosis via miR-16-5p/ACSL4 axis to alleviate diabetic nephropathy. J Diabetes Investig. 2023;14(9):1056–69.
229. Liao M, Zou S, Wu J, Bai J, Liu Y, Zhi K, Qu L. METTL3-mediated m6A modification of NORAD inhibits the ferroptosis of vascular smooth muscle cells to attenuate the aortic dissection progression in an YTHDF2-dependent manner. Mol Cell Biochem. 2024;479(12):3471–3487.
230. Zhang X, Zheng C, Zhao J, Xu X, Yao J. LncRNA MEG3 regulates ferroptosis of lens epithelial cells via PTBP1/GPX4 axis to participate in age-related cataract. J Cell Physiol. 2024;239(11):e31330.
231. Zhang M, Yu Z, Zhao L, Luo H. Long non-coding RNA PVT1 regulates atherosclerosis progression via the microRNA-106b-5p/ACSL4 axis. Biochem Biophys Res Commun. 2023;667:170–9.
232. Deng W, Zhong L, Ye S, Luo J, Ren G, Huang J, Zhuang X. Mir22hg facilitates ferritinophagy-mediated ferroptosis in sepsis by recruiting the m6A reader YTHDC1 and enhancing Angptl4 mRNA stability. J Bioenerg Biomembr. 2024;56(4):405–18.
233. Zhu C, Chen B, He X, Li W, Wang S, Zhu X, Li Y, Wan P, Li X. LncRNA MEG3 suppresses erastin-induced ferroptosis of chondrocytes via regulating miR-885-5p/SLC7A11 axis. Mol Biol Rep. 2024;51(1):139.
234. Lin P, Wang J, Li Y, Li G, Wang Y. LINC00472 Regulates Ferroptosis of Neurons in Alzheimer's Disease via FOXO1. Dement Geriatr Cogn Disord. 2024;53(3):107–18.
235. Chen B, Wang H, Lv C, Mao C, Cui Y. Long non-coding RNA H19 protects against intracerebral hemorrhage injuries via regulating microRNA-106b-5p/acyl-CoA synthetase long chain family member 4 axis. Bioengineered. 2021;12(1):4004–15.
236. Jin ZL, Gao WY, Liao SJ, Yu T, Shi Q, Yu SZ, Cai YF. Paeonol inhibits the progression of intracerebral haemorrhage by mediating the HOTAIR/UPF1/ACSL4 axis. ASN Neuro. 2021;13:17590914211010648.
237. Li Z, Zhang Y, Ji M, Wu C, Zhang Y, Ji S. Targeting ferroptosis in neuroimmune and neurodegenerative disorders for the development of novel therapeutics. Biomed Pharmacother. 2024;176: 116777.
238. Wang M, Li T, Gao R, Zhang Y, Han Y. Identifying the potential genes in alpha synuclein driving ferroptosis of Parkinson's disease. Sci Rep. 2023;13(1):16893.
239. Fang W, Xie S, Deng W. Ferroptosis mechanisms and regulations in cardiovascular diseases in the past, present, and future. Cell Biol Toxicol. 2024;40(1):17.
240. Libby P. The changing landscape of atherosclerosis. Nature. 2021;592(7855):524–33.
241. You Z, Ye X, Jiang M, Gu N, Liang C. lnc-MRGPRF-6:1 Promotes ox-LDL-Induced Macrophage Ferroptosis via Suppressing GPX4. Mediators Inflamm. 2023;2023:5513245.
242. Tang F, Tian LH, Zhu XH, Yang S, Zeng H, Yang YY. H19 lncRNA triggers ferroptosis, exacerbating ox-LDL-induced artery endothelial cell damage in vitro. Clin Hemorheol Microcirc. 2024;88(2):263–275.
243. Banerjee S, Sarkar R, Mukherjee A, Mitra S, Gope A, Chawla-Sarkar M. Rotavirus-induced lncRNA SLC7A11-AS1 promotes ferroptosis by targeting cystine/glutamate antiporter xCT (SLC7A11) to facilitate virus infection. Virus Res. 2024;339: 199261.
244. Xu L, Zhang L, Xiang Y, Zhang X. Knockdown of lncRNA NEAT1 suppresses streptococcus pneumoniae-induced ferroptosis in alveolar epithelial cells by regulating the Nrf2-GPX4 pathway. Toxicon. 2024;243: 107705.
245. Huang Y, Li L, Li Y, Lu N, Qin H, Wang R, Li W, Cheng Z, Li Z, Kang P, et al. Knockdown of LncRNA Lcn2-204 alleviates sepsis-induced myocardial injury by regulation of iron overload and ferroptosis. J Mol Cell Cardiol. 2024;192:79–93.
246. Wu MY, Yiang GT, Liao WT, Tsai AP, Cheng YL, Cheng PW, Li CY, Li CJ. Current Mechanistic Concepts in Ischemia and Reperfusion Injury. Cell Physiol Biochem. 2018;46(4):1650–67.
247. Zhang M, Liu Q, Meng H, Duan H, Liu X, Wu J, Gao F, Wang S, Tan R, Yuan J. Ischemia-reperfusion injury: molecular mechanisms and therapeutic targets. Signal Transduct Target Ther. 2024;9(1):12.
248. Co HKC, Wu CC, Lee YC, Chen SH. Emergence of large-scale cell death through ferroptotic trigger waves. Nature. 2024;631(8021):654–62.
249. Chen Q, Ji H, Lin Y, Chen Z, Liu Y, Jin L, Peng R. LncRNAs regulate ferroptosis to affect diabetes and its complications. Front Physiol. 2022;13: 993904.
250. Yang J, Liu Z. Mechanistic Pathogenesis of Endothelial Dysfunction in Diabetic Nephropathy and Retinopathy. Front Endocrinol (Lausanne). 2022;13: 816400.
251. Ni T, Huang X, Pan S, Lu Z. Inhibition of the long non-coding RNA ZFAS1 attenuates ferroptosis by sponging miR-150-5p and activates CCND2 against diabetic cardiomyopathy. J Cell Mol Med. 2021;25(21):9995–10007.
252. Zondervan KT, Becker CM, Koga K, Missmer SA, Taylor RN, Vigano P. Endometriosis Nat Rev Dis Primers. 2018;4(1):9.
253. Peat G, Thomas MJ. Osteoarthritis year in review 2020: epidemiology & therapy. Osteoarthritis Cartilage. 2021;29(2):180–9.
254. Qiu Y, Yao J, Li L, Xiao M, Meng J, Huang X, Cai Y, Wen Z, Huang J, Zhu M, et al. Machine learning identifies ferroptosis-related genes as potential diagnostic biomarkers for osteoarthritis. Front Endocrinol (Lausanne). 2023;14:1198763.
255. Ahmed S, Misra DP, Agarwal V. Interleukin-17 pathways in systemic sclerosis-associated fibrosis. Rheumatol Int. 2019;39(7):1135–43.
256. Asbell PA, Dualan I, Mindel J, Brocks D, Ahmad M, Epstein S. Age-related cataract. Lancet. 2005;365(9459):599–609.
257. Wang Y, Li P, Wang C, Bao S, Wang S, Zhang G, Zou X, Wu J, Guan Y, Ji M, et al. Lens epithelium cell ferroptosis mediated by m(6)A-lncRNA and GPX4 expression in lens tissue of age-related cataract. BMC Ophthalmol. 2023;23(1):514.
258. Zhang Z, Chen K, Pan D, Liu T, Hang C, Ying Y, He J, Lv Y, Ma X, Chen Z, et al. A predictive model for preterm infants with bronchopulmonary dysplasia based on ferroptosis-related lncRNAs. BMC Pulm Med. 2023;23(1):367.
259. Qiu L, Lin X, Chen R, Wu Y, Yan J. LncRNA PSMA3-AS1 promotes preterm delivery by inducing ferroptosis via miR-224–3p/Nrf2 axis. Cell Mol Biol (Noisy-le-grand). 2023;69(13):270–8.
260. Zhang L, Bai W, Peng Y, Lin Y, Tian M. Human umbilical cord mesenchymal stem cell-derived exosomes provide neuroprotection in traumatic brain injury through the lncRNA TUBB6/Nrf2 pathway. Brain Res. 2024;1824: 148689.
261. Shao C, Chen Y, Yang T, Zhao H, Li D. Mesenchymal Stem Cell Derived Exosomes Suppress Neuronal Cell Ferroptosis Via lncGm36569/miR-5627-5p/FSP1 Axis in Acute Spinal Cord Injury. Stem Cell Rev Rep. 2022;18(3):1127–42.
262. Gai C, Liu C, Wu X, Yu M, Zheng J, Zhang W, Lv S, Li W. MT1DP loaded by folate-modified liposomes sensitizes erastin-induced ferroptosis via regulating miR-365a-3p/NRF2 axis in non-small cell lung cancer cells. Cell Death Dis. 2020;11(9):751.
263. Yin J, Zhan J, Hu Q, Huang S, Lin W. Fluorescent probes for ferroptosis bioimaging: advances, challenges, and prospects. Chem Soc Rev. 2023;52(6):2011–30.
264. Davidson AJ, Heron R, Das J, Overholtzer M, Wood W. Ferroptosis-like cell death promotes and prolongs inflammation in Drosophila. Nat Cell Biol. 2024;26(9):1535–1544.
265. Winkle M, El-Daly SM, Fabbri M, Calin GA. Noncoding RNA therapeutics - challenges and potential solutions. Nat Rev Drug Discov. 2021;20(8):629–51.

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