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Ferroptosis: A Mechanism for Programmed Cell Death

Sonia Chadha

Amity Institute of Biotechnology, Amity University Uttar Pradesh, Lucknow Campus, Lucknow, Uttar Pradesh, India.

Corresponding author
Dr Sonia Chadha

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Abstract

Ferroptosis is defined as a non-apoptotic mechanism of regulated cell death, characterized by iron dependent accumulation of lipid hydroperoxides. Since its discovery, ferroptosis has grown as a fundamental biological process implicated in several pathological conditions including neurodegeneration, ischemia-reperfusion injury, inflammatory disorders and cancer. There are two major pathways for ferroptosis-the canonical and the non- canonical pathway. The canonical pathway involves the iron dependent accumulation of lipid hydroperoxides and is regulated by three major systems (1) the glutathione peroxidase 4 (GPx4)–glutathione system which serves as the major antioxidant defense against ferroptosis, (2) the Xc− transporter system that provides raw material for fueling the GPx4 antioxidant system and (3) iron metabolism pathways that provide the catalytic substrate for lipid peroxidation via Haber -Wieiss and Fenton chemistry. The non- canonical pathways or the GPx4 independent pathways include the ferroptosis suppressor protein 1 (FSP1)–ubiquinol system, the GTP cyclohydrolase 1 (GCH1)–tetrahydrobiopterin system, and the DHODH mitochondrial defense. Thus, ferroptosis can be regarded as a multi-layered network affecting biology and progression of diseases. Ferroptosis is also regulated by transcriptional factors like the p53 tumor suppressor and Nrf2, heat shock proteins, and epigenetic modulators in a cell-type and context-dependent manner. The present review comprehensively delineates the molecular pathways of ferroptosis regulation, with emphasis on both traditional and emerging pathways, and discusses how this mechanistic understanding is being translated into therapeutic strategies for cancer sensitization and neuroprotection.

Keywords: programmed cell death, iron metabolism, lipid peroxidation, glutathione peroxidase 4, therapeutic implication.

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1. Introduction

Organismal homeostasis is maintained by cell death and cells thus possess many programmed mechanisms of cell death including apoptosis, necroptosis, pyroptosis, and autophagy-dependent cell death. Recently ferroptosis has been identified as a non-apoptotic form of regulated cell death pathway, characterized by iron-dependent accumulation of lipid hydroperoxides thereby damaging the cell membranes (Dixon et al., 2012; Dixon &

Stockwell, 2014). The term "ferroptosis" was coined by Dixon et al., in 2012 based on the studies on the compound RSL3 which caused iron-dependent cell death morphologically distinct from apoptosis or necrosis (Dixon et al., 2012; Dixon & Stockwell, 2014). Ferroptotic cells differ from that undergoing apoptosis in that they have shrunken mitochondria with increased membrane density and reduced mitochondrial cristae without plasma membrane blebbing and an intact nucleus (Galluzzi et al., 2018; Stockwell et al., 2017). Among the various pathways regulating ferroptosis, the major one is contributed by the metabolic enzyme glutathione peroxidase-4 (GPx4), which reduces phospholipid hydroperoxides into non-toxic lipid alcohol using glutathione (GSH) and thereby prevents ferroptosis (Canonical pathway). GSH depletion, inactivation of GPx4, and limited availability of cysteine and selenium results in induction of ferroptosis (Friedmann Angeli et al., 2014). Besides GPx4 other GPx4 independent pathways have also been identified as regulators of ferroptosis (Non-Canonical) (Doll et al., 2019).

Ferroptosis is proposed to have a dual biological role. On one hand ferroptosis is responsible for ischemic neuronal injury and organelle stress, while on the other hand, it is being used to target cancer cells that don't respond to therapy and have become resistant to apoptosis. This dual role makes ferroptosis one of the most actively investigated areas in modern cell biology. Thus, it is important to understand the regulatory pathways of ferroptosis which has enormous clinical relevance. The present review provides a comprehensive summary of the pathways governing ferroptosis and discusses how the mechanistic understanding of ferroptosis is being translated into therapeutic strategies for cancer sensitization and neuroprotection.

2. Mechanisms of ferroptosis

Ferroptosis proceeds through two major pathways- the canonical or GPx4 dependent pathway and the non-canonical or the GPx4 independent pathway.

2.1 Canonical Pathway

This is the best characterized pathway of ferroptosis and involves the participation of the antioxidant enzyme glutathione peroxidase 4. The canonical pathway of ferroptosis is driven by iron driven accumulation of lipid hydroperoxides and is regulated by the X*c*−-GSH-GPx4 axis.

2.1.1 Lipid peroxidation

Accumulation of oxidized phospholipids within the biological membranes which disrupt the membrane integrity and cause cell death, is a hallmark of ferroptosis. The principal substrates for oxidation are the polyunsaturated fatty acids (PUFAs) particularly arachidonic acid (AA, C20:4) and adrenic acid (AdA, C22:4) esterified to membrane phosphatidylethanolamine (PE) (Kagan et al., 2017). The PUFAs are incorporated into the membrane phospholipids by the help of the two enzymes - acyl-CoA synthetase long-chain family member 4 (ACSL4) and lysophosphatidylcholine acyltransferase 3 (LPCAT3). ACSL4 converts the PUFAs to their respective CoA thioesters thereby activating them, whereas LPCAT3 catalyzes the esterification of the activated fatty acyl CoAs into the PE head group. Dysfunctioning of either of these enzymes suppresses ferroptosis (Feng et al., 2023; Kagan et al., 2017). Oxidation of this membrane associated PUFAs occurs both enzymatically and non-enzymatically. The membrane associated 15-lipoxygenases (15-LOX) which is encoded by ALOX15/ALOX15B, oxidizes the PE- associated PUFAs generating 15-HpETE-PE that serves as death signal (Manivarma et al., 2023). Non-enzymatic lipid peroxidation is facilitated by Fenton and Haber-Weiss reactions wherein the ferrous iron (Fe^{2+}) reduces H_2O_2 to hydroxyl radical (OH), which abstracts hydrogen from PUFA bis-allylic carbons propagating a chain reaction (Zheng et al., 2024).

2.1.2 Role of Iron in Lipid Peroxidation

The redox recycling of iron between Fe^{2+} and Fe^{3+} states governs the central role of iron in ferroptosis. The ferric ion is water-insoluble and so it is bound to proteins such as transferrin for transport and ferritin for storage. Transferrin (Tf) binds to Fe^{3+} and moves it inside the cells through the transferrin receptor (TfR1) (Figure 1). Inside the cells, iron is reduced to Fe^{2+} and contributes towards the catalytically active labile iron pool (LIP). Ferroportin (encoded by the FPN1/*SLC40A1* gene) is the only known cellular iron exporter in mammals, essential for transporting iron from inside cells (such as intestinal cells and macrophages) into the bloodstream (Ru et al., 2024). Iron homeostasis is maintained by a balance between iron uptake, export, utilization, and storage which is regulated by the IRP/IRE system. The IRP/IRE system comprises of the iron regulatory proteins (IRP1/2) which bind the iron-responsive elements (IREs) in the 3′ or 5′ UTR of transcripts encoding transferrin receptor (TfR1), ferritin, and ferroportin, regulating their

stability and translation in response to iron availability (Zhou & Tan, 2017).Transferrin-bound Fe^{3+} is endocytosed by TfR1 which is followed by six-transmembrane epithelial antigen of the prostate 3 (STEAP3) metalloreductase mediated reduction of Fe^{3+} to Fe^{2+} and export into the cytosol via the divalent metal transporter 1 (DMT1/SLC11A2). The ferritin complex comprising of the ferritin heavy and light chains (FTH1/FTL) stores excess iron in a redox-inert ferric form (Ru et al., 2024). Ferritinophagy is the selective autophagic degradation of ferritin brought about by the nuclear receptor co-activator 4 (NCOA4), which releases iron from storage, elevating the LIP and thereby promoting ferroptosis (Ning et al., 2026).

2.1.3 System Xc⁻-GSH-GPx4

Glutathione peroxidase (GPx) is a protein superfamily having redox-active cysteine residue in its active site and is also known as Phospholipid Hydroperoxide Glutathione Peroxidase (PHGPx). The human GPx family has eight isoforms wherein GPx1, GPx2, GPx3, GPx4 and GPx6 are selenoenzymes (Flohé et al., 2022; Weaver & Skouta, 2022). GPx4 is unique in the sense that it reduces the lipid peroxides including oxidized phosphatidylethanolamines, phosphatidylcholines, and cholesterol hydroperoxides within the biological membrane, thereby protecting cells from oxidative damage (Weaver & Skouta, 2022). GPx4 thus acts as a suppressor of ferroptosis by detoxifying lipid hydroperoxides and thereby supporting cell survival under conditions of oxidative stress (W. Zhang et al., 2024). Glutathione availability, selenocysteine incorporation and lipid and iron metabolism are key determinants of GPx4 activity and thus disruption of these pathways may affect GPx4 availability and function, thereby influencing cell death (Friedmann Angeli et al., 2014; Yang et al., 2014).

Reduction of lipid hydroperoxides into non-toxic lipid alcohol by GPx4 requires the obligatory participation of glutathione (GSH). Therefore, the intracellular concentration of GSH is important for ferroptosis resistance. The biosynthesis of GSH involves participation of the enzymes glutamate-cysteine ligase (GCL) and glutathione synthetase (GS). GCL catalyzes the rate-limiting condensation of glutamate and cysteine to form γ-glutamylcysteine and GS then adds glycine forming GSH. GSH biosynthesis is dependent on cysteine availability (Yang et al., 2014). Cystine (oxidized form of cysteine) is acquired through the plasma heterodimeric membrane antiporter system X*c*⁻, which is composed of the catalytic subunit SLC7A11 (xCT) and the regulatory subunit SLC3A2. This transporter exchanges intracellular glutamate for extracellular cystine in a 1:1 ratio (Viswanathan et al., 2017). After import, cystine is reduced to cysteine by thioredoxin reductase 1 (TrxR1) and cytosolic thioredoxin (Trx1), or by the action of glutaredoxins. Inhibition of cysteine uptake depletes glutathione and sensitizes cells to ferroptosis (Figure 1). Therapy-resistant cancer cells have been shown to exhibit marked GPX4 dependency (Viswanathan et al., 2017). Erastin- a pharmacological inducer of ferroptosis blocks the import of cystine, thereby reducing intracellular cysteine concentration and inhibiting GPX4 activity by limiting GSH availability. On the other hand, RSL3 and ML162 induce ferroptosis by directly alkylating and inactivating GPX4 (Gan, 2023; Liang et al., 2019).

Being a selenoprotein, the amount of GPx4 is determined by the availability of selenium. Researches have shown that selenium compounds such as methylselenocysteine, selenomethionine, and selenocystamine strengthen the antioxidant defences mediated by GPX4 and thereby prevent ferroptosis strengthening the antioxidant defenses that prevent ferroptosis (Tuo et al., 2021). Paradoxically high-dose selenium is known to induce ferroptotic cell death in certain cancer cells and thus used as a therapeutic strategy.

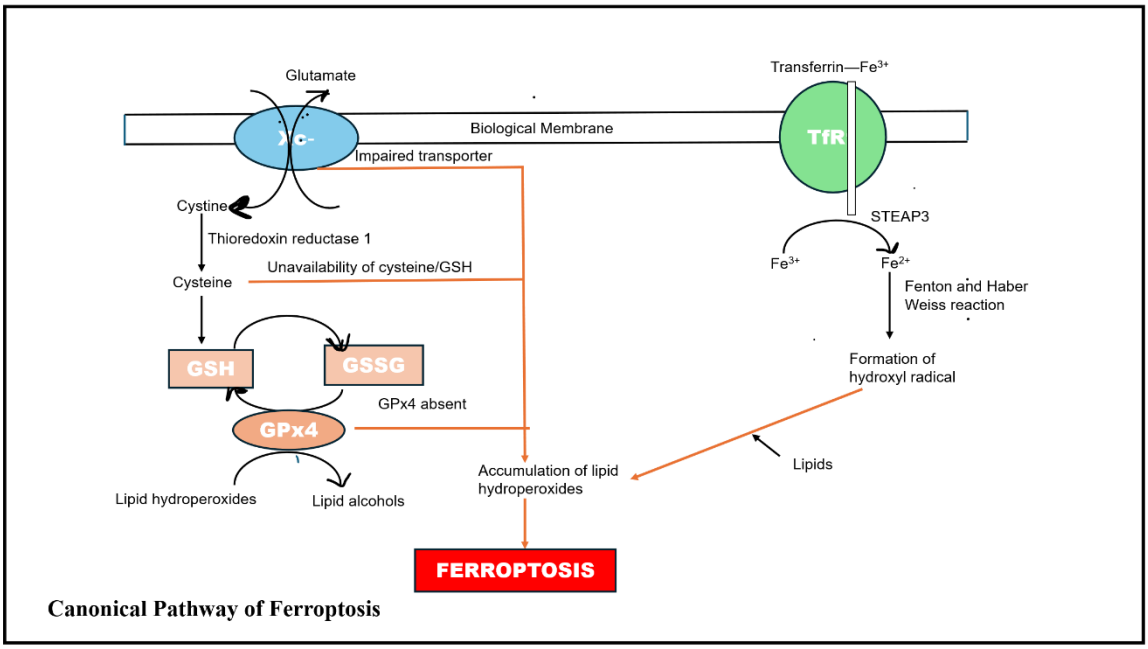

Figure 1: The Canonical of GPx4 dependent pathway of ferroptosis-The canonical pathway of ferroptosis is characterized by the iron driven accumulation of lipid hydroperoxides. Iron is transported in ferric form by the transferrin receptor (TfR1) followed by its reduction to ferrous form by STEAP3. The fenton and Haber-weiss chemistry results in the generation of hydroxyl radicals which drive lipid peroxidation. Lipid hydroperoxide accumulation is facilitated by the inactivation of glutathione peroxidase 4 (GPX4) and the failure of antioxidant defenses and /or by the inhibition of the cystine-glutamate antiporter (System Xc-), which depletes glutathione (GSH) and impairs GPx4 activity, leading to accumulation of lipid hyroperoxides facilitated by iron.

2.2 Non-Canonical Pathways

2.2.1 The FSP1–CoQ10 Pathway

GPx4 independent suppression of ferroptosis was recognized by the identification of ferroptosis suppressor protein 1 (FSP1), - a well-known apoptosis inducer in mitochondria and previously known as Apoptosis-inducing factor mitochondria-associated 2 (AIFM2) (Miyauchi et al., 2023) (Miyauchi et al., 2023). FSP1 is an NAD(P)H-dependent oxidoreductase that catalyzes the reduction of ubiquinone (coenzyme Q10, CoQ10) to ubiquinol (CoQ10H*2*) and is localized to the plasma membrane via N-terminal myristoylation. Ubiquinol helps in trapping lipid hydroperroxides in a GPx4 independent manner, directly quenching lipid peroxyl radicals and preventing the propagation of lipid peroxidation chain reactions (Y. Song et al., 2026). The FSP1–CoQ10 system thus operates parallel to GPx4, so that cells with high FSP1 expression are resistant to GPx4 inhibition, and cells with FSP1 deficiency become sensitive to GPx4 inhibitors (Y. Song et al., 2026). It has been found that in several types of cancers, that FSP1 expression is upregulated, which contributes to ferroptosis evasion and resistance to GPx4-targeted therapy. In addition, small-molecule inhibitors of FSP1, such as iFSP1 and viFSP1, have been developed and demonstrate synergistic ferroptosis induction in combination with RSL3 (Dai et al., 2024).

2.2.2 The GCH1–BH4 Pathway

Another GPX4-independent pathway involves GTP cyclohydrolase 1 (GCH1), which is the first enzyme involved in the biosynthesis of tetrahydrobiopterin (BH_4) (Kraft et al., 2020). BH_4 is a cofactor and an endogenous antioxidant required for synthesis of neurotransmitters like dopamine and nitric oxide. GCH1 was identified as one of the most effective suppressors of ferroptosis by studies carried out by Kraft et al. 2020. GCH1-mediated BH_4 production causes lipid remodeling and inhibits ferroptosis by selectively preventing depletion of phospholipids with two polyunsaturated fatty acyl tails (Kraft et al., 2020). Furthermore, BH_4 itself acts as a lipophilic radical trapping agent preventing propagation and accumulation of lipid hydroperoxides and serving as

a ferroptotic suppressor (Duo et al., 2025). Studies have shown that the GCH1 -BH_4 pathway selectively remodels PUFA containing ether phospholipids which are particularly enriched in neuronal membranes, suggesting its importance in neurological ferroptosis protection. Therefore, dietary supplementation of BH_4 or pharmacological elevation of BH_4 with sepiapterin has been proposed as a therapeutic strategy for neurodegenerative conditions associated with ferroptosis (Duo et al., 2025).

2.2.3 The Mitochondrial DHODH Pathway

Dihydroorotate dehydrogenase (DHODH) is a flavoprotein involved in the de-novo pathway for pyrimidine biosynthesis and is present in the inner mitochondrial membrane (Cao et al., 2025; Mao et al., 2021). Recent studies have shown DHODH to be a key therapeutic target for hyperproliferative disorders, parasitic infections, and viral diseases and for the treatment of autoimmune disorders, including rheumatoid arthritis and multiple sclerosis (Cao et al., 2025). DHODH inhibitors have emerged in oncology, as a promising class of anticancer agents (Cao et al., 2025). Recent studies show that DHODH serves as a suppressor of mitochondrial ferroptosis independent of GPx4, by reducing ubiquinone (CoQ10) to ubiquinol within the inner mitochondrial membrane, thereby suppressing mitochondrial lipid peroxidation (Jiang et al., 2024). This function is spatially distinct from the cytoplasmic and plasma membrane defense provided by FSP1–CoQ10, establishing DHODH as the mitochondria-specific radical trapping agent and a suppressor of ferroptosis. Studies have shown sensitization of cells to ferroptosis under conditions of GPx4 inactivation by use of pharmacological inhibitors of DHODH which has important implications for cancer therapy (Mao et al., 2021)

3. Role of Nrf2 in Ferroptosis

An important inducer of ferroptosis resistance is the nuclear factor erythroid 2-related factor 2 (Nrf2) which is encoded by NFE2L2. Nrf2 serves as the master regulator of antioxidants, and cytoprotective genes by binding to Antioxidant Response Elements (AREs) and increasing the transcription of antioxidant genes, protecting cells from oxidative stress, inflammation, and metabolic damage. The Nrf2 activity is majorly regulated by Keap 1 (Kelch-like ECH-associated protein 1) a cysteine-rich sensor protein that regulates the cellular response to oxidative and electrophilic stress by controlling the stability of Nrf2 (Jiang et al., 2024). Normally Nrf2 is bound to Keap 1 through the ETGE and DLG motifs in its Neh2 domain (Tong et al., 2006). Keap 1 acts as an adaptor for the Cul3-dependent E3 ubiquitin ligase complex, facilitating Nrf2 degradation, ensuring low levels of intracellular Nrf2. However, electrophiles and oxidants modify cysteine residues on Keap1, disrupting its interaction with Nrf2, allowing Nrf2 to dissociate from Keap1, and move to the nucleus where it increases the transcription of antioxidant genes by interacting with other protein factors (such as sMaf) and binding to the ARE (Levonen et al., 2004). Downstream Nrf2 activates promoters of *SLC7A11*, *GPX4*, *FTH1*, *HMOX1*, thereby affecting anti-ferroptotic defenses (Chen et al., 2026). Moreover, pharmacological activation of Nrf2 by sulforaphane, bardoxolone methyl have been shown to confer protection against ferroptotic stimuli in neuronal and hepatic cells (Wu et al., 2022). On the other hand, aberrant hyperactivation of Nrf2 due to KEAP1 loss-of-function mutations, Nrf2 gain-of-function mutations, or epigenetic silencing of KEAP1, suppresses ferroptosis and thereby contributes to chemoresistance in cancer cells (Kgatle et al., 2025). Thus Nrf2 may be considered as a double-edged sword, playing a cytoprotective role in degenerative disease but tumour promoting roles in relation to tumor biology.

4. Role of p53 as a Context-Dependent Modulator of Ferroptosis

The p53 protein, encoded by the *TP53* gene, acts as a complex context dependent regulator of ferroptosis. p53 plays a pro-ferroptotic role by repressing the transcription of SLC7A11 which is a critical component of system Xc- thereby causing a depletion of GSH and increasing ferroptosis susceptibility in cancer cells (Xu et al., 2023). This pro-ferroptotic role was suggested to represent a propabable mechanism by which p53 caused tumor suppression, explaining in part why p53-deficient cancers are often resistant to oxidative stress. The fact that ferroptosis represents a dispensable and detachable tumor suppressive property of p53 was shown by studies on the acetylation-deficient p53 mutant (3KR), which could not induce cell cycle arrest but were found to retain SLC7A11 repression and ferroptosis induction (Xu et al., 2023). p53 can also induce the expression of spermidine/spermine N1-acetyltransferase 1 (*SAT1*), which increases reactive oxygen species (ROS) and ALOX15 mediated lipid peroxidation thereby inducing ferroptosis (Ou et al., 2016). p53 also enhances

ferroptosis by regulating the protein ferredoxin reductase which is involved in regulating iron metabolism (Zhang et al., 2019). However, under conditions of mild or metabolic stress, p53 also serves to inhibit ferroptotic death in cells. Under conditions of metabolic stress p53 induces the transcription of CDKN1A/p21, which suppresses ferroptosis by providing sustained levels of GSH, causing a temporary delay that allows DNA repair before committing to cell death (Tarangelo & Dixon, 2018). Thus, the role of p53 may be considered as a "double-edged sword" in ferroptosis modulating the ferroptotic response in context.

5. Role of Heat Shock Proteins in ferroptosis

Heat shock proteins (HSPs) are the most abundant molecular chaperone proteins which play an important role in maintaining protein stability and thus their expression is increased under conditions of stress. HSP90 family of HSPs affects the stability of GPx4 and thus influences ferroptosis. HSPA5, also known as GRP78 or Bip, is an important member of HSP70 family. In human pancreatic ductal adenocarcinoma cells (PDAC), HSPA5 negatively regulates ferroptosis of PDAC cells through HSPA5-GPx4 signaling pathway and mediates resistance to ferroptosis (Zhu et al., 2017). HSP70 (HSPA1A) and HSP27 (HSPB1) have also been shown to suppress ferroptosis, with HSPB1 acting by reducing cellular iron levels through inhibition of the transferrin receptor internalization pathway (Sun et al., 2015). The partial overlap between the heat shock responses and suppression of ferroptosis in some tumors may thus be explained by these chaperone-mediated mechanisms which support ferroptosis resistance in cancer cells.

6. Epigenetic Regulation of ferroptosis

Epigenetics refers to heritable changes in the gene function leading to phenotypic changes without affecting the DNA sequence. Recent studies show that epigenetic regulation affects ferroptosis, and targeting epigenetic mechanisms in ferroptosis will provide a new direction for the treatment of ferroptosis-related diseases (Ouyang et al., 2024). The transcription of ACSL4 and thereby the incorporation of PUFAs in membrane lipids is repressed by the histone methyltransferase EZH2 (a component of the PRC2 complex) thus making the cells resistant to ferroptosis. On the other hand, inhibition of EZH2 sensitizes cancer cells to ferroptosis inducers (Pan et al., 2025). Similarly, the histone deacetylase HDAC1/2 can suppress *SLC7A11* promoter accessibility, providing an epigenetic route to ferroptosis sensitization (Lu et al., 2026). Moreover, histone methylation has also been shown to regulate ferroptosis. Both histone 2A ubiquitination (H2Aub) and histone 2B ubiquitination (H2Bub), have been shown to be associated with expression of SLC7A11 thus regulating ferroptosis (Xiao et al., 2025).

Ferroptosis is also regulated by many non-coding RNAs including lncRNAs and miRNAs and cirRNAs. miR-9, miR-5096, miR-375, and miR-378a-3p have been found to reduce the expression of SLC7A11 and sensitize cells to ferroptosis, while the lncRNA LINC00336 sequesters miR-6852, maintaining cysteine levels and thus preventing ferroptosis (Xiao et al., 2025). miR-15a-5p, miR-324-3p, miR-182-5p, and miR-541-3p promote ferroptosis by inhibiting GPX4 expression (Yang et al., 2023). Additionally, miR-214-3p promotes ferroptosis by targeting ATF4, which is a critical mediator of endoplasmic reticulum (ER) stress. miR-670-3p and miR-424-5p suppress ferroptosis by inhibiting ACSL4 expression (Yang et al., 2023). MiR-16-92 also causes ferroptosis resistance by inhibiting the expression of zinc lipoprotein A20, which is a molecule upstream of ACSL4 (Ojo et al., 2025). Thus, there are multiple interrelated ways by which non-coding RNAs regulate ferroptosis which need to be further studied for therapeutic targeting of ferroptosis

7. Therapeutic Implications

Ferroptosis plays a dual role in diseases- pathological in degenerative conditions and potentially beneficial in oncology. In tumor cells, the major goal is to sensitize cells to ferroptosis either by downregulating GPx4 or SLC7A11 or by potentiating iron accumulation mediated lipid peroxidation. In this context studies have shown GPx4 inhibitors (RSL3 and its derivatives, ML162, and the clinical-stage compound FINO2), system X*c*− inhibitors (erastin and its analogs imidazole ketone erastin, piperazine erastin), and iron-based nanomaterials to have preclinical efficacy in tumors resistance to standard cytotoxic agents (Ojo et al., 2025). In contrast, mesenchymal and therapy-resistant cancer cell states having elevated ACSL4 and LPCAT3 activity are susceptible to ferroptosis, suggesting therapeutic targeting of ferroptosis for metastasis and relapse. Ferroptotic cell death generates damage-associated molecular patterns (DAMPs) that can activate innate immunity and improve T cell responses against tumors (Ren et al., 2023). Moreover, iron chelators, lipophilic antioxidants and Nrf2 activators have demonstrated

protective effects in animal models of, ischemia-reperfusion injury, hemorrhagic stroke, and neurodegenerative diseases including Alzheimer's, Parkinson's, and Huntington's disease (Song & Long, 2020). The clinical translation of these agents—particularly liposome-encapsulated ferrostatin analogs—represents an active area of pharmaceutical Research (Wang et al., 2022).

Although recently several studies focus on ferroptosis as a therapeutic target in several diseases, the research is still naïve and there are several unanswered questions. The dynamics of propagation of lipid peroxidation chain reaction within membrane microdomains and mechanism by which accumulation of lipid hydroperoxides ruptures membranes whether through direct biophysical disruption or secondary pore formation and causes cell death, needs to be further studied. Furthermore, the regulation various GPX4 independent pathways of ferroptosis requires systematic elucidation. Computational modeling studies on redox fluxes, iron dynamics, and transcriptional networks should be undertaken to predict ferroptosis thresholds and optimize therapeutic windows.

8. Conclusions

Ferroptosis is a newly defined mechanism of programmed cell death with multi-layered regulatory networks encompassing Xc−-GSH-GPx4 as its central defense mechanism. Parallel GPX4 independent pathways involve FSP1–CoQ10, GCH1–BH4, and DHODH all of which are driven by iron dependent oxidative lipid damage. Ferroptosis is also regulated by epigenetics and upstream modulators such as p53, heat shock proteins, and Nrf2. Further studies will reveal other molecular pathways and regulatory nodes for ferroptosis paving the way for ferroptosis-targeted therapies and establishing ferroptotic pathway as a keystone of cell death medicine.

Declaration

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Conflict of Interest and Ethical Compliance

All authors confirm that:
i. Any potential conflicts of interest, whether financial or non-financial, have been fully disclosed. –Not Applicable
ii. All sources of funding and financial support received for the conduct of the study have been appropriately acknowledged, including any updates made during revision. –Not Applicable
iii. Necessary ethical approvals have been obtained from the relevant institutional or regulatory bodies for studies involving human participants, animals, or sensitive data, wherever applicable, and are clearly stated in the manuscript. –Not Applicable

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