# A Chapter on:

# Title: Ferroptosis: Its mechanism and role in various clinical conditions.

**Author information:**
**Binita Patel*[1],**
***[1]** CAM Institute of Allied Health Sciences & Technology,
Bhaikaka University,
Karamsad,
Gujarat, India.
Email: binitatp@charutarhealth.org
Contact number: + 91 9824229462
**Dr. Sonal Mayur Chitroda[2]**
[2]Smt. L.P.Patel Institute of Medical Laboratory Technology,
Bhaikaka University,
Karamsad,
Gujarat, India.
Email: sonalmc@charutarhealth.org
ORCID: 0000-0002-7803-3377
Contact number: +91 8980221343

**Disclaimer:** The author(s) ensure that no contractual relations or proprietary considerations exist that would affect the publication of information in the submitted manuscript. There is no conflict of interest of any sort. Neither has the membership nor one with substantially similar content under my authorship been published in any language, in any journal nor is being considered for publication elsewhere.

**Number of Figure: 00**
**Number of Table: 01**

# Ferroptosis: Its mechanism and role in various clinical conditions.


## I ABSTRACT:

Ferroptosis is a distinct iron-dependent type of nonapoptotic cell death that is induced by the oncogenic RAS-selective fatal small chemical erastin. Ferroptosis differs from apoptosis, necrosis, and autophagy in terms of morphology, biochemistry, and heredity. It is dependent on intracellular iron but no other metals. Nonapoptotic cell death mechanisms may help to selectively eliminate some tumor cells or may be induced in particular clinical conditions So, Preventing ferroptosis can defend organisms against neurodegeneration while activating it causes the nonapoptotic death of certain malignant cells.[1]



**Keywords:** ferroptosis, non-apoptotic cell death.


## II. INTRODUCTION:

The iron-dependent cell death procedure referred to as ferroptosis is distinctive from various types of cell death, especially apoptosis and necrosis. The program incorporates three main metabolic processes involving thiol, lipid, and iron, that cause lipid peroxidation which is iron-dependent and eventually, leads to cell death. Glutathione peroxidase 4 (GPx4), which triggers the reduction of lipid peroxides in a glutathione-dependent reaction, and the recently observed ferroptosis suppressor protein (FSP1), which catalyzes the regeneration of ubiquinone (Coenzyme Q10, CoQ10), that serves as a lipid peroxyl radical trap, are two of the major antioxidant systems that can prevent ferroptosis.[1,2] Iron chelators (such as deferiprone and deferoxamine) and tiny lipophilic antioxidants (such as ferrostatin and liproxstatin) can prevent the buildup of fatal lipid species that result from lipid peroxidation, which is the reason for ferroptotic cell death.[3] Ferroptotic cell death may be distinguished from other kinds of cell death through a variety of alterations in the shape of cells, metabolism, and protein expression. At the cellular and subcellular levels, ferroptotic cells takes on an unusual rounded shape prior to their death, similar to necrotic cells, but there is no cytoplasmic and organelle enlargement, and there is no injury to the plasma membrane.[1,4] Ferroptotic cells' nuclei maintain their structural integrity without the process of condensation, chromatin margination, vesication of the plasma membrane, or the formation of apoptotic bodies[1],which defines the features of apoptosis.[5] In addition, morphological features includes attributes like double-membrane encapsulated vesicles from autophagic cells, delayed blebbing, and plasma loss the membrane integrity shown in pyroptosis isn't observed in ferroptotic cells.[6] The sole distinctive morphological feature is mitochondria with smaller than usual size and enhanced membrane thickness.[1]
This chapter summarizes the ferroptosis brief introduction, history surrounding its discovery, significant research on the phenomena, its mechanism, as well as its future implications and potential study areas.

## III. DISCOVERY OF FERROPTOSIS:

Although the association between iron and lipid peroxidation has been well recognized for a long time,[7] it wasn't until Brent Stockwell and Scott J. Dixon established the term ferroptosis in 2012 and described several of its key characteristics,[1] even though Pamela Maher and David Schubert first identified the process in 2001 under the name oxytosis. Despite the fact that iron was not mentioned at the time, oxytosis and ferroptosis are now regarded to be two different terminologies for the same cell death process.[8,9]

The table below displays the overall amount of progress and research made about the phenomenon:[10]

**TABLE:1**

| YEAR | FINDINGS | NAME OF THE RESEARCHER |
|---|---|---|
| 2003 | • Erastin (mutant RAS selective compound) | B.Stockwell |
| 2007 | • VDAC2/3 (mitochondrial porins) Mutated RAS Oncogene) Vitamin E (Antioxidant) | B.Stockwell |
| 2008 | • TFRC(Iron importer)<br>• RSL 3,RSL 5 (Mutant RAS Selective compounds) DFO (Iron chelator) | B.Stockwell |
| 2010 | • ML 162, ML210 (Mutant RAS Selective compounds) | S.Schreiber |
| 2012 | • SLC7A11(Cystine/glutamate transporter; coins the term ferroptosis)<br>• Ferrostatin-1(Ferroptosis inhibitor) Sufasalazine(SLCA11 inhibitor)<br>• DPI GKT137831(NOX inhibitor) | B.Stockwell |
| 2014 | • GPX (Phospholipid hydroperoxidase)<br>• Sorafenib (SLC7A11 inhibitor) | B.Stockwell |
| 2014 | • Liprox-statin-1(Ferroptosis inhibitor)<br>• Zileuton (ALOX inhibitor) | M.Conrad |
| 2015 | • SLC38A1(Glutamine transporter) | X.Jiang |
| 2015 | • HSPB1(Heat shock protein) | D.Tang |
| 2015 | • TP53(Transcription factor) | W.Gu |
| 2015 | • Artesunate (Antimalarial agent) | N.Brady |
| 2015 | • IKE(SLC7A11 inhibitor) | B.Stockwell |
| 2016 | • ACSL4 (Lipidbiosynthesis) | D.Tang,M.Conrad, V.Kagan |
| 2016 | • NEF2L2(Transcription factor) | D.Tang |
| 2016 | • NCOA4 (Ferritinophagy) | D.Tang,X.Jiang |
| 2016 | • ALOXs (Lipoxygenase), FIN56(GPX4 and CoQ10 inhibitor), Statins (HMG-CoA reductase) | B.Stockwell |
| 2016 | • $FINO_2$ (GPX4 inactivation and iron oxidation) | K.Woerpel |
| 2017 | • BID (BCL2 family) | C.Culmsee |
| 2017 | • ZEB1(EMT-activator) | S.Schreiber |
| 2017 | • ITGA6, ITGB4 (Cell adhesion) | A.Mercurio |
| 2017 | • Hemoglobin Hemin (Iron containing protein) | R.Ratan |
| 2017 | • Rosiglitazone (ACSL4 inhibitor) | M.Conrad |
| 2018 | • BAP1 (Epigenetic regulation) | B.Gan |
| 2018 | • NECTIN4 (Cell clustering) | A.Mercurio |
| 2018 | • CTSB (Lysosomal cell death) | D.Tang |
| 2018 | • Withaferin A (Increase Iron), LOX-Block-1 (ALOX inibitor) | T.Vanden Berghe |
| 2019 | • YAP,NF2,WWTR1(Cell contact) | X.Jiang, J.Chi |
| 2019 | • AIFM2 (CoQ10 Production) | M.Conrad, J.Olzmann |
| 2019 | • Cyst(e)inase (Cysteine depletion) | W.Zou |
| 2019 | • Ferroptocide (Thioredoxin inhibitor) | P.Hergenrother |
| 2019 | • iFSP (AIFM2 inhibitor) | M.Conrad |
| 2020 | • PEX10, PEX3 (Peroxisome) | S.Schreiber |
| 2020 | • GCH1 ($BH_4$ production) | J.Schick |
| 2020 | • CHMP5, CHMP6 (ESCRT-III membrane repair) | D.Tang |
| 2020 | • POR (Phospholipid peroxidation) | S.Schreiber |

| | | |
|---|---|---|
| 2020 | • Zalcitabine (Antiretroviral agent) | D.Tang |
| 2020 | • Quercetin (Antioxidant agent) | D.Chen |

## MECHANISM OF FERROPTOSIS:

The iron-dependent accumulation of oxidatively damaged phospholipids (also known as lipid peroxides) is the distinguishing characteristic of oxytosis/ferroptosis. Sequestering iron in lysosomes can take advantage of a Fenton chemistry property that is essential for the production of reactive oxygen species.[11] When free radicals remove electrons from a lipid molecule (which is usually affecting polyunsaturated fatty acids), they can lead to the oxidation of phospholipids. Glutathione peroxidase 4 (GPX4), a glutathione-dependent hydroperoxidase that transforms lipid peroxides into non-toxic lipid alcohols, mediates the main cellular defense againstoxytosis/ferroptosis.[12] Recently two laboratories identified a second parallel protactive route involving the oxidoreductase FSP1which is also known as AIFM2. According to their research,FSP1 degrades non-mitochondrial enzyme Q10 enzymetically to produce a powerful lipophilic antioxidant that inhibits the growth of lipid peroxides[13,14] Tetrahydrobiopterin (BH4), a byproduct of the rate-limiting enzyme GCH1, was also shown to have a similar mechanism for a cofactor acting as a diffusable antioxidant in the same year.[15,16] Small compounds that induce oxytosis/ferroptosis, such as erastin, sulfasalazine, sorafenib, (1S, 3R)-RSL3, ML162, and ML210, are known to suppress the proliferation of tumor cells. These substances do not cause chromatin margination or poly (ADP-ribose) polymerase (PARP) cleavage because they do not cause apoptosis. Instead, oxytosis/ferroptosis alters the phenotype of the mitochondria. Small-molecule oxytosis/ferroptosis induction also requires iron, therefore iron chelators can block these substances. Erastin works by preventing the cystine/glutamate transporter, which results in lower intracellular glutathione (GSH) concentrations.[1] Because GPX4 depends on GSH for proper operation, its loss might cause ferroptotic cell death.[17] Oxytosis/ferroptosis can also be induced through inhibition of GPX4, as is the molecular mechanism of action of RSL3, ML162, and ML210.[16] In some cells, FSP1 compensates for loss of GPX4 activity, and both GPX4 and FSP1 must be inhibited simultaneously to induce oxytosis/ferroptosis.[18]

## FUTURE ASPECTS OF FERROPTOSIS:

With advances in the field of research, ferroptosis has been discovered in the pathophysiological mechanisms of an increasing number of illnesses, and it offers a novel therapeutic approach.Additionally, ferroptosis, an independent method of cell death, can contribute to illnesses in conjunction with other types of cell death, opening the door to the collaborative use of current treatment plans and assisting in the resolution of drug resistance difficulties in specific diseases. Ferroptosis research, however, is still in its infancy, and there are still many of issues to be resolved.[1] Ferroptosis inducers or inhibitors are effective treatments for a variety of illnesses. Tumors, neurological disorders, organ damage, etc. have all been treated by ferroptosis. Several investigations have presented proof that ferroptosis can stop tumor development. It has been shown that ferroptosis inducers are cytotoxic to a variety of tumor cells both in vivo and in vitro.[1,19,20] Ferroptosis inducers can also be transported by some specific carriers as an alternative to direct administration of ferroptosis agents, which revealed improved anticancer results.[21,22] Since certain nanoparticles, like C' dots, may cause ferroptosis, altering these nanoparticles is another efficient technique to cause ferroptosis particularly in tumor tissues. For instance, different-sized Fe3O4 nanoparticles have demonstrated variable capacities to cause ferroptosis.[23] Additionally, one strategy to improve the effectiveness of tumor immunotherapy is to control the immune cells' susceptibility to ferroptosis.[24] Ferroptosis is also linked to a few neurological conditions. According to a recent research, the lipid-transporting glycoprotein known as apolipoprotein E (ApoE), a key protein in Alzheimer's disease**.**[25] can shield cells against substances that cause ferroptosis, such as erastin and SAS. By lowering iron release from ferritin by activating the PI3K/AKT pathway, apoE prevents ferroptosis[26] Ferroptosis inhibitors can improve these symptoms since the Alzheimer's mice model had down-regulated ferroportin1, a nonheme iron exporter that triggers ferroptosis, neuronal death, and memory impairment**.**[27] A stroke sub-type associated with ferroptosis is intracerebral hemorrhage. In intracerebral hemorrhage, blocking ferroptosis has a therapeutic impact, [28] also the emergence and development of a few other neurological conditions that are linked to ferroptosis, such as Huntington's disease, Parkinson's disease, and amyotrophic lateral sclerosis.[20] One of the causes of glaucoma, as recently found by Yao et al., is ferroptosis of retinal ganglion cells caused by pathologically high intraocular pressure.[29] Ferroptosis may control illnesses including TB and autoimmune disorders in addition to cancer and neurological disorders. Mycobacterium tuberculosis (Mtb) is the cause of TB. Ferroptosis has been demonstrated to be one of the processes by which Mtb infection results in necrosis of host cells**.**[30] Neutrophils from people with systemic lupus erythematosus exhibit ferroptosis, according to a recent research. The expression of GPX4 was suppressed in the neutrophils of patients**.**[31] Ferroptosis' mechanism and pertinent metabolic route still require investigation. New questions also emerge as research is continually advanced. For instance, the propagation of waves in ferroptosis

is a rare phenomenon.[32] The mechanism behind GPX4's apparent requirement for propagation is currently unknown.[33] With the investigation of the ferroptosis mechanism, various possible inducers and inhibitors are also presented. For instance, the activity of mTOR, a key regulator of cell growth and proliferation, can be inhibited by torin 1. Under conditions of low glucose, Torin 1 has been demonstrated to protect cells by lowering the activity of System Xc.[34] More research is required to determine whether Torin 1 can be used as an inducer of ferroptosis. Furthermore, certain substances may have many roles. A proteasome inhibitor is MG132. Since the deubiquitinase OTUB1 may stabilize System Xc in a proteasome-dependent manner, treatment with MG132 enhanced the expression of System Xc.[34,35] In this sense, MG132 may be a potential inhibitor of ferroptosis. Fortunately a different investigation found that ferroptosis inducers prevented the proteasome from being expressed. Thus, encouraging proteasome expression is advantageous for cells undergoing ferroptosis.[36]

## CONCLUSION:

In conclusion, the discovery of ferroptosis has created a new platform for the study of diseases, and its clinical importance in the onset, progression, and management of illnesses has slowly become apparent. Ferroptosis research is still in its early stages at the moment. Exploring the mechanism of ferroptosis and its impact in many illnesses as well as suggesting efficient and highly focused therapeutics have significant scientific and practical utility. Ferroptosis research will continue in this manner in the future. The development of inducers and inhibitors is crucial to research on ferroptosis, and the ongoing discovery of new ferroptosis targets and mechanisms leads to new therapeutic drugs and methods for various types of diseases. In conclusion, ferroptosis is a form of programmed cell death with high application prospects but still needs further study.

## REFERENCES:


1. Dixon SJ, Lemberg KM, Lamprecht MR, Skouta R, Zaitsev EM, Gleason CE, Patel DN, Bauer AJ, Cantley AM, Yang WS, Morrison B 3rd, Stockwell BR. Ferroptosis: an iron-dependent form of nonapoptotic cell death. Cell. 2012 May 25;149(5):1060-72. doi:10.1016/j.cell.2012.03.042. PMID: 22632970; PMCID: PMC3367386.
2. Bersuker, K. et al. The CoQ oxidoreductase FSP1 acts parallel to GPX4 to inhibit ferroptosis. Nature 575, 688–692 (2019)
3. Yan, Hf., Zou, T., Tuo, Qz. *et al*. Ferroptosis: mechanisms and links with diseases. *Sig Transduct Target Ther* **6**, 49 (2021). https://doi.org/10.1038/s41392-020-00428-9
4. Yagoda, N. et al. RAS-RAF-MEK-dependent oxidative cell death involving voltage-dependent anion channels. Nature 447, 864–868 (2007).
5. Ke, B. et al. Targeting programmed cell death using small-molecule compounds to improve potential cancer therapy. Med. Res. Rev. 36, 983–1035 (2016).
6. Liang, C., Zhang, X., Yang, M. & Dong, X. Recent progress in ferroptosis inducers for cancer therapy. Adv. Mater. 31, e1904197 (2019).
7. Gutteridge JM (July 1984). Lipid peroxidation initiated by superoxide-dependent hydroxyl radicals using complexed iron and hydrogen peroxide.FEBS Letters. 172 (2):245–9. doi:10.1016/0014-5793(84)81134-5. PMID 6086389. S2CID 22040840.
8. Tan S, Schubert D, Maher P. Oxytosis: A novel form of programmed cell death. Curr Top Med Chem. 2001 Dec;1(6):497-506. doi: 10.2174/1568026013394741. PMID: 11895126.
9. Maher P, Currais A, Schubert D. Using the Oxytosis/Ferroptosis Pathway to Understand and Treat Age-Associated Neurodegenerative Diseases. Cell Chem Biol. 2020 Dec 17;27(12):1456-1471. doi: 10.1016/j.chembiol.2020.10.010. Epub 2020 Nov 10. PMID: 33176157; PMCID: PMC7749085.
10. Tang, D., Chen, X., Kang, R. *et al.* Ferroptosis: molecular mechanisms and health implications. *Cell Res* **31**, 107–125 (2021). doi:10.1038/s41422-020-00441-1
11. Mai TT, Hamaï A, Hienzsch A, Cañeque T, Müller S, Wicinski J, Cabaud O, Leroy C, David A, Acevedo V, Ryo A, Ginestier C, Birnbaum D, Charafe-Jauffret E, Codogno P, Mehrpour M, Rodriguez R. Salinomycin kills cancer stem cells by sequestering iron in lysosomes. Nat Chem. 2017 Oct;9(10):1025-1033. doi: 10.1038/nchem.2778. Epub 2017 May 16. PMID: 28937680; PMCID: PMC5890907.
12. Yang WS, Stockwell BR. Ferroptosis: Death by Lipid Peroxidation. Trends Cell Biol. 2016 Mar;26(3):165-176. doi: 10.1016/j.tcb.2015.10.014. Epub 2015 Dec 2. PMID: 26653790; PMCID: PMC4764384.
13. Bersuker K, Hendricks JM, Li Z, Magtanong L, Ford B, Tang PH, Roberts MA, Tong B, Maimone TJ, Zoncu R, Bassik MC, Nomura DK, Dixon SJ, Olzmann JA. The CoQ oxidoreductase FSP1 acts parallel to GPX4 to inhibit ferroptosis. Nature. 2019 Nov;575(7784):688-692. doi: 10.1038/s41586-019-1705-2. Epub 2019 Oct 21. PMID: 31634900; PMCID: PMC6883167.
14. Doll S, Freitas FP, Shah R, Aldrovandi M, da Silva MC, Ingold I, et al. (November 2019). FSP1 is a glutathione-independent ferroptosis supressor *Nature*. **575** (7784): 693-698.Bibcode:2019Natur.575..693D. doi:10.1038/s41586-019-1707-0. hdl:10044/1/75345. PMID 31634899. S2CID 204833583.
15. Kraft VAN, Bezjian CT, Pfeiffer S, Ringelstetter L, Müller C, Zandkarimi F, Merl-Pham J, Bao X, Anastasov N, Kössl J, Brandner S, Daniels JD, Schmitt-Kopplin P, Hauck SM, Stockwell BR, Hadian K, Schick JA. GTP Cyclohydrolase 1/Tetrahydrobiopterin Counteract Ferroptosis through Lipid Remodeling. ACS Cent Sci. 2020 Jan 22;6(1):41-53. doi: 10.1021/acscentsci.9b01063. Epub 2019 Dec 27. PMID: 31989025; PMCID: PMC6978838.

16. Soula M, Weber RA, Zilka O, Alwaseem H, La K, Yen F, Molina H, Garcia-Bermudez J, Pratt DA, Birsoy K. Metabolic determinants of cancer cell sensitivity to canonical ferroptosis inducers. Nat Chem Biol. 2020 Dec;16(12):1351-1360. doi: 10.1038/s41589-020-0613-y. Epub 2020 Aug 10. PMID: 32778843; PMCID: PMC8299533.
17. Cao JY, Dixon SJ. Mechanisms of ferroptosis. Cell Mol Life Sci. 2016 Jun;73(11-12):2195-209. doi: 10.1007/s00018-016-2194-1. Epub 2016 Apr 5. PMID: 27048822; PMCID: PMC4887533.
18. Eaton JK, Furst L, Ruberto RA, Moosmayer D, Hilpmann A, Ryan MJ, Zimmermann K, Cai LL, Niehues M, Badock V, Kramm A, Chen S, Hillig RC, Clemons PA, Gradl S, Montagnon C, Lazarski KE, Christian S, Bajrami B, Neuhaus R, Eheim AL, Viswanathan VS, Schreiber SL. Selective covalent targeting of GPX4 using masked nitrile-oxide electrophiles. Nat Chem Biol. 2020 May;16(5):497-506. doi: 10.1038/s41589-020-0501-5. Epub 2020 Mar 30. PMID: 32231343; PMCID: PMC7251976.
19. Kim SE, Zhang L, Ma K, Riegman M, Chen F, Ingold I, et al. Ultrasmall nano particles induce ferroptosis in nutrient-deprived cancer cells and suppress tumour growth. Nat Nanotechnol. 2016;11:977–85.
20. Li J, Cao F, Yin H-L, Huang Z-J, Lin Z-T, Mao N, et al. Ferroptosis: past, present and future. Cell Death Dis. 2020;11:88.
21. Yang J, Jia Z, Zhang J, Pan X, Wei Y, Ma S, et al. Metabolic intervention nanoparticles for triple-negative breast cancer therapy via overcoming FSP1- mediated ferroptosis resistance. Adv Health Mater. 2022;11:2102799.
22. Guan Q, Guo R, Huang S, Zhang F, Liu J, Wang Z, et al. Mesoporous polydopamine carrying sorafenib and SPIO nanoparticles for MRI-guided ferroptosis cancer therapy. J Control Release. 2020;320:392–403.
23. Tian X, Ruan L, Zhou S, Wu L, Cao J, Qi X, et al. Appropriate size of Fe3O4 nanoparticles for cancer therapy by ferroptosis. ACS Appl Bio Mater. 2022;5:1692–99.
24. Xu H, Ye D, Ren M, Zhang H, Bi F. Ferroptosis in the tumor microenvironment: perspectives for immunotherapy. Trends Mol Med. 2021;27:856–67.
25. Mahoney-Sanchez L, Belaidi AA, Bush AI, Ayton S. The complex role of apolipoprotein E in Alzheimer's disease: an overview and update. J Mol Neurosci. 2016;60:325–35.
26. Belaidi AA, Masaldan S, Southon A, Kalinowski P, Acevedo K, Appukuttan AT, et al. Apolipoprotein E potently inhibits ferroptosis by blocking ferritinophagy. Mol Psychiatry. 2022; https://doi.org/10.1038/s41380-022-01568-w.
27. Bao W-D, Pang P, Zhou X-T, Hu F, Xiong W, Chen K, et al. Loss of ferroportin induces memory impairment by promoting ferroptosis in Alzheimer's disease. Cell Death Differ. 2021;28:1548–62.
28. Alim I, Caulfield JT, Chen Y, Swarup V, Geschwind DH, Ivanova E, et al. Selenium drives a transcriptional adaptive program to block ferroptosis and treat stroke. Cell. 2019;177:1262–79.
29. Yao F, Peng J, Zhang E, Ji D, Gao Z, Tang Y, et al. Pathologically high intraocular pressure disturbs normal iron homeostasis and leads to retinal ganglion cell ferroptosis in glaucoma. Cell Death Differ. 2022; https://doi.org/10.1038/s41418-022-01046-4.
30. Amaral EP, Costa DL, Namasivayam S, Riteau N, Kamenyeva O, Mittereder L, et al. A major role for ferroptosis in Mycobacterium tuberculosis–induced cell death and tissue necrosis. J Exp Med. 2019;216:556–70.
31. Li P, Jiang M, Li K, Li H, Zhou Y, Xiao X, et al. Glutathione peroxidase 4–regulated neutrophil ferroptosis induces systemic autoimmunity. Nat Immunol. 2021;22:1107–17.
32. Nishizawa H, Matsumoto M, Chen G, Ishii Y, Tada K, Onodera M, et al. Lipid peroxidation and the subsequent cell death transmitting from ferroptotic cells to neighboring cells. Cell Death Dis. 2021;12:332.
33. Riegman M, Sagie L, Galed C, Levin T, Steinberg N, Dixon SJ, et al. Ferroptosis occurs through an osmotic mechanism and propagates independently of cell rupture. Nat Cell Biol. 2020;22:1042–48.
34. Yamaguchi I, Yoshimura SH, Katoh H. High cell density increases glioblastoma cell viability under glucose deprivation via degradation of the cystine/glutamate transporter xCT (SLC7A11). J Biol Chem. 2020;295:6936–45
35. Liu T, Jiang L, Tavana O, Gu W. The deubiquitylase OTUB1 mediates ferroptosis via stabilization of SLC7A11. Cancer Res. 2019;79:1913–24.
36. Kotschi S, Jung A, Willemsen N, Ofoghi A, Proneth B, Conrad M, et al. NFE2L1- mediated proteasome function protects from ferroptosis. Mol Metab.
2022;57:101436.