ISSN 1007-9327 (print)
ISSN 2219-2840 (online)

World Journal of *Gastroenterology*

World J Gastroenterol 2024 September 7; 30(33): 3791-3849

Published by Baishideng Publishing Group Inc

World Journal of Gastroenterology

Contents

Weekly Volume 30 Number 33 September 7, 2024

EDITORIAL

ORIGINAL ARTICLE

Retrospective Cohort Study

Observational Study

LETTER TO THE EDITOR

ABOUT COVER

Editorial Board Member of *World Journal of Gastroenterology*, Sung-Chul Lim, MD, PhD, Professor, Department of Pathology, Chosun University Hospital, Gwangju 501-717, South Korea. sclim@chosun.ac.kr

AIMS AND SCOPE

The primary aim of *World Journal of Gastroenterology* (*WJG*, *World J Gastroenterol*) is to provide scholars and readers from various fields of gastroenterology and hepatology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online. *WJG* mainly publishes articles reporting research results and findings obtained in the field of gastroenterology and hepatology and covering a wide range of topics including gastroenterology, hepatology, gastrointestinal endoscopy, gastrointestinal surgery, gastrointestinal oncology, and pediatric gastroenterology.

INDEXING/ABSTRACTING

The *WJG* is now abstracted and indexed in Science Citation Index Expanded (SCIE), MEDLINE, PubMed, PubMed Central, Scopus, Reference Citation Analysis, China Science and Technology Journal Database, and Superstar Journals Database. The 2024 edition of Journal Citation Reports® cites the 2023 journal impact factor (JIF) for *WJG* as 4.3; Quartile: Q1. The *WJG*'s CiteScore for 2023 is 7.8.

RESPONSIBLE EDITORS FOR THIS ISSUE

NAME OF JOURNAL
World Journal of Gastroenterology

ISSN
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

LAUNCH DATE
October 1, 1995

FREQUENCY
Weekly

EDITORS-IN-CHIEF
Andrzej S Tarnawski

EXECUTIVE ASSOCIATE EDITORS-IN-CHIEF
Jian-Gao Fan (Chronic Liver Disease)

EDITORIAL BOARD MEMBERS
http://www.wjgnet.com/1007-9327/editorialboard.htm

PUBLICATION DATE
September 7, 2024

PUBLISHING PARTNER
Shanghai Pancreatic Cancer Institute and Pancreatic Cancer Institute, Fudan University
Biliary Tract Disease Institute, Fudan University

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION ETHICS
https://www.wjgnet.com/bpg/GerInfo/288

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

POLICY OF CO-AUTHORS
https://www.wjgnet.com/bpg/GerInfo/310

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
https://www.wjgnet.com/bpg/GerInfo/239

ONLINE SUBMISSION
https://www.f6publishing.com

PUBLISHING PARTNER's OFFICIAL WEBSITE
https://www.shca.org.cn
https://www.zs-hospital.sh.cn

World Journal of Gastroenterology

Submit a Manuscript: https://www.f6publishing.com

World J Gastroenterol 2024 September 7; 30(33): 3791-3798

DOI: 10.3748/wjg.v30.i33.3791

ISSN 1007-9327 (print) ISSN 2219-2840 (online)

EDITORIAL

Targeting both ferroptosis and pyroptosis may represent potential therapies for acute liver failure

Zhong-Yuan Xing, Chuan-Jie Zhang, Li-Juan Liu

Specialty type: Gastroenterology and hepatology

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's classification
Scientific Quality: Grade B
Novelty: Grade B
Creativity or Innovation: Grade B
Scientific Significance: Grade B

P-Reviewer: Cheng TH

Received: March 18, 2024
Revised: August 10, 2024
Accepted: August 16, 2024
Published online: September 7, 2024
Processing time: 167 Days and 13.8 Hours

Zhong-Yuan Xing, Li-Juan Liu, Department of Medical Microbiology, School of Basic Medical Sciences, Wuhan University, Wuhan 430071, Hubei Province, China

Chuan-Jie Zhang, Department of Children Health Care, Wuhan Children's Hospital (Wuhan Maternal and Child Healthcare Hospital), Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430061, Hubei Province, China

Co-corresponding authors: Chuan-Jie Zhang and Li-Juan Liu.

Corresponding author: Li-Juan Liu, PhD, Lecturer, Department of Medical Microbiology, School of Basic Medical Sciences, Wuhan University, No. 185 Donghu Road, Wuhan 430071, Hubei Province, China. lijuanliu@whu.edu.cn

Abstract

In this editorial, we comment on the article published in the recent issue of the *World Journal of Gastroenterology*. Acute liver failure (ALF) is a fatal disease that causes uncontrolled massive hepatocyte death and rapid loss of liver function. Ferroptosis and pyroptosis, cell death forms that can be initiated or blocked concurrently, can play significant roles in developing inflammation and various malignancies. However, their roles in ALF remain unclear. The article discovered the positive feedback between ferroptosis and pyroptosis in the progression of ALF, and revealed that the silent information regulator sirtuin 1 (SIRT1) inhibits both pathways through p53, dramatically reducing inflammation and protecting hepatocytes. This suggests the potential use of SIRT1 and its downstream molecules as therapeutics for ALF. Thus, we will discuss the role of ferroptosis and pyroptosis in ALF and the crosstalk between these cell death mechanisms. Additionally, we address potential treatments that could alleviate ALF by simultaneously inhibiting both cell death pathways, as well as examples of SIRT1 activators being used as disease treatment strategies, providing new insights into the therapy of ALF.

Key Words: Acute liver failure; Ferroptosis; Pyroptosis; Crosstalk; Silent information regulator sirtuin 1; P53; Glutathione peroxidase 4; Gasdermin D; Treatment

Core Tip: Acute liver failure (ALF) is a life-threatening disease characterized by uncontrolled death of hepatocytes. Ferroptosis and pyroptosis are two recently discovered types of cell death that can occur simultaneously. However, their roles in ALF remain unclear. The findings show that these two cell death pathways work together to advance ALF and suggest that silent information regulator sirtuin 1 (SIRT1) and its downstream molecules could be potential therapeutics for ALF. Therefore, we will discuss the roles and crosstalk of ferroptosis and pyroptosis in ALF. Activation of SIRT1 and suppression of both cell death pathways may offer new insights into therapeutic targets for ALF.

Citation: Xing ZY, Zhang CJ, Liu LJ. Targeting both ferroptosis and pyroptosis may represent potential therapies for acute liver failure. *World J Gastroenterol* 2024; 30(33): 3791-3798
URL: https://www.wjgnet.com/1007-9327/full/v30/i33/3791.htm
DOI: https://dx.doi.org/10.3748/wjg.v30.i33.3791

INTRODUCTION

Acute liver failure (ALF) is an acute clinical syndrome that occurs in patients without a history of liver disease and is life-threatening[1]. In developed countries, there are approximately 1–6 cases per million individuals. Although the incidence is rare, ALF causes a mortality rate as high as 30%[2,3]. The most prevalent causes of ALF are hepatic toxicity induced by medications or poisons, acute viral hepatitis, autoimmune and metabolic disorders, and unexplained cryptogenic liver failure[1,3]. ALF can lead to severe complications, including coagulopathy, elevated transaminases, hepatic encephalopathy, and multi-organ failure. This is often attributed to a series of severe proinflammatory states triggered by extensive hepatocyte damage, resulting in DNA damage, oxidative stress, and an accompanying inflammatory factor storm[4-6].

The main event in ALF is the excessive and uncontrolled death of hepatocytes by apoptosis, necroptosis, and necrosis [5,7,8]. Further study has found that various types of cell death are related to liver diseases such as ALF, including ferroptosis and pyroptosis[9]. These cell death pathways can coexist in a pathological environment, and several shared overlapping mechanisms can be used as "backup" death strategies to maintain biological balance within the organism when the death induction threshold is reached, mediating various immune effects and inflammatory responses[10].

FERROPTOSIS IN ALF

Dixon *et al*[11] originally described ferroptosis, an iron-dependent regulated cell death, in 2012. It is characterized by iron metabolism disorder and an accumulation of excessive intracellular lipid peroxides, which lead to redox imbalance and ultimately cell death[12].

When iron metabolism is disrupted, excess iron can be released from iron storage proteins into the cytoplasm or other organelles. Free iron can react with intracellular hydrogen peroxide or other oxidants to cause lipid peroxidation of polyunsaturated fatty acids in the cell membrane *via* the Fenton reaction, which produces a variety of reactive oxygen species (ROS) and lipid peroxidation radicals[13,14]. System X_c^- is a key regulatory component of ferroptosis, consisting of solute carrier family 7 member 11 (SLC7A11) and solute carrier family 3 member 2[15], whose antioxidant system typically protects cells from oxidative stress[16]. However, during ferroptosis, the antioxidant system may fail to efficiently neutralize the produced ROS, resulting in the cell's incapacity to withstand lipid peroxidation[17].

The *p53* gene is essential in the cellular response to a variety of stressors, including DNA damage, hypoxia, nutrient starvation, and oncogene activation[18]. P53 can also regulate ferroptosis by directly acting on the SLC7A11 promoter to reduce its expression, thereby reducing extracellular cystine intake, decreasing glutathione synthesis, lowering glutathione peroxidase 4 (GPX4) activity, increasing lipid peroxide levels, and ultimately leading to ferroptosis[19]. P53 can also recruit the deubiquitinase ubiquitin-specific peptidase 7 to the histone H2B monoubiquitination modification (H2Bub1) in the promoter region of SLC7A11, reducing H2Bub1 on the SLC7A11 gene, resulting in lower SLC7A11 protein levels and ferroptosis[20]. However, in addition to promoting ferroptosis, p53 may also inhibit it by regulating the localization and activity of dipeptidyl peptidase 4 and other pathways, thereby promoting cell survival[21]. Therefore, p53 may exhibit a "dual role" in the regulation of ferroptosis.

Ferroptosis is thought to play a substantial role in hepatocyte death in ALF[22-24]. One study reported that the ferroptosis inhibitor ferrostatin-1 significantly prevented hepatotoxicity and lipid peroxidation in mice with acetaminophen (APAP) induced ALF, lowering the mortality rate[25]. Another study revealed similar outcomes[26]. The iron inhibitor UAMC3203 and the iron chelator deferoxamine both protected against APAP-induced liver damage by reducing ferroptosis[26-28]. Moreover, various medicines or biological extracts, such as sulforaphane[29], (+)-clausenamide[30], nitroflurbiprofen[31], avicularin[32], and glycyrrhizin[33], have been demonstrated to reduce liver damage by ferroptosis inhibition. These studies highlight the importance of ferroptosis in ALF, suggesting that blocking the ferroptosis pathway could be a viable strategy for ALF treatment. According to the study by Zhou *et al*[34], histone deacetylases silent information regulator sirtuin 1 (SIRT1) regulates ferroptosis through the p53 pathway, offering a prospective therapeutic option.

PYROPTOSIS IN ALF

Pyroptosis is a type of immunogenic cell death mediated by caspases during microbial infections[35]. It helps the body eliminate invading pathogens. The gasdermin D (GSDMD) protein is the central driver of pyroptosis. When a cell receives signals such as pathogen-associated molecular patterns, damage-associated molecular patterns, and lipopolysaccharide (LPS) *via* classical or non-classical pathways, caspases-1 and caspases-4/5/11 are recruited and activated. The activated caspases perform proteolytic activity, leading to the formation of the active N-terminal fragment of GSDMD (GSDMD-N)[35]. It also promotes the cleavage of interleukin-1beta precursor and interleukin-18 precursor to produce mature cytokines[36,37]. Subsequently, GSDMD-N binds to acidic phospholipids on the cell membrane, forming oligomerized death-inducing pores and increasing intracellular osmotic pressure, leading to cell swelling and rupture[38-40]. It leads to the release of interleukin-1beta (IL-1β), interleukin (IL)-18, tumor necrosis factor-alpha (TNFα), ATP, and other substances into the extracellular space, attracting immune cells to the injury site and mediating the inflammatory immune response[37,41,42].

Previous studies have indicated that pyroptosis plays a crucial role in liver diseases. ALF patients' liver tissue exhibits elevated levels of molecules associated with pyroptosis, including GSDMD-N, caspases-1/4, IL-1β, IL-18, and TNFα. *In vitro* research has shown that reducing GSDMD can lower MCP1/CCR2 protein levels, thereby decreasing neutrophil-mediated immune injury in the liver. In mouse models, deletion of the *GSDMD* gene effectively reduces liver inflammatory injury and increases survival rates in mice with D-Galn/LPS-induced ALF[43]. Moreover, several studies have shown that the use of pyroptosis inhibitors such as VX-765[44], GSDMD inhibitor necrosulfonamide[45], GSK3β inhibitor TDZD-8[46], limonin[47], 3,4-dihydroxyphenylethanol glycoside (DAG)[48], and tyrosine-alanine (YA)[49], can alleviate liver cell pyroptosis, reduce oxidative stress and inflammation, and improve liver injury. However, the regulatory mechanisms remain unclear. Additionally, p53-induced pyroptosis has been reported in several studies[50-53], but it is rarely reported in the liver.

CROSSTALK BETWEEN FERROPTOSIS AND PYROPTOSIS IN ALF

Given that pyroptosis and ferroptosis are often simultaneously inhibited or encouraged in tissue injury or cancers[54-56], researchers have explored their relationship. Some studies have demonstrated a mutual regulatory link between ferroptosis and pyroptosis. For example, a deficiency of GPX4 in bone marrow cells might increase GSDMD production *via* caspase-1/11, resulting in pyroptosis[57]. In the diabetic retinopathy model, the ferroptosis inhibitor Ferr-1 can reduce GSDMD expression, thereby inhibiting pyroptosis and improving retinal tissue damage[58]. Chlorpyrifos promotes GSDMD cleavage and increases intracellular ROS levels, which in turn enhances p53-mediated ferroptosis[59]. The Stat3/p53/nuclear factor-E2-related factor 2 axis regulates both ferroptosis and pyroptosis in colorectal cancer cells[60]. These findings indicate that there may be crosstalk between ferroptosis and pyroptosis in diseases.

ALF is characterized by excessive death of hepatocytes. Therefore, crosstalk and co-activation of multiple death pathways are likely important mechanisms. However, there is currently little research on the combined role of ferroptosis and pyroptosis in ALF. A report revealed that treatment with YA and DAG can simultaneously reduce ferroptosis and pyroptosis in an ALF mouse model, thereby protecting the liver from damage and reducing mouse mortality[48,49]. Zhou *et al*[34] found that both ferroptosis and pyroptosis are triggered in the liver tissue of ALF patients. Inhibiting ferroptosis or pyroptosis protected mice from LPS/D-GalN-induced ALF. Furthermore, in the LPS/D-GalN-induced ALF mouse model, inhibiting GPX4 promoted ferroptosis and increased the expression of the pyroptosis marker GSDMD. Supplementation with GPX4 inhibited both ferroptosis and pyroptosis. It was found that the absence of GSDMD reduces not only pyroptosis but also ferroptosis in GSDMD knockout mice[34]. As a result, ferroptosis has a positive feedback regulatory effect on pyroptosis (Figure 1). Further identification of critical molecules or drugs that target the ferroptosis and pyroptosis processes may reveal potential strategies for ALF prevention and treatment.

SIRT1 SERVES AS A THERAPEUTIC TO ALLEVIATE ALF VIA INHIBITING BOTH FERROPTOSIS AND PYROPTOSIS

SIRT1 is a class of nicotinamide adenine dinucleotide (+)-dependent histone deacetylases that regulate the deacetylation of histones and other proteins. The targets include p53, forkhead box class O1/3/4, heat shock factor1, hypoxia-inducible factor 1alpha, nuclear factor kappa B[61,62]. SIRT1 regulates a variety of activities associated with anti-aging and oxidative stress, including apoptosis, autophagy, mitochondrial function, DNA damage repair, metabolism, and inflammation[62,63]. SIRT1 down-regulation correlates with cell aging and increased inflammatory factors, such as IL6, IL8, and IL1B/IL-1β[64]. A recent study found that activating SIRT1 could inhibit ferroptosis induced by excessive iron through autophagy in foam cells, providing a new therapeutic target for atherosclerosis[65].

SIRT1 also plays a role in ALF (Table 1)[66-73]. Several studies have shown that the SIRT1 signal in ALF reduces cellular oxidative stress and inhibits hepatocyte death[66-68,74,75]. Further studies revealed that the p53 signaling pathway is involved in the process[69,70,76]. SIRT1 can deacetylate p53, promote autophagy, inhibit oxidative stress, and reduce inflammatory responses[70].

Zhou *et al*[34] discovered that SIRT1 expression was reduced in human ALF liver tissue. Using SIRT1 activators or overexpressing SIRT1 could inhibit both ferroptosis events (reduced iron deposition and ROS activity, decreased

Table 1 Current studies on the role of silent information regulator sirtuin 1 in acute liver failure

Article title	Core tips	Ref.
Sirtuin 1 attenuates ALF by reducing reactive oxygen species *via* hypoxia-inducible factor 1α	Resveratrol, a SIRT1 activator, deacetylates hypoxia-inducible factor 1alpha and inhibits its activity, reducing ALF caused by hypoxia, reactive oxygen species, and apoptosis	Cao *et al* [66]
Short-term fasting attenuates lipopolysaccharide/D-galactosamine-induced ALF through SIRT1-autophagy signaling in mice	Short-term dietary restriction activates the SIRT1 signaling pathway, regulates autophagy, and reduces hepatocytes apoptosis in ALF	Long *et al*[67]
Fusobacterium nucleatum promotes the development of ALF by inhibiting the NAD+ salvage metabolic pathway	Fusobacterium nucleatum suppresses NAD+ and the SIRT1/adenosine monophosphate activated protein kinase signaling pathway, causing liver damage in ALF	Cao *et al* [68]
Hepato-protective effect of resveratrol against acetaminophen-induced liver injury is associated with inhibition of CYP-mediated bioactivation and regulation of SIRT1-p53 signaling pathways	Resveratrol helps to heal liver impairment caused by APAP by blocking CYP-mediated APAP bioactivation and regulating SIRT1, p53, cyclin D1, and proliferating cell nuclear antigen	Wang *et al*[69]
Apigenin prevents acetaminophen-induced liver injury by activating the SIRT1 pathway	Apigenin prevents acetaminophen-induced liver injury by regulating the SIRT1-p53 axis, which promotes autophagy and reduces the inflammatory response and oxidative stress caused by acetaminophen	Zhao *et al*[70]
Sirtuin-activating compounds alleviate D-galactosamine/lipopolysaccharide-induced hepatotoxicity in rats: Involvement of sirtuin 1 and heme oxygenase 1	Quercetin and SRT1720 can activate SIRT1 protein and inhibit HO-1 expression, reducing liver damage caused by D-galactosamine/lipopolysaccharide in rats	Kemelo *et al*[71]
The sirtuin 1 activator SRT1720 alleviated endotoxin-induced fulminant hepatitis in mice	SRT1720, a SIRT1 activator, reduces fulminant hepatitis caused by lipopolysaccharide/D-Gal, potentially through inhibiting tumor necrosis factor-alpha production and activating the apoptotic cascade	Zhou *et al*[72]
Evaluation of the reparative effect of SIN in an acetaminophen-induced liver injury model	SIN successfully treats acetaminophen-induced liver injury by restoring SIRT1 levels, lowering oxidative stress, and repairing cell damage	Kayalı *et al*[73]

ALF: Acute liver failure; APAP: Acetaminophen; CYP: Cytochrome; NAD+: Nicotinamide adenine dinucleotide; SIN: Sinomenine; SIRT1: Silent information regulator sirtuin 1.

expression of Acyl-CoA synthetase long-chain family 4, and increased expression of SLC7A11 and GPX4) and the expression of the pyroptosis marker GSDMD, thereby alleviating acute liver injury. In LPS/D-GalN-induced *in vitro* and *in vivo* models, the deactivation of SIRT1 increased ferroptosis and pyroptosis, exacerbating liver injury. Further research revealed that the inhibition of ferroptosis and pyroptosis by SIRT1 may depend on p53 deacetylation[34]. These results suggest that SIRT1 may serve as a molecular target to suppress multiple death processes and as a potential treatment for ALF.

Classical SIRT1 activators have been discovered, including natural ones like resveratrol, and synthetic compounds derived from the core structure of imidazole (1,2-b) thiazole, such as SRT1720 and SRT2104[77]. There have been no known clinical investigations on ALF treatment using SIRT1 activators. However, SIRT1 activators have shown an excellent safety profile and positive therapeutic effects on several diseases. Clinical trial results indicate that the natural SIRT1 activator resveratrol is effective in treating Alzheimer's disease[78], obesity and metabolic disorders[79], and polycystic ovary syndrome[80]. The synthetic SIRT1 activator SRT2104 has been demonstrated to ameliorate sepsis[81], psoriasis[82], and blood lipid profiles in older adults[83]. Although natural drugs have some cytotoxicity, synthetic SIRT1 activators address these concerns. However, current medication development remains challenging, and clinical investigations have shown that orally administered SRT2104 has an absolute bioavailability of only 14% (NCT00937872), which is inadequate. Therefore, it may be necessary to develop appropriate drug delivery techniques, modify pharmacochemical structures, or use combination therapy. Kemelo *et al*[71] reported that quercetin (a natural polyphenol) and SRT1720 showed the ability to improve disease in a rat ALF model, providing evidence that combination therapy may be effective in ALF treatment. In addition, further clinical research will advance the application of SIRT1 activators in ALF treatment.

CONCLUSION

Various forms of cell death, such as apoptosis, necroptosis, necrosis, ferroptosis, and pyroptosis, have been implicated in ALF. However, the crosstalk between them remains unclear. Zhou *et al*[34] proved that the positive feedback between ferroptosis and pyroptosis plays an important role in hepatocyte mortality in ALF. Mutual stimulation of these cell death pathways may significantly reduce the survival rates of ALF patients. Thus, identifying targets that control the activation of these cell death pathways, as well as medicines that directly suppress these cell death pathways, may provide novel therapeutic strategies to treat ALF. SIRT1 could act as a treatment for ALF, influencing both ferroptosis and pyroptosis. However, it is unclear if SIRT1 can influence other death pathways, such as apoptosis, necroptosis, and necrosis, all of which play essential roles in ALF. Molecular targets capable of effectively controlling multiple cell death pathways have not been reported either. In addition, the efficacy of SIRT1 activation in the clinical treatment of ALF has not been reported. Therefore, addressing these concerns may provide therapeutic targets for treating ALF.

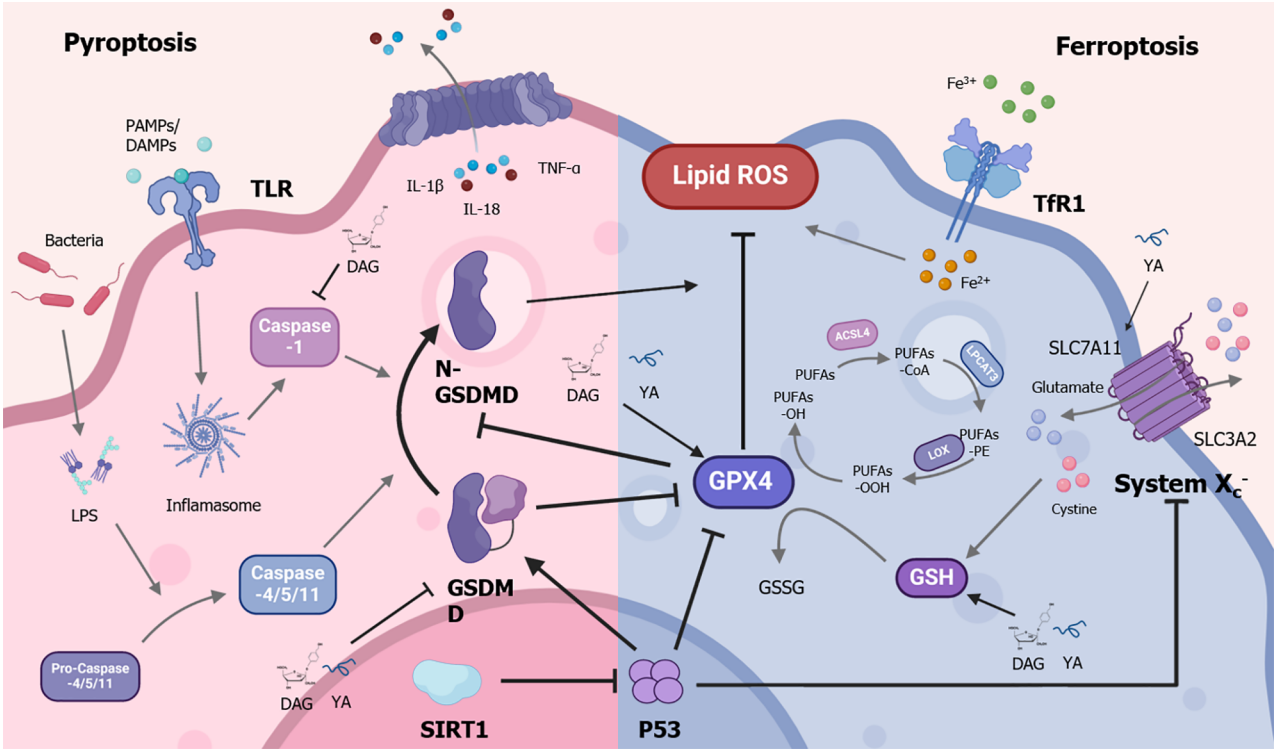

Figure 1 The positive feedback loop between ferroptosis and pyroptosis in acute liver failure, as well as possible treatments that target ferroptosis and pyroptosis. Glutathione peroxidase 4 (GPX4) reduces the expression of gasdermin D (GSDMD), a pyroptosis marker. In turn, GSDMD can reduce the level of GPX4. Silent information regulator sirtuin 1 can inhibit GSDMD expression while elevating System X_c^- *via* p53, hence targeting ferroptosis and pyroptosis. Acute liver failure mice treated with tyrosine-alanine or 3,4-dihydroxyphenylethanol glycoside (DAG) show a similar role in suppressing both cell death pathways. GSDMD-N: N-terminal fragment of gasdermin D; GSSG: Oxidized glutathione; IL-1β: Interleukin-1beta; IL-18: Interleukin-18; LPCAT3: Lysophosphatidylcholine acyltransferase 3; LPS: Lipopolysaccharide; PUFAs: Polyunsaturated fatty acids; ROS: Reactive oxygen species; SIRT1: Silent information regulator sirtuin 1; SLC7A11: Solute carrier family 7 member 11; SLC3A2: Solute carrier family 3 member 2; TLR: Toll-like receptors; TNFα: Tumor necrosis factor-alpha; YA: Tyrosine-alanine.

FOOTNOTES

Author contributions: Liu LJ and Zhang CJ designed the overall concept and outline of the manuscript; Xing ZY contributed to the discussion and design of the manuscript, as well as illustrations; Xing ZY, Zhang CJ, and Liu LJ contributed to the writing and editing of the manuscript and review of the literature; All authors have read and approved the final manuscript.

Supported by The Hubei Provincial Natural Science Foundation of China, No. 2020CFB656.

Conflict-of-interest statement: The authors declare that they have no conflicts of interest to disclose.

Country of origin: China

ORCID number: Chuan-Jie Zhang 0000-0003-0404-6615; Li-Juan Liu 0000-0002-2549-5463.

S-Editor: Luo ML
L-Editor: Filipodia
P-Editor: Yu HG

REFERENCES

1 **Stravitz RT**, Fontana RJ, Karvellas C, Durkalski V, McGuire B, Rule JA, Tujios S, Lee WM; Acute Liver Failure Study Group. Future directions in acute liver failure. *Hepatology* 2023; **78**: 1266-1289 [PMID: 37183883 DOI: 10.1097/HEP.0000000000000458]
2 **Stravitz RT**, Lee WM. Acute liver failure. *Lancet* 2019; **394**: 869-881 [PMID: 31498101 DOI: 10.1016/S0140-6736(19)31894-X]

3 **Shingina A**, Mukhtar N, Wakim-Fleming J, Alqahtani S, Wong RJ, Limketkai BN, Larson AM, Grant L. Acute Liver Failure Guidelines. *Am J Gastroenterol* 2023; **118**: 1128-1153 [PMID: 37377263 DOI: 10.14309/ajg.0000000000002340]

4 **Brenner C**, Galluzzi L, Kepp O, Kroemer G. Decoding cell death signals in liver inflammation. *J Hepatol* 2013; **59**: 583-594 [PMID: 23567086 DOI: 10.1016/j.jhep.2013.03.033]

5 **Luedde T**, Kaplowitz N, Schwabe RF. Cell death and cell death responses in liver disease: mechanisms and clinical relevance. *Gastroenterology* 2014; **147**: 765-783 [PMID: 25046161 DOI: 10.1053/j.gastro.2014.07.018]

6 **Vasques F**, Cavazza A, Bernal W. Acute liver failure. *Curr Opin Crit Care* 2022; **28**: 198-207 [PMID: 35142727 DOI: 10.1097/MCC.0000000000000923]

7 **Schwabe RF**, Luedde T. Apoptosis and necroptosis in the liver: a matter of life and death. *Nat Rev Gastroenterol Hepatol* 2018; **15**: 738-752 [PMID: 30250076 DOI: 10.1038/s41575-018-0065-y]

8 **Shojaie L**, Iorga A, Dara L. Cell Death in Liver Diseases: A Review. *Int J Mol Sci* 2020; **21**: 9682 [PMID: 33353156 DOI: 10.3390/ijms21249682]

9 **Aizawa S**, Brar G, Tsukamoto H. Cell Death and Liver Disease. *Gut Liver* 2020; **14**: 20-29 [PMID: 30917630 DOI: 10.5009/gnl18486]

10 **Gautheron J**, Gores GJ, Rodrigues CMP. Lytic cell death in metabolic liver disease. *J Hepatol* 2020; **73**: 394-408 [PMID: 32298766 DOI: 10.1016/j.jhep.2020.04.001]

11 **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; **149**: 1060-1072 [PMID: 22632970 DOI: 10.1016/j.cell.2012.03.042]

12 **Galluzzi L**, Vitale I, Aaronson SA, Abrams JM, Adam D, Agostinis P, Alnemri ES, Altucci L, Amelio I, Andrews DW, Annicchiarico-Petruzzelli M, Antonov AV, Arama E, Baehrecke EH, Barlev NA, Bazan NG, Bernassola F, Bertrand MJM, Bianchi K, Blagosklonny MV, Blomgren K, Borner C, Boya P, Brenner C, Campanella M, Candi E, Carmona-Gutierrez D, Cecconi F, Chan FK, Chandel NS, Cheng EH, Chipuk JE, Cidlowski JA, Ciechanover A, Cohen GM, Conrad M, Cubillos-Ruiz JR, Czabotar PE, D'Angiolella V, Dawson TM, Dawson VL, De Laurenzi V, De Maria R, Debatin KM, DeBerardinis RJ, Deshmukh M, Di Daniele N, Di Virgilio F, Dixit VM, Dixon SJ, Duckett CS, Dynlacht BD, El-Deiry WS, Elrod JW, Fimia GM, Fulda S, García-Sáez AJ, Garg AD, Garrido C, Gavathiotis E, Golstein P, Gottlieb E, Green DR, Greene LA, Gronemeyer H, Gross A, Hajnoczky G, Hardwick JM, Harris IS, Hengartner MO, Hetz C, Ichijo H, Jäättelä M, Joseph B, Jost PJ, Juin PP, Kaiser WJ, Karin M, Kaufmann T, Kepp O, Kimchi A, Kitsis RN, Klionsky DJ, Knight RA, Kumar S, Lee SW, Lemasters JJ, Levine B, Linkermann A, Lipton SA, Lockshin RA, López-Otín C, Lowe SW, Luedde T, Lugli E, MacFarlane M, Madeo F, Malewicz M, Malorni W, Manic G, Marine JC, Martin SJ, Martinou JC, Medema JP, Mehlen P, Meier P, Melino S, Miao EA, Molkentin JD, Moll UM, Muñoz-Pinedo C, Nagata S, Nuñez G, Oberst A, Oren M, Overholtzer M, Pagano M, Panaretakis T, Pasparakis M, Penninger JM, Pereira DM, Pervaiz S, Peter ME, Piacentini M, Pinton P, Prehn JHM, Puthalakath H, Rabinovich GA, Rehm M, Rizzuto R, Rodrigues CMP, Rubinsztein DC, Rudel T, Ryan KM, Sayan E, Scorrano L, Shao F, Shi Y, Silke J, Simon HU, Sistigu A, Stockwell BR, Strasser A, Szabadkai G, Tait SWG, Tang D, Tavernarakis N, Thorburn A, Tsujimoto Y, Turk B, Vanden Berghe T, Vandenabeele P, Vander Heiden MG, Villunger A, Virgin HW, Vousden KH, Vucic D, Wagner EF, Walczak H, Wallach D, Wang Y, Wells JA, Wood W, Yuan J, Zakeri Z, Zhivotovsky B, Zitvogel L, Melino G, Kroemer G. Molecular mechanisms of cell death: recommendations of the Nomenclature Committee on Cell Death 2018. *Cell Death Differ* 2018; **25**: 486-541 [PMID: 29362479 DOI: 10.1038/s41418-017-0012-4]

13 **Lei P**, Bai T, Sun Y. Mechanisms of Ferroptosis and Relations With Regulated Cell Death: A Review. *Front Physiol* 2019; **10**: 139 [PMID: 30863316 DOI: 10.3389/fphys.2019.00139]

14 **Tang D**, Chen X, Kang R, Kroemer G. Ferroptosis: molecular mechanisms and health implications. *Cell Res* 2021; **31**: 107-125 [PMID: 33268902 DOI: 10.1038/s41422-020-00441-1]

15 **Lewerenz J**, Hewett SJ, Huang Y, Lambros M, Gout PW, Kalivas PW, Massie A, Smolders I, Methner A, Pergande M, Smith SB, Ganapathy V, Maher P. The cystine/glutamate antiporter system x(c)(-) in health and disease: from molecular mechanisms to novel therapeutic opportunities. *Antioxid Redox Signal* 2013; **18**: 522-555 [PMID: 22667998 DOI: 10.1089/ars.2011.4391]

16 **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**: 34 [PMID: 30925886 DOI: 10.1186/s13045-019-0720-y]

17 **Jiang X**, Stockwell BR, Conrad M. Ferroptosis: mechanisms, biology and role in disease. *Nat Rev Mol Cell Biol* 2021; **22**: 266-282 [PMID: 33495651 DOI: 10.1038/s41580-020-00324-8]

18 **Kastenhuber ER**, Lowe SW. Putting p53 in Context. *Cell* 2017; **170**: 1062-1078 [PMID: 28886379 DOI: 10.1016/j.cell.2017.08.028]

19 **Jiang L**, Kon N, Li T, Wang SJ, Su T, Hibshoosh H, Baer R, Gu W. Ferroptosis as a p53-mediated activity during tumour suppression. *Nature* 2015; **520**: 57-62 [PMID: 25799988 DOI: 10.1038/nature14344]

20 **Wang Y**, Yang L, Zhang X, Cui W, Liu Y, Sun QR, He Q, Zhao S, Zhang GA, Wang Y, Chen S. Epigenetic regulation of ferroptosis by H2B monoubiquitination and p53. *EMBO Rep* 2019; **20**: e47563 [PMID: 31267712 DOI: 10.15252/embr.201847563]

21 **Kang R**, Kroemer G, Tang D. The tumor suppressor protein p53 and the ferroptosis network. *Free Radic Biol Med* 2019; **133**: 162-168 [PMID: 29800655 DOI: 10.1016/j.freeradbiomed.2018.05.074]

22 **Mancardi D**, Mezzanotte M, Arrigo E, Barinotti A, Roetto A. Iron Overload, Oxidative Stress, and Ferroptosis in the Failing Heart and Liver. *Antioxidants (Basel)* 2021; **10**: 1864 [PMID: 34942967 DOI: 10.3390/antiox10121864]

23 **Guo G**, Yang W, Sun C, Wang X. Dissecting the potential role of ferroptosis in liver diseases: an updated review. *Free Radic Res* 2023; **57**: 282-293 [PMID: 37401821 DOI: 10.1080/10715762.2023.2232941]

24 **Lu Y**, Hu J, Chen L, Li S, Yuan M, Tian X, Cao P, Qiu Z. Ferroptosis as an emerging therapeutic target in liver diseases. *Front Pharmacol* 2023; **14**: 1196287 [PMID: 37256232 DOI: 10.3389/fphar.2023.1196287]

25 **Yamada N**, Karasawa T, Kimura H, Watanabe S, Komada T, Kamata R, Sampilvanjil A, Ito J, Nakagawa K, Kuwata H, Hara S, Mizuta K, Sakuma Y, Sata N, Takahashi M. Ferroptosis driven by radical oxidation of n-6 polyunsaturated fatty acids mediates acetaminophen-induced acute liver failure. *Cell Death Dis* 2020; **11**: 144 [PMID: 32094346 DOI: 10.1038/s41419-020-2334-2]

26 **Lőrincz T**, Jemnitz K, Kardon T, Mandl J, Szarka A. Ferroptosis is Involved in Acetaminophen Induced Cell Death. *Pathol Oncol Res* 2015; **21**: 1115-1121 [PMID: 25962350 DOI: 10.1007/s12253-015-9946-3]

27 **Schnellmann JG**, Pumford NR, Kusewitt DF, Bucci TJ, Hinson JA. Deferoxamine delays the development of the hepatotoxicity of acetaminophen in mice. *Toxicol Lett* 1999; **106**: 79-88 [PMID: 10378453 DOI: 10.1016/s0378-4274(99)00021-1]

28 **Niu B**, Lei X, Xu Q, Ju Y, Xu D, Mao L, Li J, Zheng Y, Sun N, Zhang X, Mao Y, Li X. Protecting mitochondria *via* inhibiting VDAC1 oligomerization alleviates ferroptosis in acetaminophen-induced acute liver injury. *Cell Biol Toxicol* 2022; **38**: 505-530 [PMID: 34401974

DOI: 10.1007/s10565-021-09624-x]

29 **Liu J**, Huang C, Liu J, Meng C, Gu Q, Du X, Yan M, Yu Y, Liu F, Xia C. Nrf2 and its dependent autophagy activation cooperatively counteract ferroptosis to alleviate acute liver injury. *Pharmacol Res* 2023; **187**: 106563 [PMID: 36410674 DOI: 10.1016/j.phrs.2022.106563]

30 **Wang M**, Liu CY, Wang T, Yu HM, Ouyang SH, Wu YP, Gong HB, Ma XH, Jiao GL, Fu LL, Wu QS, Kurihara H, Li YF, Shen T, He RR. (+)-Clausenamide protects against drug-induced liver injury by inhibiting hepatocyte ferroptosis. *Cell Death Dis* 2020; **11**: 781 [PMID: 32951003 DOI: 10.1038/s41419-020-02961-5]

31 **Zhong X**, Fan XG, Chen R. Repurposing Niclosamide as a Therapeutic Drug against Acute Liver Failure by Suppressing Ferroptosis. *Pharmaceutics* 2023; **15**: 1950 [PMID: 37514136 DOI: 10.3390/pharmaceutics15071950]

32 **Shi P**, Zhu W, Fu J, Liang A, Zheng T, Wen Z, Wu X, Peng Y, Yuan S, Wu X. Avicularin alleviates acute liver failure by regulation of the TLR4/MyD88/NF-κB and Nrf2/HO-1/GPX4 pathways to reduce inflammation and ferroptosis. *J Cell Mol Med* 2023; **27**: 3326-3338 [PMID: 37644784 DOI: 10.1111/jcmm.17905]

33 **Wang Y**, Chen Q, Shi C, Jiao F, Gong Z. Mechanism of glycyrrhizin on ferroptosis during acute liver failure by inhibiting oxidative stress. *Mol Med Rep* 2019; **20**: 4081-4090 [PMID: 31545489 DOI: 10.3892/mmr.2019.10660]

34 **Zhou XN**, Zhang Q, Peng H, Qin YJ, Liu YH, Wang L, Cheng ML, Luo XH, Li H. Silent information regulator sirtuin 1 ameliorates acute liver failure *via* the p53/glutathione peroxidase 4/gasdermin D axis. *World J Gastroenterol* 2024; **30**: 1588-1608 [PMID: 38617450 DOI: 10.3748/wjg.v30.i11.1588]

35 **Gao W**, Wang X, Zhou Y, Wang X, Yu Y. Autophagy, ferroptosis, pyroptosis, and necroptosis in tumor immunotherapy. *Signal Transduct Target Ther* 2022; **7**: 196 [PMID: 35725836 DOI: 10.1038/s41392-022-01046-3]

36 **Rathinam VA**, Fitzgerald KA. Inflammasome Complexes: Emerging Mechanisms and Effector Functions. *Cell* 2016; **165**: 792-800 [PMID: 27153493 DOI: 10.1016/j.cell.2016.03.046]

37 **Wu J**, Lin S, Wan B, Velani B, Zhu Y. Pyroptosis in Liver Disease: New Insights into Disease Mechanisms. *Aging Dis* 2019; **10**: 1094-1108 [PMID: 31595205 DOI: 10.14336/AD.2019.0116]

38 **Aglietti RA**, Estevez A, Gupta A, Ramirez MG, Liu PS, Kayagaki N, Ciferri C, Dixit VM, Dueber EC. GsdmD p30 elicited by caspase-11 during pyroptosis forms pores in membranes. *Proc Natl Acad Sci USA* 2016; **113**: 7858-7863 [PMID: 27339137 DOI: 10.1073/pnas.1607769113]

39 **Liu X**, Zhang Z, Ruan J, Pan Y, Magupalli VG, Wu H, Lieberman J. Inflammasome-activated gasdermin D causes pyroptosis by forming membrane pores. *Nature* 2016; **535**: 153-158 [PMID: 27383986 DOI: 10.1038/nature18629]

40 **Sborgi L**, Rühl S, Mulvihill E, Pipercevic J, Heilig R, Stahlberg H, Farady CJ, Müller DJ, Broz P, Hiller S. GSDMD membrane pore formation constitutes the mechanism of pyroptotic cell death. *EMBO J* 2016; **35**: 1766-1778 [PMID: 27418190 DOI: 10.15252/embj.201694696]

41 **Yu P**, Zhang X, Liu N, Tang L, Peng C, Chen X. Pyroptosis: mechanisms and diseases. *Signal Transduct Target Ther* 2021; **6**: 128 [PMID: 33776057 DOI: 10.1038/s41392-021-00507-5]

42 **Wei X**, Xie F, Zhou X, Wu Y, Yan H, Liu T, Huang J, Wang F, Zhou F, Zhang L. Role of pyroptosis in inflammation and cancer. *Cell Mol Immunol* 2022; **19**: 971-992 [PMID: 35970871 DOI: 10.1038/s41423-022-00905-x]

43 **Li H**, Zhao XK, Cheng YJ, Zhang Q, Wu J, Lu S, Zhang W, Liu Y, Zhou MY, Wang Y, Yang J, Cheng ML. Gasdermin D-mediated hepatocyte pyroptosis expands inflammatory responses that aggravate acute liver failure by upregulating monocyte chemotactic protein 1/CC chemokine receptor-2 to recruit macrophages. *World J Gastroenterol* 2019; **25**: 6527-6540 [PMID: 31802832 DOI: 10.3748/wjg.v25.i44.6527]

44 **Jiao M**, Wang J, Liu W, Zhao X, Qin Y, Zhang C, Yin H, Zhao C. VX-765 inhibits pyroptosis and reduces inflammation to prevent acute liver failure by upregulating PPARα expression. *Ann Hepatol* 2023; **28**: 101082 [PMID: 36893888 DOI: 10.1016/j.aohep.2023.101082]

45 **Wu YL**, Ou WJ, Zhong M, Lin S, Zhu YY. Gasdermin D Inhibitor Necrosulfonamide Alleviates Lipopolysaccharide/D-galactosamine-induced Acute Liver Failure in Mice. *J Clin Transl Hepatol* 2022; **10**: 1148-1154 [PMID: 36381100 DOI: 10.14218/JCTH.2021.00560]

46 **Zhang D**, Shi C, Zhang Q, Wang Y, Guo J, Gong Z. Inhibition of GSK3β activity alleviates acute liver failure *via* suppressing multiple programmed cell death. *J Inflamm (Lond)* 2023; **20**: 24 [PMID: 37443080 DOI: 10.1186/s12950-023-00350-1]

47 **Yang R**, Yu H, Chen J, Zhu J, Song C, Zhou L, Sun Y, Zhang Q. Limonin Attenuates LPS-Induced Hepatotoxicity by Inhibiting Pyroptosis *via* NLRP3/Gasdermin D Signaling Pathway. *J Agric Food Chem* 2021; **69**: 982-991 [PMID: 33427450 DOI: 10.1021/acs.jafc.0c06775]

48 **Liu T**, Yang L, Gao H, Zhuo Y, Tu Z, Wang Y, Xun J, Zhang Q, Zhang L, Wang X. 3,4-dihydroxyphenylethyl alcohol glycoside reduces acetaminophen-induced acute liver failure in mice by inhibiting hepatocyte ferroptosis and pyroptosis. *PeerJ* 2022; **10**: e13082 [PMID: 35310165 DOI: 10.7717/peerj.13082]

49 **Siregar AS**, Nyiramana MM, Kim EJ, Cho SB, Woo MS, Lee DK, Hong SG, Han J, Kang SS, Kim DR, Choi YJ, Kang D. Oyster-Derived Tyr-Ala (YA) Peptide Prevents Lipopolysaccharide/D-Galactosamine-Induced Acute Liver Failure by Suppressing Inflammatory, Apoptotic, Ferroptotic, and Pyroptotic Signals. *Mar Drugs* 2021; **19**: 614 [PMID: 34822485 DOI: 10.3390/md19110614]

50 **Ranjan A**, Iwakuma T. Non-Canonical Cell Death Induced by p53. *Int J Mol Sci* 2016; **17**: 2068 [PMID: 27941671 DOI: 10.3390/ijms17122068]

51 **Saha G**, Chiranjivi AK, Khamar BM, Prerna K, Kumar M, Dubey VK. BLIMP-1 Mediated Downregulation of TAK1 and p53 Molecules Is Crucial in the Pathogenesis of Kala-Azar. *Front Cell Infect Microbiol* 2020; **10**: 594431 [PMID: 33194842 DOI: 10.3389/fcimb.2020.594431]

52 **Yuliana ND**, Tuarita MZ, Khatib A, Laila F, Sukarno S. GC-MS metabolomics revealed protocatechuic acid as a cytotoxic and apoptosis-inducing compound from black rice brans. *Food Sci Biotechnol* 2020; **29**: 825-835 [PMID: 32523792 DOI: 10.1007/s10068-019-00725-2]

53 **Zhu A**, Cheng C, Lin S, Hong Z, Shi Z, Deng H, Zhang G. Silence of linc00023 inhibits pyroptosis and promotes cell proliferation *via* regulating p53. *Gene* 2023; **882**: 147628 [PMID: 37429368 DOI: 10.1016/j.gene.2023.147628]

54 **Tang R**, Xu J, Zhang B, Liu J, Liang C, Hua J, Meng Q, Yu X, Shi S. Ferroptosis, necroptosis, and pyroptosis in anticancer immunity. *J Hematol Oncol* 2020; **13**: 110 [PMID: 32778143 DOI: 10.1186/s13045-020-00946-7]

55 **Cao Z**, Qin H, Huang Y, Zhao Y, Chen Z, Hu J, Gao Q. Crosstalk of pyroptosis, ferroptosis, and mitochondrial aldehyde dehydrogenase 2-related mechanisms in sepsis-induced lung injury in a mouse model. *Bioengineered* 2022; **13**: 4810-4820 [PMID: 35188436 DOI: 10.1080/21655979.2022.2033381]

56 **Wan S**, Zhang G, Liu R, Abbas MN, Cui H. Pyroptosis, ferroptosis, and autophagy cross-talk in glioblastoma opens up new avenues for glioblastoma treatment. *Cell Commun Signal* 2023; **21**: 115 [PMID: 37208730 DOI: 10.1186/s12964-023-01108-1]

57 **Kang R**, Zeng L, Zhu S, Xie Y, Liu J, Wen Q, Cao L, Xie M, Ran Q, Kroemer G, Wang H, Billiar TR, Jiang J, Tang D. Lipid Peroxidation Drives Gasdermin D-Mediated Pyroptosis in Lethal Polymicrobial Sepsis. *Cell Host Microbe* 2018; **24**: 97-108 [PMID: 29937272 DOI: 10.1016/j.chom.2018.05.009]

58 **Shao J**, Bai Z, Zhang L, Zhang F. Ferrostatin-1 alleviates tissue and cell damage in diabetic retinopathy by improving the antioxidant capacity of the Xc(-)-GPX4 system. *Cell Death Discov* 2022; **8**: 426 [PMID: 36284090 DOI: 10.1038/s41420-022-01141-y]

59 **Han C**, Sheng J, Pei H, Sheng Y, Wang J, Zhou X, Li W, Cao C, Yang Y. Environmental toxin chlorpyrifos induces liver injury by activating P53-mediated ferroptosis *via* GSDMD-mtROS. *Ecotoxicol Environ Saf* 2023; **257**: 114938 [PMID: 37099958 DOI: 10.1016/j.ecoenv.2023.114938]

60 **Wu Y**, Pi D, Zhou S, Yi Z, Dong Y, Wang W, Ye H, Chen Y, Zuo Q, Ouyang M. Ginsenoside Rh3 induces pyroptosis and ferroptosis through the Stat3/p53/NRF2 axis in colorectal cancer cells. *Acta Biochim Biophys Sin (Shanghai)* 2023; **55**: 587-600 [PMID: 37092860 DOI: 10.3724/abbs.2023068]

61 **Sauve AA**, Wolberger C, Schramm VL, Boeke JD. The biochemistry of sirtuins. *Annu Rev Biochem* 2006; **75**: 435-465 [PMID: 16756498 DOI: 10.1146/annurev.biochem.74.082803.133500]

62 **Yang Y**, Liu Y, Wang Y, Chao Y, Zhang J, Jia Y, Tie J, Hu D. Regulation of SIRT1 and Its Roles in Inflammation. *Front Immunol* 2022; **13**: 831168 [PMID: 35359990 DOI: 10.3389/fimmu.2022.831168]

63 **Singh CK**, Chhabra G, Ndiaye MA, Garcia-Peterson LM, Mack NJ, Ahmad N. The Role of Sirtuins in Antioxidant and Redox Signaling. *Antioxid Redox Signal* 2018; **28**: 643-661 [PMID: 28891317 DOI: 10.1089/ars.2017.7290]

64 **Wang L**, Xu C, Johansen T, Berger SL, Dou Z. SIRT1 - a new mammalian substrate of nuclear autophagy. *Autophagy* 2021; **17**: 593-595 [PMID: 33292048 DOI: 10.1080/15548627.2020.1860541]

65 **Su G**, Yang W, Wang S, Geng C, Guan X. SIRT1-autophagy axis inhibits excess iron-induced ferroptosis of foam cells and subsequently increases IL-1B and IL-18. *Biochem Biophys Res Commun* 2021; **561**: 33-39 [PMID: 34000515 DOI: 10.1016/j.bbrc.2021.05.011]

66 **Cao P**, Chen Q, Shi CX, Wang LW, Gong ZJ. Sirtuin1 attenuates acute liver failure by reducing reactive oxygen species *via* hypoxia inducible factor 1α. *World J Gastroenterol* 2022; **28**: 1798-1813 [PMID: 35633910 DOI: 10.3748/wjg.v28.i17.1798]

67 **Long B**, Tao H, Tong S, Wang X, Yin W. Short-term fasting attenuates lipopolysaccharide/D-galactosamine-induced acute liver failure through Sirt1-autophagy signaling in mice. *MedComm (2020)* 2023; **4**: e412 [PMID: 38020718 DOI: 10.1002/mco2.412]

68 **Cao P**, Chen Q, Shi C, Wang L, Gong Z. Fusobacterium nucleatum promotes the development of acute liver failure by inhibiting the NAD(+) salvage metabolic pathway. *Gut Pathog* 2022; **14**: 29 [PMID: 35765030 DOI: 10.1186/s13099-022-00503-2]

69 **Wang Y**, Jiang Y, Fan X, Tan H, Zeng H, Wang Y, Chen P, Huang M, Bi H. Hepato-protective effect of resveratrol against acetaminophen-induced liver injury is associated with inhibition of CYP-mediated bioactivation and regulation of SIRT1-p53 signaling pathways. *Toxicol Lett* 2015; **236**: 82-89 [PMID: 25956474 DOI: 10.1016/j.toxlet.2015.05.001]

70 **Zhao L**, Zhang J, Hu C, Wang T, Lu J, Wu C, Chen L, Jin M, Ji G, Cao Q, Jiang Y. Apigenin Prevents Acetaminophen-Induced Liver Injury by Activating the SIRT1 Pathway. *Front Pharmacol* 2020; **11**: 514 [PMID: 32425778 DOI: 10.3389/fphar.2020.00514]

71 **Kemelo MK**, Kutinová Canová N, Horinek A, Farghali H. Sirtuin-activating compounds (STACs) alleviate D-galactosamine/lipopolysaccharide-induced hepatotoxicity in rats: involvement of sirtuin 1 and heme oxygenase 1. *Physiol Res* 2017; **66**: 497-505 [PMID: 28248534 DOI: 10.33549/physiolres.933488]

72 **Zhou D**, Yang F, Lin L, Tang L, Li L, Yang Y, Liu D, Zhang C, Wu T, Wei H, Zhang X, Zhang L. The sirtuin 1 activator SRT1720 alleviated endotoxin-induced fulminant hepatitis in mice. *Exp Anim* 2021; **70**: 302-310 [PMID: 33678756 DOI: 10.1538/expanim.20-0014]

73 **Kayalı A**, Bora ES, Acar H, Erbaş O. Evaluation of the Reparative Effect of Sinomenine in an Acetaminophen-Induced Liver Injury Model. *Curr Issues Mol Biol* 2024; **46**: 923-933 [PMID: 38275673 DOI: 10.3390/cimb46010059]

74 **Zhang J**, Hu C, Li X, Liang L, Zhang M, Chen B, Liu X, Yang D. Protective Effect of Dihydrokaempferol on Acetaminophen-Induced Liver Injury by Activating the SIRT1 Pathway. *Am J Chin Med* 2021; **49**: 705-718 [PMID: 33657990 DOI: 10.1142/S0192415X21500324]

75 **Cao P**, Chen Q, Shi C, Pei M, Wang L, Gong Z. Pinocembrin ameliorates acute liver failure *via* activating the Sirt1/PPARα pathway in vitro and in vivo. *Eur J Pharmacol* 2022; **915**: 174610 [PMID: 34951978 DOI: 10.1016/j.ejphar.2021.174610]

76 **Nakamura K**, Zhang M, Kageyama S, Ke B, Fujii T, Sosa RA, Reed EF, Datta N, Zarrinpar A, Busuttil RW, Araujo JA, Kupiec-Weglinski JW. Macrophage heme oxygenase-1-SIRT1-p53 axis regulates sterile inflammation in liver ischemia-reperfusion injury. *J Hepatol* 2017; **67**: 1232-1242 [PMID: 28842295 DOI: 10.1016/j.jhep.2017.08.010]

77 **Chang N**, Li J, Lin S, Zhang J, Zeng W, Ma G, Wang Y. Emerging roles of SIRT1 activator, SRT2104, in disease treatment. *Sci Rep* 2024; **14**: 5521 [PMID: 38448466 DOI: 10.1038/s41598-024-55923-8]

78 **Moussa C**, Hebron M, Huang X, Ahn J, Rissman RA, Aisen PS, Turner RS. Resveratrol regulates neuro-inflammation and induces adaptive immunity in Alzheimer's disease. *J Neuroinflammation* 2017; **14**: 1 [PMID: 28086917 DOI: 10.1186/s12974-016-0779-0]

79 **Timmers S**, Konings E, Bilet L, Houtkooper RH, van de Weijer T, Goossens GH, Hoeks J, van der Krieken S, Ryu D, Kersten S, Moonen-Kornips E, Hesselink MKC, Kunz I, Schrauwen-Hinderling VB, Blaak E, Auwerx J, Schrauwen P. Calorie restriction-like effects of 30 days of resveratrol supplementation on energy metabolism and metabolic profile in obese humans. *Cell Metab* 2011; **14**: 612-622 [PMID: 22055504 DOI: 10.1016/j.cmet.2011.10.002]

80 **Ardehjani NA**, Agha-Hosseini M, Nashtaei MS, Khodarahmian M, Shabani M, Jabarpour M, Fereidouni F, Rastegar T, Amidi F. Resveratrol ameliorates mitochondrial biogenesis and reproductive outcomes in women with polycystic ovary syndrome undergoing assisted reproduction: a randomized, triple-blind, placebo-controlled clinical trial. *J Ovarian Res* 2024; **17**: 143 [PMID: 38987824 DOI: 10.1186/s13048-024-01470-9]

81 **van der Meer AJ**, Scicluna BP, Moerland PD, Lin J, Jacobson EW, Vlasuk GP, van der Poll T. The Selective Sirtuin 1 Activator SRT2104 Reduces Endotoxin-Induced Cytokine Release and Coagulation Activation in Humans. *Crit Care Med* 2015; **43**: e199-e202 [PMID: 25978169 DOI: 10.1097/CCM.0000000000000949]

82 **Krueger JG**, Suárez-Fariñas M, Cueto I, Khacherian A, Matheson R, Parish LC, Leonardi C, Shortino D, Gupta A, Haddad J, Vlasuk GP, Jacobson EW. A Randomized, Placebo-Controlled Study of SRT2104, a SIRT1 Activator, in Patients with Moderate to Severe Psoriasis. *PLoS One* 2015; **10**: e0142081 [PMID: 26556603 DOI: 10.1371/journal.pone.0142081]

83 **Libri V**, Brown AP, Gambarota G, Haddad J, Shields GS, Dawes H, Pinato DJ, Hoffman E, Elliot PJ, Vlasuk GP, Jacobson E, Wilkins MR, Matthews PM. A pilot randomized, placebo controlled, double blind phase I trial of the novel SIRT1 activator SRT2104 in elderly volunteers. *PLoS One* 2012; **7**: e51395 [PMID: 23284689 DOI: 10.1371/journal.pone.0051395]

Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: office@baishideng.com
Help Desk: https://www.f6publishing.com/helpdesk
https://www.wjgnet.com