

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 80852

Title: A review of ferroptosis in colorectal cancer: Friends or Foes?

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06409416

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: China

Manuscript submission date: 2022-10-14

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-10-28 03:16

Reviewer performed review: 2022-11-07 12:03

Review time: 10 Days and 8 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous



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statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

It is my honor to be invited by your journal to be the reviewer of this review. I have carefully read the manuscript. It is a topic of interest to researchers in the related areas because of the popularity of ferroptosis recently. The expression of this whole review is comprehensive, but the paper still needs some improvements before acceptance for publication. My detailed comments are as follows: 1. In this article, the author discussed the mechanism of ferroptosis and its signaling pathway. However, the relevant information we see in the article is complex and cluttered. And the organization of the article needs to be adjusted. In addition, it is suggested to add the correlation with colorectal cancer. 2. The title of the author revolves around friends or enemies, but the explanation in the article is insufficient. It is suggested to add relevant content. 3. At the end of the article, the practical clinical significance of inducing ferroptosis was described, it is suggested to supplement other aspect that inhibit the effect of ferroptosis on tumor, so as to better respond to the enemy in title.

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Peer-review model: Single blind

Reviewer's code: 04410177

Position: Peer Reviewer

Academic degree: PhD

Professional title: Assistant Professor, Senior Statistician, Statistical Worker, Statistician

Reviewer's Country/Territory: Taiwan

Author's Country/Territory: China

Manuscript submission date: 2022-10-14

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-11-08 10:11

Reviewer performed review: 2022-11-08 11:50

Review time: 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
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Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous

statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

In this paper, the authors aimed to elucidate the underlying mechanisms of ferroptosis in colorectal cancer by literature review. This study is some interesting and the results may be useful. However, some critical concerns should be addressed before publish. 1
Title: Appropriate. But, I suggested to add study design or article type in the title. 2
Abstract: Well described in the manuscript. 3 Key words: Appropriate. 4 Background: Please add references about review article related to similar issue. 5 Methods: Appropriate. 6 Results: Appropriate. 7 Discussion: I am not familiar the hypothesis proposed in this study. The authors should clarify this concern for discussion. 8
Illustrations and tables: I am not familiar in vivo model. Please introduce commonly used illustrations and tables for predictive model. Does any vitro model involve the similar topic? 9 Biostatistics: Not applicable. 10 Units: Does the manuscript meet the requirements of use of international system of units? 11 References: Please cite appropriately the latest, important and authoritative references in the introduction and discussion sections. 12 Quality of manuscript organization and presentation: Please provide English editing certificate. 13 Research methods and reporting: Please provide appropriate research methods and reporting. Authors should have prepared their manuscripts according to manuscript type and the appropriate categories, as follows: (1) CARE Checklist (2013) - Case report; (2) CONSORT 2010 Statement - Clinical Trials study, Prospective study, Randomized Controlled trial, Randomized Clinical trial; (3) PRISMA 2009 Checklist - Evidence-Based Medicine, Systematic review, Meta-Analysis; (4) STROBE Statement - Case Control study, Observational study, Retrospective Cohort study; and (5) The ARRIVE Guidelines - Basic study. 14 Ethics statements: Please provide appropriate ethics approval.

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Manuscript NO: 80852

Title: A review of ferroptosis in colorectal cancer: Friends or Foes?

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06412958

Position: Peer Reviewer

Academic degree: MD

Professional title: Doctor

Reviewer's Country/Territory: China

Author's Country/Territory: China

Manuscript submission date: 2022-10-14

Reviewer chosen by: AI Technique

Reviewer accepted review: 2022-11-08 10:47

Reviewer performed review: 2022-11-14 09:42

Review time: 5 Days and 22 Hours

Scientific quality	<input checked="" type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous

SPECIFIC COMMENTS TO AUTHORS

First, focusing on CRC, this manuscript illustrates the molecular mechanisms and pathways of ferrochrysetic disease and proposes that cancer therapy based on ferrochrysetic disease may not be suitable for all cancer types, or even for different clinical stages of the same type. The TP53-induced glycolysis and apoptosis regulator (TIGAR) is a potential regulator of iron sag in the development of colorectal cancer, and TIGAR is a potential negative regulator of iron sag. In addition, factors regulating gpx4 may be involved in the regulation of ferrolapse. GTP loop hydrolase 1 (GCH1), a rate-limiting enzyme that synthesizes free radicals to capture the antioxidant tetrahydrotrexate (BH4), has been found to inhibit ferrolapse in a GPX4-independent manner, and it has been clinically proposed that inducing ferrolapse in cancer cells may induce vaccine-like effects. The idea of stimulating anti-tumor immunity to overcome immunotherapy resistance and of immunosuppressive cells in TME contributing to immunotherapy resistance is constructive and instructive. Second, this manuscript mainly plays a role of summary and inspiration in this field. The content structure is logical, the language narrative is organized, and the illustrations are concise and clear. The background investigation and summary are carried out by the literature discovery method, and the summary is comprehensive and complete. It will further help the specific mechanisms involved in the occurrence, development and metastasis of colorectal cancer. Third, many studies have proposed possible pathways for iron sag in colorectal cancer, but the specific mechanisms of its involvement in the onset, progression and metastasis of colorectal cancer remain unclear. In the classical pathway, GPX4 can be used as a target for tumor therapy, but inhibition of GPX4 may have side effects on its protective effect against beta-amyloid toxicity in neurons. In addition, p53



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has conflicting effects on iron lobe, but its mechanism in colorectal cancer is unique. Future research could explore how to switch between the "brake" and the "accelerator" in the regulation of iron sag. In addition to classical mechanisms, other potential regulatory pathways need to be discovered. Therefore, it is very necessary for the majority of researchers to learn from the systematic knowledge framework of the paper on the basis of theory combined with clinical practice to further research on colorectal cancer iron ptosis.