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PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 83685

Title: Clinical significance and potential application of cuproptosis-related genes in gastric cancer

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03468910
Position: Editorial Board
Academic degree: PhD
Professional title: Assistant Professor, Surgeon
Reviewer's Country/Territory: Italy
Author's Country/Territory: China

Manuscript submission date: 2023-02-04

Reviewer chosen by: Yu-Lu Chen

Reviewer accepted review: 2023-02-28 06:34

Reviewer performed review: 2023-03-04 12:24

Review time: 4 Days and 5 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No creativity or innovation

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Scientific significance of the conclusion in this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No scientific significance
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [Y] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The topic of this manuscript falls within the scope of World Journal of Gastrointestinal Oncology. The Authors explored the molecular biological mechanisms of cuproptosis-related genes in gastric cancer, and constructed a significant prognostic normogram model for gastric cancer, and found that FDX1, LIAS and MTF1 (genes that function closely with cuproptosis) could serve as potential prognostic biomarkers for gastric cancer patients and provide novel targest for immunotarget therapy. It is a interesting manuscript that makesd a contribution to therapy for gastric cancer. It is well organized and well written.The manuscript methodologically sound well. The conclusions are supported by results. Complete the References. Tables anf Figures are good.

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Reviewer's code: 05687852
Position: Peer Reviewer
Academic degree: MD, PhD
Professional title: Doctor, Professor
Reviewer's Country/Territory: Taiwan
Author's Country/Territory: China

Manuscript submission date: 2023-02-04

Reviewer chosen by: Geng-Long Liu

Reviewer accepted review: 2023-03-14 05:15

Reviewer performed review: 2023-03-17 14:34

Review time: 3 Days and 9 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [Y] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [Y] Grade C: Fair [ ] Grade D: No creativity or innovation

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Language quality	[ ] Grade A: Priority publishing [ ] Grade B: Minor language polishing [Y] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The author systematically analyzed the molecular alterations of cuproptosis -related genes (CRGs) and constructed a novel prognostic nomogram model in GC using bioinformatics technology. The findings aim to offer new insights to predict GC prognosis and provide multiple therapeutic targets for future therapy. Albeit, I consider these findings to provide new insight into cancer-related fields, I still have some suggestions. 1, The title focus on “cuproptosis”-related genes, why does the author mention “Pyroptosis” in the introduction part. For example, ……All of this evidence suggests that “pyroptosis” influences the development and distal survival time of GC. For example, ……In our study, we systematically analyzed the molecular alterations of “pyroptosis”-related genes (CRGs)….. 2, Same as Discussion part, …..The prognostic models constructed in our study consisted of three “pyroptosis”-related genes (FDX1, LIAS, MTF1). As we all know, FDX1, LIAS, MTF1 are “cuproptosis”-related genes NOT “pyroptosis”-related genes 3, Most figures and tables are highly professional; however, the authors should guide the readers to the meaning of the images and tables appropriately; otherwise, it is likely to cause misunderstandings. Therefore, I suggest the

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author consider revising these figures and table legends again. 4, In the discussion part, the author mentions about……we explored the mechanisms of how prognosis - related CRGs influenced distal prognosis at the DNA methylation level and immune cell infiltration level. However, where is the DNA methylation-related data? Please perform pertinent bioinformatic analyses and provide examples of studies investigating miRNA alteration or DNA methylation (https://biit.cs.ut.ee/methsurv/) (PMID: 29264942, 34834441, 33437202). 5, The author demonstrated that FDX1, LIAS, and MTF1 could serve as potential prognostic biomarkers for GC patients and provide novel targets for immunotarget therapy. So far, the tumor infiltrates immune cells and is vital for patient survival. Therefore, it is worth validating their data correlated with immune cells by using the "TIMER" (http://timer.cistrome.org) analysis tool (PMID: 32442275, 34329194, 35454940). 6, Since Connectivity Map (CMap) can be used to discover the mechanism of action of small molecules, functionally annotate genetic variants of disease genes, and inform clinical trials. It would be fascinating if these data could be correlated with other clinical databases. Therefore, I suggest the authors can validate their data via CMap or proteinatlas, and discuss these methodologies and literature as well as the validated data for cancer recurrence or metastasis in the manuscript (PMID: 17008526, 29195078, 32064155). 7, There are few typo issues for the authors to pay attention to; please also unify the writing of scientific terms. “Italic, capital”? The font is too small for some of the current figures; meanwhile, the manuscript also needs English proofreading.