Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Oncology

Manuscript NO: 64687

Title: Novel perspective in pancreatic cancer therapy: Targeting ferroptosis pathway

Reviewer's code: 05429162
Position: Peer Reviewer
Academic degree: MD
Professional title: Academic Fellow, Doctor, Research Fellow
Reviewer's Country/Territory: Japan
Author's Country/Territory: China

Manuscript submission date: 2021-02-22
Reviewer chosen by: AI Technique
Reviewer accepted review: 2021-02-23 12:06
Reviewer performed review: 2021-02-28 12:44
Review time: 5 Days

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] 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

Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

SPECIFIC COMMENTS TO AUTHORS

Summary Yang et al. reviewed a current situation and future perspectives of the ferroptosis for pancreatic cancer treatment. Although the manuscript well described, there are some major point to be revised. Major points [Introduction] 1) Page 2 line 22; The author used the term of "deterioration". This term is not quite commonly used in the practice. Please specify what you would like to indicate using this term and consider changing the term from another proper technical term. 2) Page 3 line 1-2; The recent adjuvant chemotherapy for PDAC should be considered. Please refer the following articles: a) Uesaka et al. Lancet. 2016 Jul 16;388(10041):248-57. doi: 10.1016/S0140-6736(16)30583-9. (Adjuvant S-1 chemotherapy) b) Conroy et al. N Engl J Med. 2018 Dec 20;379(25):2395-2406. doi: 10.1056/NEJMoa1809775. (Adjuvant modified FOLFIRINOX) 3) Page 3 line 15-16; The author stated "More than 90% of PDAC have mutations in KRAS that both promote proliferation and alter cellular metabolism". The reference No.12 does not contain the role of KRAS mutation. Please add correct reference article. Also, the oncogenic KRAS plays a key role for invasion and metastasis of pancreatic cancer. Please mention about these roles of KRAS and cite appropriate articles. 4) Page 3 line 21-22; Indeed, the ferroptosis plays a critical role for RCD, the following sentence may give readers an impression of authors' personal opinions. Please reconsider the sentence.: "Ferroptosis is closely related to cystine/cysteine and ROS, so we consider that ferroptosis is a critical RCD of PDAC that may be selectively targeted as an anticancer therapy." [2.2 Characteristic] 1) Page 4 line 1; The authors stated the points of difference of ferroptosis from other RCDs. However, the points of difference between ferroptosis and each RCD should be clarified. Please describe these points by each RCD (necrosis, apoptosis and autophagy). It may be more easily to understand if the authors make a figure or table describing the points of difference. [3 Current status of ferroptosis in PDAC] 1) Page 5 line 8-11; In the figure2, it is not clearly stated that the

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

relation between ferroptosis and PDAC. The figure should describe the relation between PDAC and ferroptosis depending on the citation articles. Also, the contents of the figure should be written in the main text. Please reconsider the contents of the figure2 and main text. [3.1 Ferroptosis regulated by iron metabolism in PDAC] 1) Page 5 line 14-24; the dynamics of Fe3+ is relatively complicated. Please consider making a figure to explain the main text in this section. [3.2 Autophagy-dependent ferroptosis in PDAC] 1) Page 7 line 4-7; the sorafenib failed to show the significant contribution for overall survival in pancreatic cancer. If authors would like to mention about the sorafenib, please refer the following article related to sorafenib and pancreatic cancer and explain why the sorafenib failed to this clinical trial: Sinn et al. Eur J Cancer. 2020 Oct;138:172-181. doi: 10.1016/j.ejca.2020.06.032. [3.5 Ferroptosis regulated by tumor microenvironment in PDAC] 1) Page 10 line 3-6; the authors stated "The tumor microenvironment, including tumor cells, tumor vascular system, extracellular matrix, and immune cells, is an important factor affecting tumor therapy. An article reported that a kind of ferroptosis inducer works by affecting the tumor microenvironment, such as blood flow status, oxygen content, pH value, etc". This paragraph seems a summary of ferroptosis. If the authors would like to describe multiple roles of ferroptosis in this section, please make a table or figure to explain specific key roles of ferroptosis by each points of view (pH, immune system etc). [5 Summary and perspective] 1) Page 12 line 27-28; In this section, the authors mentioned about the photo dynamic therapy (PDT). There are few evidences to prove the PDT contributes pancreatic cancer patients' survival (Wang et al. Photodiagnosis Photodyn Ther. 2020 Sep;31:101876. doi: 10.1016/j.pdpdt.2020.101876.). Also, there is no citation to reveal the relations between PDT and pancreatic cancer, and PDT and ferroptosis. If the authors would like to mention about PDT, please describe specific mechanism why the PDT contributes to pancreatic cancer treatment, or, please consider cut these sentences. Minor points

Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

[Introduction] 1) Page 2 line 23; There is a significant consideration whether the following sentence is grammatically correct: “Surgery is the only cure for PDAC, but most patients are diagnosed as advanced and lack of opportunity for radical surgery due to the absence of distinctive clinical symptoms.” [3.4 Ferroptosis regulated by lipid metabolism in pancreatic cancer] 1) Page 9 line 7-8; The author stated “Therefore, we can study ferroptosis by studying the key enzymes (ACSL4, LPDACAT3, and ALOXs) in lipid oxidation.” It seems that the sentence includes the authors speculation. Please consider to move this sentence for “4 Inducing ferroptosis to treat pancreatic cancer” section.

Baishideng Publishing Group

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: World Journal of Gastrointestinal Oncology

Manuscript NO: 64687

Title: Novel perspective in pancreatic cancer therapy: Targeting ferroptosis pathway

Reviewer's code: 05429162
Position: Peer Reviewer
Academic degree: MD
Professional title: Academic Fellow, Doctor, Research Fellow
Reviewer's Country/Territory: Japan
Author's Country/Territory: China

Manuscript submission date: 2021-02-22
Reviewer chosen by: Jia-Ru Fan
Reviewer accepted review: 2021-04-23 10:34
Reviewer performed review: 2021-04-23 11:17
Review time: 1 Hour

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [Y] Major revision [ ] Rejection
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Yang et al. reviewed a current situation and future perspectives of the ferroptosis for

7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

pancreatic cancer treatment. The manuscript was well revised, however, the figures and tables should be included in the revised file, even if the tables and figures has not been changed.