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PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 69607

Title: Propofol induces ferroptosis and inhibits malignant phenotypes of gastric cancer cells by regulating miR-125b-5p/STAT3 axis

Reviewer's code: 02729532
Position: Editorial Board
Academic degree: MBBS, MD
Professional title: Associate Professor
Reviewer's Country/Territory: India
Author's Country/Territory: China
Manuscript submission date: 2021-07-06
Reviewer chosen by: AI Technique
Reviewer accepted review: 2021-07-06 06:51
Reviewer performed review: 2021-07-10 02:17
Review time: 3 Days and 19 Hours

Scientific quality	[ ] Grade A: Excellent [Y] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
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	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

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SPECIFIC COMMENTS TO AUTHORS

very much interesting and novel research idea. Congratulations.

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Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 69607

Title: Propofol induces ferroptosis and inhibits malignant phenotypes of gastric cancer cells by regulating miR-125b-5p/STAT3 axis

Reviewer's code: 00003880
Position: Peer Reviewer
Academic degree: MD, PhD
Professional title: Associate Professor
Reviewer's Country/Territory: Japan
Author's Country/Territory: China

Manuscript submission date: 2021-07-06

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-07-08 07:18

Reviewer performed review: 2021-07-17 13:21

Review time: 9 Days and 6 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish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
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SPECIFIC COMMENTS TO AUTHORS

The study by Liu and colleagues investigates the inhibitory effect of propofol on the progression of gastric cancer which is associated with the regulation of ferroptosis. They firstly presented that propofol decreased the growth and promoted apoptosis of gastric cancer cell lines. Propofol also impaired invasion and migration of gastric cancer cells, which were closely related with the induction of ferroptosis. Furthermore, propofol suppressed STAT3 expression which was mediated by miR-125b-5p. These findings could provide novel insights for gastric cancer prevention and treatment. The study is well conducted and the methods used are appropriate. These findings will be of interest to researchers involved in the treatment of gastric cancer. However, I regret to inform you that your manuscript could not be considered for publication in its present form. My comments are as follows. Major comments; 1. There have been a variety of papers describing the underlying mechanism for the effect of propofol on the proliferation of gastric cancer. Certainly, the data of ferroptosis is novel, but it is doubtful whether ferroptosis is a more important factor for the effect of propofol on malignant phenotypes of gastric cancer compared with apoptosis. How the authors translate this question? Targeting ferroptosis is promising strategy for gastric cancer therapy? 2. Overexpression of STAT3 reversed expression of ferroptosis associated proteins, it would be good to see they were also regulated by miR125b-5p treatments. 3. The results of proliferation, colony formation and invasion assays of two different gastric cacner cell lines are so similar. The authors should explain why the differences between two cell lines are so small in most experiments. 4. Figure 1 A & B; In order to assess the growth effects, the proliferation assay should be done in various dose of propofol. The effects were obtained in a dose dependent manner? 5. The reason determining in vitro concentration of propofol should be described. 6. Inhibitory effect of propofol on invasion (about 50% at

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20 nM) looked higher compared to growth inhibition. But it is likely that inhibitory invasion ability by propofol only results in impaired growth of cell lines. How the authors explain this question? The possibility cannot be denied that this effect is induced by the inhibition of cell growth. To address this, authors should attempt to isolate factors involving in cancer invasion accelerated by propofol, by doing additional experiments, such as measurement of proteolytic activy. 7. Figure 3 & 4F; The quality of bands seems to be low, so this is hard to tell without densitometry and quantitation. 8. The evidence showing that transfection of pmirGLO-STAT3 plasmid effectively induced STAT3 expression is required. 9. The wound healing assays, shown in Figure2 C & D, need to be compared when the control wound is completely closed. The photographs do not show the clear significance by propofol treatments. 10. In vivo experiments need to be repeated at least twice and with at least 10 randomized mice for each experimental group. Did the authors report any toxic effect, as body weight loss, during the experiment? Minor comments; 1. Please provide more detail information of experimental procedure of invasion and migration assay. Matrigel was coated in the bottom of chamber? 2. Page 8 line 3-4; Please change “5mmo;/L erastin or ferrostatin (1mmol/L)” with “5mmo;/L erastin or 1mmol/L ferrostatin” or “erastin (5mmo;/L) or ferrostatin (1mmol/L”. 3. Page 12 line 12; Please change “by inhibiting miR-125b-5p in…” with “by up-regulating miR-125b-5p in…”. I think it would be serious negligence.