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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 67405

Title: Exosomal delivered microRNA-588 from M2 polarized macrophages contributes to cisplatin resistance of gastric cancer cells

Reviewer's code: 00505755
Position: Editorial Board
Academic degree: PhD
Professional title: Senior Research Fellow
Reviewer's Country/Territory: Japan
Author's Country/Territory: China

Manuscript submission date: 2021-04-23
Reviewer chosen by: AI Technique
Reviewer accepted review: 2021-04-23 23:29
Reviewer performed review: 2021-04-26 00:22
Review time: 2 Days

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish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

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SPECIFIC COMMENTS TO AUTHORS

This study describes a possible role of miR-588 in cisplatin-resistant gastric cancer. Keywords may be re-checked and revised to have miR-588.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 67405

Title: Exosomal delivered microRNA-588 from M2 polarized macrophages contributes to cisplatin resistance of gastric cancer cells

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: 2021-04-23
Reviewer chosen by: AI Technique
Reviewer accepted review: 2021-04-24 12:12
Reviewer performed review: 2021-05-06 12:25
Review time: 12 Days

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish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

The study by Cui and colleagues examined the mechanisms of exosomes-mediated cellular communication between human gastric cancer cells and tumor-associated macrophages (TAM). They firstly identified exosomes from M2 polarized macrophages which is isolated from murine bone marrow. Exosomes-treated gastric cancer cell lines impaired the effect of DDP and reduced apoptosis compared with control cancer cells. They subsequently found miR-588 was highly expressed in the exosomes by qPCR. Similarly, the expression of miR-588 was elevated in the DDP-resistant gastric cancer cells co-cultured with exosomes from macrophages. miR-588 inhibitor facilitated the apoptosis which was indicated by the prompted expression of apoptosis-related proteins. Cylindromatosis was negatively associated with miR-588. MiR-588 may be a useful tool as biomarkers and has attracted considerable attention as a novel therapeutic candidate for the development of targeted anticancer agent. These findings will be of interest to clinicians, as well as researchers 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 is no rationale for picking only miR-588 for analysis. It seems the author picked their preferred miRNA. How about other pivotal miRNA that have been described as crucial for in exosomes-mediated cellular communication? To my knowledge, it hasn't been prominently implicated in gastric cancer through interaction between tumor and surrounding microenvironment. The significance of picking up miR-588 is unclear. 2. The authors described that “CYLD knockdown reversed the effect of miR-588 inhibitor” in Results Section, but showing only data of Western blotting. To really substantiate that silencing cylindromatosis impaired the effect of miR-588, it would be important to show xenograft data. The number of mice used in the experiment should be given in the

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Figure legends. 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? 3. The authors showed the expression of miR-588 was elevated in the gastric cancer cells co-cultured with exosomes from macrophages What is the mechanism of miR-588 transfer from macrophage to cancer cells? 4. Why do the authors not evaluate the expression of cylindromatosis in macrophage in these experiments? 5. The definition of "DDP-resistant gastric cancer cells" is unclear. The authors newly established cell lines resistant to SGC7901 cells? 6. I think it should be useful if the authors gave the more information about the miR-588 inhibitor, such as chemical company. 7. In Abstract Section, the statement: "Cisplatin (DDP) is one of the most common…." should be replaced to BACKGROUND. There looks to be no AIM in Abstract. 8. In the discussion section, the authors simply repeated the experimental results they had already described in the results section. They should rather provide a more elaborate explanation of the results as they pertain to the previously raised questions. 9. Clinical translation of these experiments is entirely unclear and doubtful. Minor comments; There are too many characters corruptions in this manuscript, especially in figures. They should double-check their manuscript before submitting. 1. Page6, line12: please change "paly" to "play". 2. Page12, line 23: please change "unactivated" to "inactivated". 3. Page15, line 4: please change "regualting" to "regulating". 4. Figure 5: please change "miR-181c-5p" to "miR-558". The same mistake was also seen in the text.

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RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 67405

Title: Exosomal delivered microRNA-588 from M2 polarized macrophages contributes to cisplatin resistance of gastric cancer cells

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: 2021-04-23
Reviewer chosen by: Yun-Xiaojian Wu
Reviewer accepted review: 2021-06-16 06:15
Reviewer performed review: 2021-06-20 08:21
Review time: 4 Days and 2 Hours

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) [Y] Minor revision [ ] Major revision [ ] Rejection
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

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SPECIFIC COMMENTS TO AUTHORS

The authors investigated the role of miR-588 in exosomes derived from tumor-associated macrophages (TAM) in chemo-resistance of gastric cancer. Exosomal transfer of TAMs derived miR-588 confer DDP resistance. The manuscript is generally well modified. However, I regrettably should say that it is still immature for publication. My comments are as follows; 1. The authors claim the expression of CVLD was not differed between inactivated and M2 polarized macrophage but don't show the data. Reviewer think that evaluation of CVLD expression in macrophages is one of the important points in the manuscript and it would be highly preferable to show the data. Can the authors reflect these results in Discussion Section? 2. The revised words and/or sentences of this revised manuscript is unclear. Please show the significant changes (such as highlight in yellow in the Title).