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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 60177

Title: miR-34a demethylation up-regulates MP expression and promotes liver cancer cell apoptosis

Reviewer's code: 02441467
Position: Peer Reviewer
Academic degree: PhD
Professional title: Professor
Reviewer's Country/Territory: China
Author's Country/Territory: China

Manuscript submission date: 2020-10-20
Reviewer chosen by: AI Technique
Reviewer accepted review: 2020-10-23 00:12
Reviewer performed review: 2020-10-28 08:39
Review time: 5 Days and 8 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [Y] Grade D: Fair [ ] Grade E: Do not publish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

The title of this paper reflects the main content of the manuscript: miR-34a can up-regulate the expression of MPP2 and promote the apoptosis of liver cancer cells through demethylation, and inhibit proliferation, invasion and metastasis of cells. The idea of this paper is relatively complete, focusing on the effect of miR-34a demethylation on the biological function of liver cancer cells. However, I think the key word "caspase3" is not accurate enough, and the methods in the manuscript is not clear enough. For example, when cell proliferation is measured by MTT assay, how is cell viability calculated? what is the dilution ratio of the antibody in western blot analysis? What's the concentration of 5-za? In addition, in the Transwell experiment, NC demeth and NC pre groups images of HepG2 in figure S1 were the same, miR-34a demeth and miR-34a demeth + siMPP2 groups images of Hep3B in figure S4 were the same, please give a reasonable explanation for the above phenomenons. And in the results of western blotting assay, there were only statistical graphs and no stripes, which I thought it was not rigorous enough. Finally, if experimental conditions and time permit, it is suggested to increase animal experiments, so as to better illustrate the research topic of this paper.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 60177

Title: miR-34a demethylation up-regulates MP expression and promotes liver cancer cell apoptosis

Reviewer's code: 02259896
Position: Peer Reviewer
Academic degree: PhD
Professional title: Senior Scientist
Reviewer's Country/Territory: India
Author's Country/Territory: China

Manuscript submission date: 2020-10-20
Reviewer chosen by: Ze-Mao Gong
Reviewer accepted review: 2020-11-12 04:07
Reviewer performed review: 2020-12-02 07:27
Review time: 20 Days and 3 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) [Y] 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

The study "miR-34a demethylation up-regulates MPP2 expression and thus promotes liver cancer cell apoptosis" has been submitted to the World Journal of Gastroenterology by Li et al. The study explores the role of miR-34a and MMP2 in liver cancer and adjacent normal tissues. They subsequently find miR-34a methylation to govern the expression of MMP2, and thus propose miR methylation as a potential method for liver cancer treatment. The study is interesting but the authors should address the following concerns. 1. Apart from MMP2, please discuss other biological factors that promote the metastatic nature of liver cancer. Any redundancy between proteins of the MMP family should also be taken into account. 2. Apart from MMP2, were any other downstream targets of miR-34a found to be altered? Please elucidate 3. Mention the distance of resection margins from the site of tumors? Did the expression of miR-34a, MMP, caspase follow any specific trend with increasing or decreasing distance from tumor site should be discussed thoroughly.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 60177

Title: miR-34a demethylation up-regulates MP expression and promotes liver cancer cell apoptosis

Reviewer's code: 02440884
Position: Editorial Board
Academic degree: MD

Professional title: Chief Doctor, Full Professor, Professor, Senior Lecturer

Reviewer's Country/Territory: Germany

Author's Country/Territory: China

Manuscript submission date: 2020-10-20

Reviewer chosen by: Ze-Mao Gong

Reviewer accepted review: 2020-12-02 14:06

Reviewer performed review: 2020-12-04 17:19

Review time: 2 Days and 3 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) [Y] 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

In the experimental study methylation of miR-34a is shown as molecular mechanism in regulation of MPP2 in liver cell carcinogenesis. The authors demonstrate that miR-34a demethylation is associated with an increase in MPP2, which belongs to the membrane palmitoylated proteins. These multidomain proteins are involved in several important cellular activities. The manuscript is well written and in the scope of the Journal. The experimental setting is well and provides essential data. Comments 1. HCCs are investigated. The classification and entity should be given. 2. Page 5: MPP is for membrane palmitoylated proteins and not palmitoyl membrane protein . 3. MPPs are important in lateral membrane organization and cell adhesion. In the study apoptosis and diminished proliferation, invasion and migration of liver cells were found. It should be of interest to investigate cellular adhesions after after miR-34a demethylation and the si-MPP2 rescue.

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RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 60177

Title: miR-34a demethylation up-regulates MP expression and promotes liver cancer cell apoptosis

Reviewer's code: 02440884
Position: Editorial Board
Academic degree: MD
Professional title: Chief Doctor, Full Professor, Professor, Senior Lecturer
Reviewer's Country/Territory: Germany
Author's Country/Territory: China
Manuscript submission date: 2020-10-20
Reviewer chosen by: Le Zhang
Reviewer accepted review: 2020-12-22 19:02
Reviewer performed review: 2020-12-22 19:09
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) [Y] Minor revision [ ] Major revision [ ] Rejection
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

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In the experimental study methylation of miR-34a is shown as molecular mechanism in regulation of MPP2 in liver cell carcinogenesis. The authors demonstrate in the further revised version that miR-34a demethylation is associated with an increase in MPP2, which belongs to the membrane palmitoylated proteins. These multidomain proteins are involved in several important cellular activities. Comments 1. HCCs are investigated. The classification and entities according to WHO are not addressed in detail.