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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 53120

Title: Exosomal miR-182 regulates the effect of RECK on gallbladder cancer

Reviewer's code: 02545023
Position: Editorial Board
Academic degree: PhD
Professional title: Associate Professor
Reviewer's country: United States
Author's country: China

Reviewer chosen by: Artificial Intelligence Technique

Reviewer accepted review: 2019-12-05 19:44

Reviewer performed review: 2019-12-21 00:24

Review time: 15 Days and 4 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	[ ] Accept (High priority)	Peer-Review:
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] Accept (General priority)	[Y] Anonymous
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[Y] Minor revision	[ ] Onymous
[ ] Grade D: Fair	[ ] Grade D: Rejection	[ ] Major revision	Peer-reviewer's expertise on the topic of the manuscript:
[ ] Grade E: Do not publish		[ ] Rejection	[ ] Advanced
			[Y] General
			[ ] No expertise
			Conflicts-of-Interest:
			[ ] Yes
			[Y] No

SPECIFIC COMMENTS TO AUTHORS

Exosomal miR-182 regulates the effect of RECK on gallbladder cancer. 1. In the

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introduction, "Moreover, RECK exerts its influence on tumor progression through the regulation of miRNA." But all the following examples demonstrated that miRNAs exert influence on tumor progression through regulating RECK. 2. "Although numerous studies have elucidated the molecular mechanism of miR-182 and RECK in various cancers, yet the very role of exosomal miR-182 and RECK in GC remains unclear." The paper is about miR-182 and RECK, but the well-known or established molecular mechanism about the relationship between miR-182 and RECK was not elucidated in the introduction. 3. In the materials and methods, (Sample Collection) "The collected tissues were sectioned and stored in liquid nitrogen at -80 °C for testing" "the supernatant was collected and placed in -80℃ liquid nitrogen to be measured." Were the collected tissues stored in liquid nitrogen or at -80 °C ? 4. In methods, the expression "Cells were hydrolyzed with trypsin to make cell suspension." is not appropriate. 5. About the apoptosis assay, the author didn't mention the details in the paper, such as whether any reagent was used or not? 6. Page 11, Result "Compared with normal human blood samples, serum miR-182 level was significantly elevated in patients with GC (Figure 2B). " "Figure 2. B: Exogenous miR-182 was highly expressed in patients with GC. On the image, "exosomal miRNA182" The expression is not consistent. "Here, we compared the expression of exogenous/endogenous miR-182 in different NM phases and analyzed the correlation between miR-182 and clinical features" This author used "exogenous and endogenous" to distinguish "cell or tissue" derived and "exosome "derived miR-182, which is confusing. 7. Page 12 "Exosomal miR-182 was associated with GC metastasis" Based on figure 3 data, both cellular and exosomal miR-182 increased in cancer as compared to normal tissue. 8. Page 13, in rescue assay, "Exosomal miR-182, exosomal miR-182+RECK overexpression vector were added to GC cells for the conduction of corresponding MTT, Western blot and Transwell experiments." Is synthesized miR-182 or exosome used in this assay? If only synthesized miR-182 was

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used in this assay, this experiment may only prove miR-182 relevant to cancer, not exosomal miR-182 specifically.

INITIAL REVIEW OF THE MANUSCRIPT

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[Y] No

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[Y] No

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 53120

Title: Exosomal miR-182 regulates the effect of RECK on gallbladder cancer

Reviewer's code: 02451459
Position: Peer Reviewer
Academic degree: PhD
Professional title: Associate Professor
Reviewer's country: Singapore
Author's country: China

Reviewer chosen by: Jie Wang
Reviewer accepted review: 2019-12-19 02:58
Reviewer performed review: 2019-12-21 01:41
Review time: 1 Day and 22 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	[ ] Accept (High priority)	Peer-Review:
[Y] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] Accept (General priority)	[Y] Anonymous
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[Y] Minor revision	[ ] Onymous
[ ] Grade D: Fair	[ ] Grade D: Rejection	[ ] Major revision	Peer-reviewer's expertise on the topic of the manuscript:
[ ] Grade E: Do not publish		[ ] Rejection	[ ] Advanced
			[Y] General
			[ ] No expertise
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SPECIFIC COMMENTS TO AUTHORS

This study aims to establish the of miR-182 and RECK to gallbladder cancer. On the

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basis on a clear correlation of high miR-182 and RECK in gallbladder cancer, they went to to demonstrate that miR-182 is enriched in gall bladder cancer cells and are secreted in encapsulated form within exosomes. Introduction of such miR-182 suppressed RECK expression, and also increase proliferative and anti-apoptosis phenotype. This effect was also demonstrated using loss of function experiments where reversal of effect was seen with RECK siRNA. Therefore the strength of this work is the strong correlation between clinical findings and basic sciences. Effect is well established using a combination of both gain and loss of function studies. The dual luciferase activity provides the important linkage that miR-182 has the capacity to regulated RECK directly. The significance of this pathway, in comparison to other oncogenic proteins will need to be ascertained in future studies. Specific comments are as follow: 1. Figure 1 does not describe clearly whether the data was obtained from the cell lines or from tumor tissues derived from patients. The sample size that was used to gather this data was also not described. 2. To describe intracellular miR-182 as endogenous and exosomal miR-182 as exogenous is not appropriate. Exogenous tends to refer to materials that originate from outside the body. Therefore, exosomal miR-182 are still considered as endogenous as it is derived from host cells. 3. In the paragraph on miR-182 targeted inhibition of RECK expression, miR-182 was wrongly described as miR-195. 4. There are multiple typographical errors that need to be corrected. It is recommended that a language expert be engaged to proofread the final manuscript.

INITIAL REVIEW OF THE MANUSCRIPT

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 53120

Title: Exosomal miR-182 regulates the effect of RECK on gallbladder cancer

Reviewer's code: 00418258
Position: Editorial Board
Academic degree: PhD
Professional title: Professor
Reviewer's country: Italy
Author's country: China

Reviewer chosen by: Jie Wang

Reviewer accepted review: 2019-12-14 14:49

Reviewer performed review: 2019-12-24 18:59

Review time: 10 Days and 4 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	[Y] Accept (High priority)	Peer-Review:
[Y] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] Accept (General priority)	[Y] Anonymous
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[ ] Grade D: Fair	[ ] Grade D: Rejection	[ ] Major revision	Peer-reviewer's expertise on the topic of the manuscript:
[ ] Grade E: Do not publish		[ ] Rejection	[Y] Advanced
			[ ] General
			[ ] No expertise
			Conflicts-of-Interest:
			[ ] Yes
			[Y] No

SPECIFIC COMMENTS TO AUTHORS

This is a very interesting paper providing robust evidence for a role of miR-182 in GC,

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special attention was focused on exosomal (extracellular presence of miR-182). The Authors have also investigated the mechanism (possible) for miR-182 suggesting a role in down regulating RECK and in turn promoting migration and invasion in GC.

INITIAL REVIEW OF THE MANUSCRIPT

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