ANSWERING REVIEWERS

Jun 23, 2012

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 10173-Edited.doc).

Title: miR-374b-5p Promotes Gastric Cancer Invasion and Metastasis by suppressing RECK expression

Author: Juan Xie, Zhi-Hui Tan, Xia Tang, Ming-shu Mo, Yan-Ping Liu, Run-Liang Gan, Yi Li, Li Zhang, Guo-Qing Li

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 10173

The manuscript has been improved according to the suggestions of reviewers:
1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer(Reviewer1: 0014566 and Reviewer2: 0023587),

Reviewer 1:

The authors have published a recent paper which employs a similar approach in GC cell lines: Juan Xi et al. “miR-7 inhibits the invasion and metastasis of gastric cancer cells by suppressing epidermal growth factor receptor expression “,Oncol Rep. 2014 Apr;31(4):1715-22. My questions is wheather microRNA profiling performed in the latter study and in the current new submission involves the same experiment or is it different? The authors use the same cell lines in these two papers and seem to get different microRNA profiling results in cell lines-this needs to be explained and discussed. If there is an overlap between microarray results this needs to be stated and interpreted in terms of ?novelty.

(1). microRNA profiling performed in the latter study and in the current new submission involves the same experiment or is it different?The authors use the same cell lines in these two papers and

seem to get different microRNA profiling results in cell lines-this needs to be explained and discussed.

Answer：We thank the reviewer for the suggestion. The microRNA profiling performed in the current submission was supplied with some newly discovered miRNAs compared with the published paper(Oncol Rep. 2014 Apr;31(4):1715-22), such as ebv-mir-BART 19-3P, Kshv-miR-K12-5*, hsa-miR-20b-5p etc. And the two miRNA microarrays were performed in different time. So, they were not the same experiment. There was an overlap between the two microarray results, but some different expressed microRNAs were also found, such as hsa-miR-21, hsa-miR-26b, hsa-miR-29c etc. In this experiment, MKN45 cell line was not included which was another reason why two microarray results were different. In this revised version, the discussion has been enriched as suggested by the reviewer in Pg.10 line 19.

(2).If there is an overlap between microarray results this needs to be stated and interpreted in terms of novelty?

Answer：In previous research, we found the treatment with antisense oligonucleotide for miR-7 did not completely inhibit the metastasis of cancer cells[1]. It suggested that some other miRNAs may be also involved such as miR-374b-5p. In this revised version, we made the supplement in Pg.10 line21.

Reviewer 2:

COMMENTS TO AUTHORS:

There are numerous reports of newly identified microRNA targeted genes in cancer, however, the application of these findings in clinical practice seems to be challenged by the fact that the same microRNA may target multiple genes including both oncogenes and tumor suppressors. The authors should discuss this complexity and potential implications of their findings in the discussion section.

Answer：We thank the reviewer for the thoughtful and constructive comments. In the revised version, we made the change and supplement in Pg.9 line15. It was replaced by “It has been reported that altered miRNAs expression is associated with tumor development and progression, but little is known about the expression levels change and relative function of miRNAs in gastric cancer cells[2]. In this study, we reported differentially expressed miRNAs in gastric cancer cells compared

with normal mucosal cells, then we focused on miR-374b-5p discriminatory expression and found it was involved in tumor metastasis and invasion that had not been reported before".

Minor comments: 1) The authors must improve English and correct grammar mistakes throughout the manuscript - eg. Pg. 2 line 16 "invasiveness may-via"; pg. 7, ln 12; pg. ln 23-27 (sentence way too long and hard to follow), pg. 8 ln 21 "are" should be "is", pg 11 ln 1 "Peferences", etc. 2) Key words: "DNA microarray", is this a typo? 3) Page 8, ln 22. The authors should be more cautious when stating that "little is known about the expression levels change and relative function of miRNAs in gastric cancer cells" there are numerous recent publications on that. 4) The content in page 3, ln 17-26 should not be presented in the "Introduction" part of the article – authors should not start describing their findings in this part of the paper and should move this part to the appropriate sections below!

Answer: We thank the reviewer for raising these critical comments.

1)The authors must improve English and correct grammar mistakes throughout the manuscript.

Answer: We have made the modification as suggested by the reviewer. Pg. 2 line 16 "invasiveness may-via" was replaced by "invasiveness may via" in Pg. 2 line 25. The long sentence in pg. ln 23-27 was modified. Pg. 8 ln 21 "are", pg 11 ln 1 "Peferences" were replaced by "is" and " REFERENCES".

2). Key words: "DNA microarray", is this a typo?

Answer: The typo has been replaced by " miRNA microarray" in Pg. 2 line 30.

3) Page 8, ln 22. The authors should be more cautious when stating that "little is known about the expression levels change and relative function of miRNAs in gastric cancer cells".

Answer: The statement has been deleted and replaced by "Many miRNAs have unique and different expression pattern in certain cancer tissues. It has been reported that miR-222-3p was up-regulated and promoted proliferation and invasion in endometrial carcinoma, but

down-regulated in prostate cancer. Some researchers suggest these miRNA expression characteristics are potential biomarkers and powerful diagnostic tools for tumor classification and diagnosis." in Pg. 8 line 21.

4）The content in page 3, ln 17-26 should not be presented in the "Introduction" part of the article – authors should not start describing their findings in this part of the paper and should move this part to the appropriate sections below!

Answer: The statement in page 3, ln 17-26 has been deleted, and we added some contents in discussion (Pg. 9, ln 25-31).

[1].Xie J, Chen M, Zhou J, Mo MS, Zhu LH, Liu YP, Gui QJ, Zhang L, Li GQ. miR-7 inhibits the invasion and metastasis of gastric cancer cells by suppressing epidermal growth factor receptor expression. Oncology reports. 2014; 31: 1715-1722.

[2].Shah MA, Khanin R, Tang L, Janjigian YY, Klimstra DS, Gerdes H, Kelsen DP. Molecular classification of gastric cancer: a new paradigm. *Clinical Cancer Research.* 2011; **17**: 2693-2701.

References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology.*

Sincerely yours,

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