

ANSWERING REVIEWERS

May, 9, 2015



Dear Editor,

Thank you very much for your letter dated May 1 and for the accompanying referees' comments on my paper (WJG, ESPS Manuscript NO: 18044). I am submitting a revised manuscript that incorporates the recommendations of the reviewers. For your convenience, we have highlighted the changes made in red.

Please find enclosed the edited manuscript in Word format (file name: 18044-review.docx).

Title: Circulating microRNAs and long non-coding RNAs in gastric cancer diagnosis: An update and review

Author: Ya-Kai Huang, Jian-Chun Yu

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 18044

1 Format has been updated

SUGGESTIONS IN "The Revision Policies of BPG for Review"

Response: Our amended manuscript has been reviewed by American Journal Experts (AJE), and we have attached the file of the English language certificate

EDITOR'S SUGGESTIONS

Response: (1) We have retitled this review according to your valuable advice.

(2) We have added the full names of the authors and their institution, city, province and postcode to the manuscript.

(3) We have provided the corresponding author and corresponding address in the manuscript.

(4) We have provided the key words, core tip and audio core tip in the manuscript.

(5) We have amended the reference format in the manuscript using endnote X6.

(6) We have reformatted the tables and figures according to your revision policies.

2 The manuscript has been improved according to the suggestions of reviewers, a point-by-point response to each of the reviewers' comments is attached.

Reviewer #1

(1) It is probably an over-statement in "circulating miRNAs in GC diagnosis". The authors need to focus on their topic "the diagnosis of gastric cancer". In addition, the authors should review the difference in the expression of circulating miRNAs and lncRNAs between intestinal-type and diffuse-type gastric cancers or between early and advanced gastric cancers.

Response: We have readjusted the frame of section 2 of “primary circulating miRNAs used in GC diagnosis” and section 3 of “primary circulating lncRNAs used in GC diagnosis”, deleted the irrelevant content to make sure the manuscript focus on the topic of gastric cancer diagnosis. Concurrently, we have added the content about the circulating miRNAs and lncRNAs for detection of GC classified by tumor site, pathological type and tumor stage in section 2.4 of “Summary of circulating miRNAs used in GC diagnosis” and section 3.3 of “Summary of circulating lncRNAs used in GC diagnosis” according to your recommendation.

(2) Many syntax errors and spelling mistakes were found. The manuscript should be corrected by native English speaker.

Response: We have polished the language with assistance from American Journal Experts (AJE)

Reviewer #2

Major considerations:

- (1) The description of circulating non-coding RNAs is made monotonically and boring. In each case is simply a description of the main findings of a study, and then they comment on findings in other diseases of the mentioned non-coding RNAs. Therefore, the article could be summarized substantially

Response: We have amended the content in section 2 of “primary circulating miRNAs used in GC diagnosis” and section 3 of “primary circulating lncRNAs”, and summarized the characteristics of circulating miRNAs and lncRNAs for GC diagnosis in section 2.4 of “Summary of circulating miRNAs used in GC diagnosis” and section 3.3 of “Summary of circulating lncRNAs used in GC diagnosis” as well as in table 2 and table 4, respectively.

- (2) It is recommended that the authors note in the title that this is a review of the literature focused on findings on circulating microRNAs and long non-coding RNAs as biomarkers for gastric cancer

Response: We have amended the title according to your suggestion.

- (3) The writing must be revised and substantially improved throughout the manuscript

Response: We have polished the language with assistance from American Journal Experts (AJE)

- (4) The description of the micro RNAs seems to obey only to the order in which the authors describe the studies reviewed. The microRNAs should be classified, at least according to the reported miRNA expression abnormalities in GC: Upregulated miRNAs (oncomirs) and downregulated miRNAs (tumor-suppressor miRNAs)

Response: We have amended the frame of section 2 of “primary circulating miRNAs used in GC diagnosis” and section 3 of “primary circulating lncRNAs used in GC diagnosis”, classified descriptions of circulating miRNAs and circulating lncRNAs in GC diagnosis are performed according to their circulating expression levels in section 2.1 of “main up-regulated circulating miRNAs used in GC diagnosis”, section 2.2 of “main down-regulated circulating miRNAs used in GC diagnosis”, section 3.1 of “main up-regulated circulating lncRNAs used in GC diagnosis” and section 3.2 of “main down-regulated circulating lncRNAs used in GC diagnosis”. Concurrently, we have added the contents with respect to onco-miRNAs and tumor-suppressor miRNAs in every paragraph describing circulating miRNA or lncRNA in gastric cancer diagnosis, we have summarized the

characteristics of circulating miRNAs and lncRNAs in section 2.4 of “summary of circulating miRNAs used in GC diagnosis” and section 3.3 of “Summary of circulating lncRNAs used in GC diagnosis”, respectively. In addition, the characteristics of the microRNA and lncRNA have been presented in table 2 and table 4 according to your recommendation, respectively.

- (5) The English must be polished throughout the manuscript paying particular attention to the sections 1 and 2.

Response: We have polished the language with assistance from American Journal Experts (AJE)

Minor consideration

- (1) Please, use consistently the abbreviation GC throughout the text

Response: I have amended the corresponding content to use GC throughout the text according to your suggestion

- (2) Page 1, first paragraph. Author refers to non-invasive methods?” There were many methods for GC detection, such as serum pepsinogen, MG-7.”

Response: We means the non-invasive methods, I have amended the corresponding content to make it clear according to your suggestion

- (3) Page 2 (second paragraph) and legend of figure 2: please change “nascent RNA” for nascent mRNA.

Response: I have changed “nascent RNA” to nascent mRNA according to your suggestion

- (4) Page 2, third paragraph –Please rephrase sentence to make it more clear: “miRNAs are protected by various lipids and proteins in exosomes and other microparticles have been detected in plasma, serum, urine, saliva, and milk”.

Response: I have rephrased the sentence to make it accessible according to your proposal

“miRNAs that are protected by exosomes and other microparticles have been detected in plasma, serum, urine, saliva, and milk”

- (5) The way as heading or subtitles was used to indicate different non-coding RNAs is confusing. It is encouraged to author if possible, dividing the microRNAs mentioned in the manuscript according to the expression profile findings reported previously.

Response: According to your advice, we have amended the contents of section 2 of “primary circulating miRNAs used in GC diagnosis” and section 3 of “primary circulating lncRNAs used in GC diagnosis”, classified descriptions of circulating miRNAs and circulating lncRNAs in GC diagnosis are performed according to their circulating expression levels in section 2.1 of “main up-regulated circulating miRNAs used in GC diagnosis”, section 2.2 of “main down-regulated circulating miRNAs used in GC diagnosis”, section 3.1 of “main up-regulated circulating lncRNAs used in GC diagnosis” and section 3.2 of “main down-regulated circulating lncRNAs used in GC diagnosis”.

- (6) Although it is not the focus of the review and in several cases is unknown, if it is possible it would be interesting to make a brief description of the role of microRNAs and lncRNAs in gastric cancer (at least for those with more potential as biomarkers for GC).

Response: I have added the content with respect to the functions of microRNAs and lncRNAs in GC in paragraph 3 and paragraph 4, respectively.

(7) Throughout the manuscript, capital letters are used improperly.

Response: I have polished the language to make capital letters used correctly based on your advice

(8) Please check the use of et al. instead of etc. to indicate the logical continuation of a list (not people) through the text.

Response: I have corrected the usage of “etc” and “et al” through the text

(9) Please review the citation of authors throughout the text. It must be uniform and following the instructions for authors.

Response: I have corrected the citation of author following the instruction

(10) Page 5, second paragraph, Please rephrase sentence to make it more clear: “25 miRNAs were identified to be differently expressed, of which 11 were up-regulated and 14 were down-regulated in gastric cancer comparing to control groups, finally, miR-195-5p in gastric cancer was identified to be most significantly comparing with control groups with more than 13-fold changes in expression and was suggested to function as a novel tumor suppressor miRNA in gastric cancer development”.

Response: I have rephrased the sentence and deleted some texts to make sure of reader’s unambiguous comprehension of it

“Aysegul Gorur et al stated that plasma miR-195-5p was most significantly down-regulated, with more than 13-fold changes in the expression in GC patients compared with control groups, suggesting its potential as a biomarker for GC detection”

(11) Several abbreviations were not used uniformly throughout the text, e.g.: EGC, NSCLC, etc.

Response: I have corrected the abbreviations throughout the text

(12) Several abbreviations are not explained for the casual reader, e.g.: SNPs, CRC, etc.

Response: I have explained the abbreviations using full name

(13) Page 7, first paragraph, Please rephrase sentence to make it more clear: “In this study, in vitro experiment showed that transfection of let-7a mimics significantly inhibited CCR7 protein expression level in MNK-45 cells and the migration and invasion of MNK-45 cells.”

Response: I have rephrased the sentence deleted some texts to make it unambiguous.

“ In this study, in vitro experiments revealed that let-7a might function as a tumor suppressor miRNA in GC by suppressing CCR7”

(14) References must be showed in tables 2 a

Response: I have added the references to the table 2 (now is termed as table 3)

3 References and typesetting were corrected

We declare that this work is original, the manuscript is not under consideration by other journals. All authors approved the contents submitted. We look forward to hearing from you at your earliest convenience

I hope that my paper has been revised satisfactorily and will be accepted for publication in your journal. I look forward to your response.

Sincerely yours,

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