Author’s response to reviews

Title: Plasma expression of miRNA-21, -214, -34a, and -200a in patients with persistent HPV infections and cervical lesions

Authors:

Hongyun WANG (hongyunwangen@126.com)
Dandan ZHANG (egg81811@163.com)
Qing CHEN (964565749@qq.com)
Ying Hong (hongying@nju.edu.cn)

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Author’s response to reviews:

Catherine Rice
BMC Cancer
August 12, 2019
Dear Catherine,

We would like to thank the editors for their hard work. We have significantly revised our manuscript, which is now titled “Plasma expression of miRNA-21, -214, -34a, and -200a in patients with persistent HPV infection and cervical lesions”. We would like to submit our revised manuscript for consideration for publication as a research article in BMC Cancer.

Please find our point-by-point responses to the comments of the reviewers below. The revised manuscript and the point-by-point response letter have been submitted. Our revised manuscript accurately shows the amendments to the manuscript text, and the specific page numbers and line numbers associated with the content changes are provided in the response letter for easy review.

We confirm that this paper has not been published elsewhere in whole or in part and does not contain any individual person’s data. All authors have read and approved the content and have agreed to submit the manuscript for consideration for publication in this journal. The authors have no conflicts of interest to declare.

I hope that, with your help, the revised article can be published.

I look forward to hearing from you soon.

Yours sincerely,
Editor Comments:

1. We note that the current submission contains some textual overlap with other previously published works, in particular in the Discussion section. Please see the attached screenshots for more detail. While we understand that you may wish to express some of the same ideas contained in these publications, please be aware that we cannot condone the use of text from previously published work. Please re-phrase these sections to minimise overlap.

Response
The editor’s comment is correct. We have modified the text as follows (Discussion, line 24, page 11-line 23, page 23):

According to a report by Nambaru et al., in 121 cervical cancer biopsy specimens collected [14], episomal forms were more frequent in the HPV16 type, and integrated forms were more frequent in the HPV18 type (p=0.011). The study found 53 miRNAs near the integration sites, 39 of which were related to cancer. The incidence of miRNAs near the HPV integration site was 78.3%, and in HPV16 type cases, the incidence was more frequent.

According to a report by Arroyo et al., miRNA circulates in the blood in a fairly stable extracellular form and has been developed as a blood biomarker for cancer and other diseases. However, the mechanism of this significant stability in the blood environment is not clear. According to the current model, cyclic miRNA is protected by membrane-bound vesicles (such as exosomes), but this has not been further studied. [15].

In a report by Allegra et al., cell data related to the role of miRNAs in the pathogenesis of various diseases are reviewed, and the latest information concerning the role of circulating miRNAs is compiled. In addition, the role of circulating miRNAs in tumour disease may be particularly important. At least 79 miRNAs are reported to be plasma or serum miRNA biomarkers of solid and blood tumours. Cyclic miRNA profiles can improve cancer diagnosis and predict the prognosis of cancer patients, while changes in circulating levels may indicate cancer susceptibility and through analysis can be used to help determine therapeutic goals [16].

According to a report by Zen et al., miRNAs, once thought to be unstable RNA molecules, are now known to be stably expressed in serum, plasma, urine, saliva and other body fluids. In addition, the unique expression patterns of miRNAs in these cycles are associated with certain human diseases, including various types of cancer. Therefore, tumour-derived miRNA levels in serum or plasma are becoming a new blood-based fingerprint to detect human cancer, especially in the early stages.[17]

2. We note that you have included a ‘Consent for publication’ section in the Declarations. Consent for publication refers to consent for the publication of identifying images or other personal or clinical details of participants that compromise anonymity. Seeing as this is not applicable to your manuscript please state “Not Applicable” in this section.

Response
The editor’s comment is correct. We have modified the text as follows ( Declarations, line 17-23, page 13):

Consent for publication
The manuscript does not contain any individual person’s data in any form. This paper has not been published elsewhere in whole or in part. Our manuscript does not contain any individual person’s data,
and thus, the 'Consent for publication' section is not applicable.
All authors have read and approved the manuscript content and agreed to submission of the manuscript for consideration for publication in the journal.

3. If abbreviations are used in the text they should be defined in the text at first use, and a list of abbreviations should be provided in the Declarations.
Response
The editor’s comment is correct. We have modified the text as follows (Methods, lines 4-5, page 5):
After cervical conization, formalin-fixed paraffin-embedded (FFPE) tissue samples were prepared and assessed.

4. At this stage, please upload your manuscript as a single, final, clean version that does not contain any tracked changes, comments, highlights, strikethroughs or text in different colours. All relevant tables/figures/additional files should also be clean versions. Figures (and additional files) should remain uploaded as separate files. Please ensure that all figures, tables and additional/supplementary files are cited within the text.
Response
The editor’s comment is correct. We have modified the text.

Reviewer reports:
If improvements to the English language within your manuscript have been requested, you should have your manuscript reviewed by someone who is fluent in English. If you would like professional help in revising this manuscript, you can use any reputable English language editing service. We can recommend our affiliates Nature Research Editing Service (http://bit.ly/NRES_BS) and American Journal Experts (http://bit.ly/AJE_BS) for help with English usage. Please note that use of an editing service is neither a requirement nor a guarantee of publication. Free assistance is available from our English language tutorial (https://www.springer.com/gb/authors-editors/authorandreviewertutorials/writinginenglish) and our Writing resources (BMC_WRITING_RESOURCES_URLhttp://www.biomedcentral.com/getpublished/writing-resources). These cover common mistakes that occur when writing in English.
Response
The editor’s comment is correct. We have asked AJE to revise the paper.