Author’s response to reviews

Title: miR-221-5p enhances cell proliferation and metastasis through post-transcriptional regulation of SOCS1 in human prostate cancer

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Author’s response to reviews:

Dear Editor in Chief,

Thank you very much for your letter and advice. We have revised the manuscript, and would like to re-submit it for your consideration. We have addressed the comments raised by the reviewers, and resubmitted the revised manuscript. Point by point responses to the reviewers’ comments are listed below this letter.

We hope that the revised version of the manuscript is now acceptable for publication in your journal.

I look forward to hearing from you soon.

With best wishes,

Yours sincerely,
Jinying Zhang

We would like to express our sincere thanks to the reviewers for the constructive and positive comments.

Replies to Reviewer 1

Minor critiques:
Comment 1. The authors may describe a strong rationale for miR-221-5p, thus why miR-221-5p was selected. The authors described simply as "Gene microarray data have shown the abnormal expression and paradoxical role of ...." They can describe more in detail.

Answer: Thank you for your reminding. It is a critical question about why we choose the mir-221-5p in this study. I’m so sorry that my description in the manuscript is not detailed enough. In addition to gene microarray data, we have done some work about the correlation between miR-221-5p and prostate cancer patient samples in an unpublished article. In my new submission of manuscript, we detect the expression of miR-221-5p and SOCS1 in cancer tissues and adjacent tissues of 20 prostate cancer patients, which is collected from Second People’s Hospital of Wuxi Affiliated to Nanjing Medical University in the last four months. We found that it is a clear correlation between the miR-221-5p and prostate cancer (Fig1A and 3A). This clinical data also provide a more solid data base for our research.

Comment 2. This reviewer found typo errors in multiple places in the text.

Answer: Thank you for your reminding. I have already changed it.

Replies to Reviewer 2

Comment 1: This is a fairly good study of miR-221-5p in prostate cancer, with both in vitro cell line experiments and an in vivo experiment.

I see that Fig. 5 says how many mice per group, but the Methods section must state how many total mice and how many mice per group, and what was done to each group. The details on this are lacking.

Answer: Thank you for your reminding. I have already changed it in my manuscript.

Comment 2: There are still numerous problems in grammar, spelling, random punctuation, incorrect word spacing, and English usage which make the paper hard to read. As an example, under "methods" in the Abstract, "We established PC3 stably cell lines that are overspression or silenced of..." should be "We established PC3 cell lines with stable overexpression or silencing of...." "stably cells" is incorrect. The last heading of the Results section in the main manuscript is "miR-221-5p promotes the xenograft of the prostate cancer in vivo." This should read, miR-221-5p promotes prostate cancer xenograft growth in vivo.

Please don't think that these are the only examples, as there are many more. Therefore, revision by a native English speaker or a Chinese person skilled in correct English usage is needed before publication can be considered.

Answer: Thank you very much for your questions and reminding. I've modified the grammatical problems in my manuscript.
Comment 3: The reference list needs to be updated. How do the authors reconcile their findings with:

Comprehensive proteomic profiling identifies the androgen receptor axis and other signaling pathways as targets of microRNAs suppressed in metastatic prostate cancer.


... in which miR-221-5p is found to be suppressed in metastatic prostate cancer? Coarfa et al. found that miR-221-5p is epigenetically silenced in prostate cancer cells. They found that the decrease of this miR is associated with significantly worse clinical outcome, and that miR--221-5p could suppress TMPRSS2 (which is a good thing). The current paper's authors found that overexpression of miR-221-5p promotes cell proliferation, migration, colony formation, and growth of xenografts. Please reconcile your findings with Coarfa et al. They seem to be totally opposite.

Answer: Thank you very much for your question, which is of great guiding significance to our work, and let us note that miR-221-5p may have a completely different way of acting in prostate cancer.

In clinical samples, We also found that in some tumor samples, the expression of miR-221-5p in the adjacent tissues was elevated and decreased in the cancer tissue, which indicated that the patient had obvious heterogeneity, but in the whole clinical data, mir-221-5p was related to the development of prostate cancer(Fig 1A,3A). miR-221-5p may have different effects at different stages of prostate cancer, but the number of prostate cancer samples currently collected is only 20, which is not enough to illustrate the problem. We will also collect more patient samples in subsequent trials to analyze the relationship between mir-221-5p and prostate cancer during different stages of development.

In the previous manuscript we had only experimented with PC3 cells, and in the submission process, we constructed the DU145 stable cells of miR-221-5p overexpression or silenced to further verify whether the mir-221-5p also regulates cell proliferation and migration in other prostate cancer cells. The cell proliferation assays(Fig 1D,1E,1F) and cell migration assay (Fig.2B) were carried out to further explain the effect of mir-221-5p on the proliferation and migration of prostate cancer cells.