Author’s response to reviews

Title: MiR-182-5p and its target HOXA9 in non-small cell lung cancer: a clinical and in-silico exploration with the combination of RT-qPCR, miRNA-seq and miRNA-chip

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Author’s response to reviews:

Response letter
Dec 7th, 2019

To: Editor-in-Chief
BMC Medical Genomics

Dear Editors and Reviewers:
On behalf of my co-authors, we thank you very much for giving us an opportunity to revise our manuscript; we appreciate the editors and reviewers very much for your comments on our paper submitted to BMC Medical Genomics (ID: MGNM-D-19-00182 R1). We have revised the manuscript according to your kind advices and here are our replies to the remarks.
A clean revised manuscript is going to be resubmitted simultaneously with the current response letter. The followings are responses to each point brought up:
Assistant Editor Comments:
1. Conclusion

We note that your manuscript does not include a ‘Conclusions’ section.
In order to be in line with journal requirements, please ensure that you include the following sections within your manuscript: Background, Methods, Results, Discussion, Conclusions.
This section should state clearly the main conclusions of the research article and provide an explanation of the importance and relevance of the study reported.
Reply: Thank you very much for your precious advice.
We have included the section of “Conclusions” in the manuscript:

Conclusions
In conclusion, the oncogenic role of miR-182-5p in NSCLC was confirmed by comprehensively analyzing data obtained from RT-qPCR assays, miRNA-seq and miRNA-chip database. Multiple target genes, including HOXA9, may play a role in the molecular mechanism of HOXA9 in NSCLC.

2. Declarations heading

Please ensure that you include a ‘Declarations’ heading and that it is placed after the Abbreviations in your manuscript.
The Declarations section encompasses the sub-sections: Ethics approval and consent to participate, Consent for publication, Availability of data and material, Competing interests, Funding, Authors’ contributions, Acknowledgements.
Reply: Thank you very much for your precious advice.
We have included a “Declarations” heading as you suggested:

Declarations
Ethics approval and consent to participate
The study was approved by the Ethics Committee of the First Affiliated Hospital of Guangxi Medical University. Written informed consent was obtained from all of the patients.

Consent for publication
Not applicable.

Availability of data and materials
The datasets generated and/or analysed during the current study are available in the TCGA (https://portal.gdc.cancer.gov/), GEO (https://www.ncbi.nlm.nih.gov/gds/), miRWalk (http://zmf.umm.uni-heidelberg.de/apps/zmf/mirwalk2/) and TargetScanHuman (http://www.targetscan.org/vert_72/) databases.

Competing interests
The authors declare that they have no competing interests.

Funding
The study was supported by funds from National Natural Science Foundation of China (NSFC81560469, NSFC81360327), Natural Science Foundation of Guangxi, China (2015GXNSFCA139009, 2017GXNSFAA198016), Guangxi Medical University Training Program for Distinguished Young Scholars (2017) and Innovation Project of Guangxi Graduate Education (201710598080), Guangxi Degree and Postgraduate Education Reform and Development Research Projects, China (JGY2019050), Medical Excellence Award Funded by the Creative Research Development Grant from the First Affiliated Hospital of Guangxi Medical University, Science and
Technology Innovation Training Program for College Students in the First Clinical Medical College of Guangxi Medical University in 2018. The funding bodies played no role in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

Author’s contributions
All authors have contributed to this study for submission. The contributions are as following:
LG analyzed all experiment results, prepared for tables and figures, and revised the manuscript.
SBY contributed to data analysis and paper writing.
JY contributed to the conception, modification of the study and instruction of experiment and revision work.
JLK contributed to the conception, modification of the study and instruction of experiment and revision work.
KS contributed to the conception and modification of the study, and writing of the paper draft.
FCM contributed to the conception and modification of the study, and writing of the paper draft.
LZH helped to perform the RT-qPCR and analyze the RT-qPCR data.
JL contributed to analyze the target genes by GO, KEGG pathway and PPI network and corrected the paper.
SYY analyzed the data from RT-qPCR, GEO and TCGA database and wrote the results.
RQH performed RT-qPCR, collected and analyzed the data from TCGA and GEO database and corrected the part of the results.
XHH contributed to the design of the study, guided the study method, and corrected the paper.
GC contributed to the design of the study, supervised all experiments and corrected the paper.
All authors read and approved the final manuscript.

Acknowledgements
We expressed sincere thanks to the patients included in this study, the target gene prediction tools (miRWalk, Micr54, miRanda, mirbridge, miRDB, miRMap, miRNAMap, Pictar2, PITA, RNA22, RNAhybrid, Tarbase and mirTarbase), and the TCGA, GEO and STRING databases.

3. Consent to participate
Please include the following statement in the Ethics approval and consent to participate section of your manuscript: “Written informed consent was obtained from all of the patients”.
Reply: Thank you very much for your precious advice.
We have added the statement in the manuscript as you suggested:
Ethics approval and consent to participate
The study was approved by the Ethics Committee of the First Affiliated Hospital of Guangxi Medical University. Written informed consent was obtained from all of the patients.

4. Role of funding bodies
Please provide more details regarding the specific role of each of the funding bodies in your study. If the funding bodies only provided the financial means to allow the authors to carry out the study, please state “The funding bodies played no role in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript” and include this statement in the Funding section of your manuscript.
However, if each of the funding bodies took part in the design of the study and collection, analysis, and interpretation of data, and the writing of the manuscript, this must be stated in the Competing Interests section of your manuscript.  

Reply: Thank you very much for your precious advice.  

We have included the statement in the manuscript as you suggested:  

Funding  
The study was supported by funds from National Natural Science Foundation of China (NSFC81560469, NSFC81360327), Natural Science Foundation of Guangxi, China (2015GXNSFCA139009, 2017GXNSFAA198016), Guangxi Medical University Training Program for Distinguished Young Scholars (2017) and Innovation Project of Guangxi Graduate Education (201710598080), Guangxi Degree and Postgraduate Education Reform and Development Research Projects, China (JGY2019050), Medical Excellence Award Funded by the Creative Research Development Grant from the First Affiliated Hospital of Guangxi Medical University, Science and Technology Innovation Training Program for College Students in the First Clinical Medical College of Guangxi Medical University in 2018. The funding bodies played no role in the design of the study and collection, analysis, and interpretation of data and in writing the manuscript.

5. Availability of data and materials

a) Please note that BMC mandates data deposition for the following:

• Protein sequences
• DNA and RNA sequences
• DNA and RNA sequencing data
• Genetic polymorphisms
• Linked genotype and phenotype data
• Macromolecular structure
• Microarray data (must be MIAME compliant)
• Crystallographic data for small molecules

As such, we ask that you please provide the relevant accession numbers if your data has been deposited into a data bank or the appropriate web links if the data has been uploaded into a repository. If the data has not yet been deposited, please do so and provide the relevant information needed to access it in the ‘Availability of data and materials’ section in your manuscript. Please ensure all data is already released and that any accession numbers/web links are in the ‘Availability of Data and Materials’ in their final form, and that all links and accessions allow access to public data.

Your data availability statement can take the following form: “The datasets generated and/or analysed during the current study are available in the [NAME] repository, [PERSISTENT WEB LINK OR ACCESSION NUMBER TO DATASETS]”.
b) Please remove the statement “And all patients signed informed consent” from the Availability of data and materials section of your manuscript.
Reply: Thank you very much for your precious advice.
We have revised the section of “Availability of data and materials” as you suggested:

Availability of data and materials
The datasets generated and/or analysed during the current study are available in the TCGA (https://portal.gdc.cancer.gov/), GEO (https://www.ncbi.nlm.nih.gov/gds/), miRWalk (http://zmf.umm.uni-heidelberg.de/apps/zmf/mirwalk2/) and TargetScanHuman (http://www.targetscan.org/vert_72/) databases.

6. Authors’ contributions
Please clarify whether all of the authors of this manuscript have read and approved the final manuscript in the Authors’ contributions section of your manuscript.
If so, please include the statement “All authors read and approved the final manuscript.” in the Authors’ contributions section of your manuscript.
Reply: Thank you very much for your precious advice.
We have included the statement in the manuscript as you suggested:

Author’s contributions
All authors have contributed to this study for submission. The contributions are as following:
LG analyzed all experiment results, prepared for tables and figures, and revised the manuscript.
SBY contributed to data analysis and paper writing.
JY contributed to the conception, modification of the study and instruction of experiment and revision work.
JLK contributed to the conception, modification of the study and instruction of experiment and revision work.
KS contributed to the conception and modification of the study, and writing of the paper draft.
FCM contributed to the conception and modification of the study, and writing of the paper draft.
LZH helped to perform the RT-qPCR and analyze the RT-qPCR data.
JL contributed to analyze the target genes by GO, KEGG pathway and PPI network and corrected the paper.
SYY analyzed the data from RT-qPCR, GEO and TCGA database and wrote the results.
RQH performed RT-qPCR, collected and analyzed the data from TCGA and GEO database and corrected the part of the results.
XHH contributed to the design of the study, guided the study method, and corrected the paper.
GC contributed to the design of the study, supervised all experiments and corrected the paper.
All authors read and approved the final manuscript.

7. Remove attachments
Please remove the additional file entitled ‘Response letter.docx’ from your manuscript and from the file inventory as it is no longer needed at this stage.
Reply: Thank you very much for your precious advice.
We have removed the file as you suggested.

8. 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. Should you wish to respond to these revision requests, please put your responses to the reviewers’/editors’ comments in the Response to Reviewers box in Editorial Manager. Please do not upload a separate letter.

Reply: Thank you very much for your precious advice.

We have uploaded our manuscript as a single, final, clean version that did not contain any tracked changes, comments, highlights, strikethroughs or text in different colours. All relevant tables/figures/additional files were clean versions.

We hope that the revision is acceptable and look forward to hearing from you soon.

Yours Sincerely,

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