Author's response to reviews

Title: Characterization of human gastric carcinoma-related methylation of 9 miR CpG islands and repression of their expressions in vitro and in vivo

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Author's response to reviews:

We received the review of above manuscript on March 26. We appreciate that these reviewers find that the study to be interesting and important in its field.

According to the Editorial requests, we have defined the name of the ethics committee at our hospital that gave the ethics approval (#2011041207) for the present study in the Methods section. A method section was added in the revised abstract.

A native English speaker has edited the revised manuscript. A marked-up copy of the changes made from the previous article file by MS Word has been uploaded.

All the comments and suggestions made by the reviewers were constructive and useful. We have now addressed all these comments in the revised version of the paper.

Yours sincerely,
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Reviewer #1. We appreciate the constructive comments made by this reviewer. In addressing them, we have made the manuscript more clear.
I “no standard deviation among the histograms in the figures....” We added the standard deviation data into the Figure 3, Table 1, Table 2 (footnote), and
Supplementary Table 4.

I “no strong evidence to show that the 9 microRNAs used for analyzing the methylation status were representative” It is a huge work to demonstrate the miR methylation-transcription association in the genome wide scale. Compared to the hundred miR CpG islands in the human genome, we agree that 9 miR CpG islands is a small number. We modified the Abstract of the manuscript to reflect this. To best of my knowledge, this is a first effort to explore the methylation-transcription association of group of miR CpG islands in vitro and in vivo. This kind of association has not been reported for miR-9-3, miR-200b, and miR-210 yet.

I “English…” A native English speaker has edited the revised version of the manuscript.

Reviewer #2. We appreciate that this reviewer for the very constructive comments.
1. “Conclusions in the Abstract…” We modified the conclusion in the revised version.
2. “Conclusions in the Discussion…” We modified them and described them consistently.
3. “description on target mRNAs of miR…” We described the target mRNAs and biological function of these tested miRNAs in the revised manuscript and added more references.
4. “AZA treatment…” As we summarized on the Supplementary Table 2, other scientists have studied the reactivation of miR-9-1, miR-193b, and miR-203 in different cell line by AZA. According to the work published by Professor Weiguo Zhu and his colleagues (Ref.35), AZA interferes mainly DNA methylation through DNA damage-repair pathways. There are also a number of reports to show that instead of inhibiting DNMT1, AZA can indirectly change the expression status of many genes, whether they host a CpG island or not. Thus, we do not carry out AZA experiments to support the conclusion of this study.

Reviewer #3. We appreciate that this reviewer for the careful proofreading and useful suggestions.
1. “the particular regions chosen for methylation analysis…” We tried to analyze the methylation status of CpG island regions embedded or flanked the corresponding miR gene. The exact location of amplicons is dependent on the available CpG-free primer set used in the present study. We mentioned this in the revised paper.
2. “numerical scale…” We added a numerical scale on the new Supplementary Figure 1.
3. “Numerical inconsistencies or errors…” The error in the Abstract has been corrected. The “Figure 2A-G” was a mistyping. It is replaced with “Figure 3A-G”.

Reviewer #4. We appreciate that this reviewer for the helpful suggestions. We have now addressed all statistical comments in the revised version.