Author's response to reviews

Title: Altered expression of microRNAs in the myocardium of rats with acute myocardial infarction

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Author's response to reviews: see over
Dear Editor

Re: 1269673356319990

Thank you for giving us the chance to revise our manuscript. We made modifications according to your advice and reviewer’s comments.

Our responses to reviewer’s comments are attached to this message.

We hope our revisions can meet the requirements.

Best Regards,

Wei Gao

Editor requests

Comment
Microarray data, Please provide the relevant accession numbers for your microarray data under the Methods section of the revised manuscript.

Response
The entire datasets (for miRNA) described here are available from the Gene Expression Omnibus (GEO, http://www.ncbi.nlm.nih.gov/geo/) through series accession number GSE19695.

Comment
Financial competing interests? In the past five years have you received reimbursements, fees, funding, or salary from an organization that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

Response
In the past five years we have not received reimbursement, fees, funding, or salary from an organization that may in any way gain or lose financially from the publication of this manuscript, either now or in the future.

Comment
Is such an organization financing this manuscript (including the article-processing charge)

Response
There is not such an organization financing this manuscript.
Do you hold any stocks or shares in an organization that may in any way gain or lose financially from the publication of this manuscript, either now or in the future?

**Response**

We don’t hold any stocks or shares in an organization that may in any way gain or lose financially from the publication of this manuscript, either now or in the future.

**Comment**

Do you hold or are you currently applying for any patents relating to the content of the manuscript?

**Response**

We do not hold and haven’t applied for any patents relating to the content of the manuscript.

**Comment**

Have you received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript?

**Response**

We have not received reimbursements, fees, funding, or salary from an organization that holds or has applied for patents relating to the content of the manuscript.

**Comment**

Do you have any other financial competing interests?

**Response**

We don’t have other financial competing interests.

**Comment**

Are there any non-financial competing interests (political, personal, religious, academic, ideological, intellectual, commercial or any other) to declare in relation to this manuscript?

**Response**

There are no non-financial competing interests (political, personal, religious, academic, ideological, intellectual, commercial or any other) to declare in relation to this manuscript.

**Comment**

Please indicate how the language corrections have been attended to in the cover letter that will accompany your resubmission.

**Response**
We asked a native English speaker to edit our manuscript.

**Comment**
Please also ensure that your revised manuscript conforms to the journal style (http://www.biomedcentral.com/info/ifora/medicine_journals).

**Response**
We revised our manuscript to conform to the journal style.

**REFEREE 1**
No Comment.

**REFEREE 2**

**Comment**
There are some minor points of criticism, including the used biochip. This chip contains 924 miRNAs mixed up from three organisms, human, rat and mouse. However, currently, many more miRNAs in these three organisms are known. The authors should comment why they do not use a biochip just for the investigated species containing all miRNAs but a mix of species while losing some potentially important ones.

**Response**
In August 2008, when we used the chip from Capitalbio corporation to do the experiments of miRNA microarray, the chip (microarray mammalian V3.0) contain 924 miRNAs mixed from three organisms: human, rat and mouse. We asked scientists from Capitalbio to explain why three organisms were put together. Their answer is that the three organisms are mostly frequently investigated in miRNA microarray, and the chip containing 924 miRNAs taken from the three organisms can satisfy the requirements of microarray detection.

**Comment**
In addition, the authors should comment whether they find miRNAs that are deregulated only in the target species or whether they detect also de-regulated human miRNAs.

**Response**
We detected has-miR-214 in circulation in patients who suffer from AMI. The level of expression of miR-214 on day2 and day7 after AMI are up-regulated.

**REFEREE 3**

**Comment**
The author’s should include error bars in their real-time PCR measurements to show how consistent the changes in microRNA expression were between animals in each treatment group.
Response
We re-did the qRT-PCR analysis and generated the error bars in the new Figure 3.

Comment
The Tarbase database is quite limited since many experimentally validated microRNA targets are not included. For example, many targets for miR-1 and miR-126 have been experimentally validated, but are not included in this database. Because the number of differentially expressed microRNAs identified in this study is relatively small, the author should combine their Tarbase analysis with an extensive literature search to identify all of the known targets of these microRNAs.

Response
We manually literature-curated through PubMed and collected all experimentally supported targets for deregulated miRNAs reported in the literature (see sheet “miR-target from literature” in Additional File 1). The reported functions of miRNA-target interactions in corresponding literature was also curated.

Comment
It was not clear in the methods what the control population was. Were sham-operated animals used as controls for each of time-points, or were untreated controls used?

Response
In this study, sham-operated animals were used as controls for each of the time-points. In the modified manuscript, we’ve already edited the sentence, “In the sham-control group, rats were exposed to all surgical procedures except the ligation of the anterior descending coronary artery” (line 6-7 of page 4) so that the control population is more clearly identified.

Comment
In the myocardial infarction methods it should be “border-zone” rather than “bordline”

Response
In the modified manuscript, we have corrected the error in spelling. The modified sentence follows; “We utilized an in vivo rat model to study the altered expression of miRNA in the border zone myocardium of rats with AMI” (line 1-2 of page 4)

Comment
In table 2 the authors indicate that miR-1 is located in an intron of MIB-1. This is incorrect since miR-1 is actually transcribed in the opposite direction of MIB-1

Response
We removed miR-1 and MIB-1 issue from Table 2.
Comment
The following sentence near the beginning of the discussion needs to be edited for grammar, “the expression levels of miRNAs have dynamic changes change with the time when the AMI occurs in rats”

Response
In the modified manuscript, the sentence has been edited from “the expression levels of miRNAs have dynamic changes change with the time when the AMI occurs in rats” to “Our data shows that the change of expression levels of miRNAs is in accordance with the progression of AMI” (line 1-3 of page 10)

Comment
Typo in the following sentence at the end of the discussion, “in conclusion, we identified some miRNAs that showed altered expression during AMI”

Response
In the modified manuscript, the sentence “in conclusion, we identified some miRNAs that showed altered expression during AMI” has been edited to “In conclusion, we identified some miRNAs that showed altered expressions in rat myocardium with acute myocardial infarction”. (line 20-21 of page 10)

REFEREE 4
No Comment.