Author's response to reviews

Title: Plasma Metabolomics Study on Chinese Medicine Syndrome Evolution of Heart Failure Rats caused by LAD Ligation

Authors:

qi qiu Dr. (qiugi@anzhengcp.com)
chun li Dr. (huaixiaokui@yahoo.com.cn)
yong wang Dr. (doctor_wangyong@sina.com)
cheng xiao Dr. (xc2002812@126.com)
Yu Li Dr. (liyubeijing1973@163.com)
Yongxiang Wei Dr. (yongxiang_wei@163.com)
Yang Lin Dr. (linyang@anzhengcp.com)
Wei Wang Dr. (wangwei26960@126.com)

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Author's response to reviews: see over
Dear Editors and Reviewers:
Thank you for your letter and for the reviewers’ comments concerning our manuscript entitled “Plasma Metabonomics Study on Chinese Medicine Syndrome Evolution of Heart Failure Rats Caused by LAD Ligation” (MS: 1675597752106092). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. All changes to the text were marked in red, using the "Track Changes" function in Microsoft Word. The format of the revised vision was adjusted to conform to the journal style (http://www.biomedcentral.com/info/ifora/medicine_journals). The main corrections in the paper and the responds to the reviewer’s comments are as flowing:

Reviewer: Zhigang Lu
Reviewer's report:
The manuscript described the research about Plasma Metabonomics Study on Chinese Medicine Syndrome Evolution of Heart Failure Rats Caused by LAD Ligation. But some minor revisions are needed:

1. Page 4th, “The line 5 from the bottom, symbol “°C” should be corrected. Same problem is page 7th, 8th.
Answer: We’re sorry for the incorrect expression, and have corrected in the manuscript.

2. In the methods part, Evaluation of Rat Model with MI, Qi Deficiency and Blood Stasis Syndrome was done following the basic phenotypic changes, ECG, echocardiography, colorimetric analysis of images of the auricle, plantar and tongue, and blood studies. Can the author offer the reference standard recognized by academic field? Here the author needs to add some references.
Answer: The discussion part was rewritten, and some references were added, we hope it meet with approval.

3. In the GC/TOF-MS analysis, amino acid metabolites and the glucose metabolites staff were observed, and performed Correlation Analysis with animal models. In Fig 4, 5 and 6, they show there is significant correlation between the observed amino acid metabolites and the glucose metabolites and different time animal models but, in Fig7 there is no common region of the 4d, 21d, 45 day. The author should give more explain in the discussion part.
Answer: The instruction was added in the result and discussion part.
Reviewer: Sherry Sachdeva

Reviewer's report:

Comments:

Major Compulsory Revisions

i. Authors mentioned the mice in Echocardiography “The mice were anesthetized with a pentobarbital sodium (1%, 20 mg kg⁻¹ IP) at 4, 7, 14, 21, 28, 45 and 60 days after surgery”. Whether the author used ‘rat or mice model’ for this study. Clear this confusion.

Answer: We’re sorry for the negligence, and have corrected in the manuscript.

ii. Samples analysed for plasma metabolomics “Methyl cyanide (250 µL) was mixed into 100-µL aliquots of the plasma samples……… in split mode (25:1, v/v)”. Is this a standard method then provide the reference of this methodology.

Answer: Reference was added in the manuscript.

iii. Why the 4, 21 and 45 days are chosen for the analysis of the samples? What is their significance?

Answer: The period from 7 to 28 days is the stable ischemic heart failure qi deficiency and blood stasis (QDBS) time window, and the two periods, 1-4 days and 45-60 days after the operation were diagnosed as the qi deficiency. So each time point in the three periods 4, 21, and 45 day after operation was selected to do the GC-MS analysis. This explanation was added in the result of the manuscript.

iv. Experimental design is unclear and requires better presentation.

Answer: The part of experimental designs was modified in the manuscript.

v. Literature survey is poor and many important and recent references are missing, such as, Li et al., 2010. Zhongguo Zhong Xi Yi Jie He Za Zhi.30 (9): 919-21, Ren et al., 2010 .Zhongguo Zhong Xi Yi Jie He Za Zhi. 30(4): 352-6.

Answer: The discussion part was rewritten, and some references including those two literatures were added.

vi. Results for body weight should also included, what changes in body weight takes place at different time periods? No tables or figures have been included in the manuscript providing information regarding this.

Answer: Results for body weight were added in to the supplemental table 1.

vii. Table 1, 2 and 3 symbols of statistics are missing. What this # arrows signify. Is these arrows for increase and decrease, then how many fold or percentage change noted must be denoted by double arrows or some other symbols.

Answer: The arrows were denoted in the tables and the notes were also added.

viii. In Fig-7, author mentioned the Venn diagrammatic representation of plasma metabolite changes at the time of operation. It should be discussed in results and what conclusion drawn from this figure.
Answer: The conclusion was added in the result and discussion part.

Minor Essential Revisions
i. Conclusion: Seems to be too vague and lengthy. Should be more crisp and concise.
   Answer: Conclusion part was rewritten in the revision. We hope it meet with approval.

ii. Discussion requires improvement. Also it should be shortened as it is unnecessary lengthy and redundant.
   Answer: Discussion was modified in the revision. We hope it meet with approval.

iii. Heating rate (/ min), temperature ( ) etc. mentioned at many places in the manuscript. Check it properly.
   Answer: We’re sorry for the incorrect expression, and have corrected in the manuscript.

Discretionary Revisions
i. Authors should also focussed on Ultrasonic cardiographic (USCG) parameters, including left ventricular end-systolic diameter (LVEDs), left ventricular end-diastolic diameter (LVEDd) etc were measured for supporting their results of Heart failure.
   Answer: We’re really appreciated to the suggestion, in this manuscript 2-dimensionally guided M-mode was used, but the three-dimensional biplane Simpson’s method was needed to evaluate the LVEDs and LVEDd.

Moreover, we found some mistakes in Figure7 and corrected them in the revision.

We tried our best to improve the manuscript and made some changes in the manuscript. These changes will not influence the content and framework of the paper. We appreciate for Editors/Reviewers’ warm work earnestly, and hope that the correction will meet with approval.

Once again, thank you very much for your comments and suggestions.

Thank you and best regards.

Yours sincerely,
Qi Qiu
E-mail: qiuqi@anzhengcp.com

Corresponding author:
Name: Wei Wang

E-mail: wangwei26960@126.com