Author's response to reviews

Title: Proprotein convertase subtilisin/kexin type 9 expression is transiently up-regulated in the acute period of myocardial infarction in rat

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Author's response to reviews: see over
Dear editor,

We would like to re-submit the enclosed manuscript entitled "Proprotein convertase subtilisin/kexin type 9 expression is transiently up-regulated in the acute period of myocardial infarction in rat (7203209451394225)", which we wish to be considered for publication in BMC Cardiovascular Disorders.

I formally state that all the co-authors have read and approved the final manuscript for publication and the manuscript is submitted solely to BMC Cardiovascular Disorders. No conflict of interest exists in this manuscript. None of the paper’s contents, in whole or in part, have been previously published elsewhere. If at any time you have any questions concerning the manuscript, please kindly feel free to contact with me.

Would you please kindly find our response point-by-point for reviewers followed by the cover letter.

Thank you and best regards,

Yours sincerely,

Jian-Jun Li, MD, PhD, Corresponding Author.

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Response to editor and reviewers:

Thank you very much for editor and reviewers’ positive comments on our manuscript. We have made the appropriate changes in revised manuscript according to your kind suggestions.

Reviewer 1
Questions 1 (major comments)
Answers: Thanks for the reviewer’s scientific comments on this section. Indeed, the diet may influence the expression of lipid parameters after acute myocardial infarction, and we also took this issue into consideration before our experiment. In the current study, all the blood and tissue samples were obtained after the 8-12 hour fast before the sacrifice. Animals with longer period of occlusion (24h, 48h, and 96h as the reviewer kindly mentioned) were free access to food and water immediately after recovery but still need to be fast 8-12h before the sacrifice. Therefore, we think the influence of diet on the lipid parameters was balanced among groups.

Questions 2 (major comments)
Answers: Thanks for reviewer’s careful comments on our manuscript. In the present study, the sacrifice was performed at the same time of the day (around 8:00 am) for animals with 24, 48 or 96 h of occlusion.

Questions 3 (major comments)
Answers: Thanks for reviewer’s kind suggestion. The rats were given normal diet with 4.62% fat content. We have added this information into our revised manuscript.

Questions 4 (major comments)
Answers: According to the reviewer’s scientific suggestion, we performed the one-way analysis of variance (ANOVA) to test the
difference among control and different acute myocardial infarction groups. Furthermore, the comparison between two groups were used the Dunnett’s T3 test (unequal variances) or Bonferroni test (equal variances) in our revised manuscript.

Questions 5 (minor comments)
Answers: Thanks for the reviewer’s scientific comments on this issue. In a model of myocardial infarction involving ligation of the proximal left anterior descending branch of the coronary artery in rats, the major factors related to the infarct size are not the surgery but animal individual differences per se. Recently, PCSK9, a secreted protease synthesized mainly in the liver, has been established as a potential risk factor for coronary artery disease. However, no current data revealed the relationship between infarction size and PCSK9 level during the acute period of myocardial infarction. In the present study, we observed that the PCSK9 level was transiently up-regulated but we did not explore the exact mechanisms. Whether there existed any relationship with the infarct size was just a tentative speculation. Nonetheless, the explanation of such speculation should be very careful due to the lack of related study. Therefore, more detailed experiments are warranted to test this speculation in the future. We believe that such study will be very interesting and useful in this field.

Reviewer 2
Questions 1 (minor comments)
Answers: Based on the reviewer’s scientific suggestion, we added the data of the plasma inflammatory marker, white blood cell counts, into our revised manuscript. It has been well established that multiple inflammatory markers are involved in the pathogenesis of acute myocardial infarction such as white blood cell counts and C-reactive protein (kindly see reference 26). However, in the preliminary stage of our study, we only measured white blood cell counts at 3h, 6h, and
12h post the infarction for the limitation of blood sample. We think this marker may partly reflect the inflammatory status at the acute period of myocardial infarction. Nonetheless, thanks very much for the reviewer’s scientific suggestion due to the guiding significance for our future experiments.