Reviewer's report

Title: Molecular mechanisms of hydrogen sulfide against uremic accelerated atherosclerosis through cPKCβII/Akt signal pathway

Version: 0 Date: 24 Jun 2019

Reviewer: Marco Colucci

Reviewer's report:

In this study, Xiong and Colleagues aimed to elucidate the possibly protective role of hydrogen sulphide containing compounds against the uremia accelerated atherosclerosis in ApoE -/- mouse model. The Authors showed more cPKCβII membrane translocation in UAAS mice; they also pointed out a protective effect of L-cys and NaHS administration, while PPG injection seemed to worsen the condition.

MAJOR COMMENTS

- The reviewer strongly advises deep review of the whole Materials and Methods section: the study design is not described; no reason is given for the various groups, and moreover treatment with various substances is not explained (NaHS? PPG?), nor these substances are mentioned in the introduction. It is stated that these substances were injected intraperitoneally after surgery; how long after surgery? Did they receive single or multiple injection? What dosage of the various substances was administered? The administration of these substances did happen before or after the 6 weeks of high fat diet? Moreover, it is stated that "When the modeling was completed, mice were sacrificed": when the modelling was considered complete? Please review.

- The review recommends general revision of written English for the whole paper. Some suggestions are made as minor comments; however the whole text would benefit a revision, in order to enhance its accessibility and enabling the reader to focus on the good job done.

- The study performed seems very interesting, with noteworthy results; however, extensive revisions are recommended before the manuscript could be considered for publishing.

MINOR COMMENTS

- Page 3, line 25-26: "The damage of arterial endothelium is recognized as initial factor for cardiovascular, and vascular endothelial damage plays an important role in the occurrence and development of cardiovascular diseases". Please review and reformulate the sentence.
- Page 3, line 30: As CSE/H2S system seems to be protective against UAAS, the reviewer suggests to modify the sentence as follows: "Our group found that there was a relationship between endogenous cystathionine-γ-lyase/hydrogen sulfide (CSE/H2S) system and the risk of cardiovascular disease in maintenance hemodialysis patients".

- Please provide more information about the role of Akt phosphorylation in the Introduction.

- In the Introduction, the Authors stress the role of PKC activation in favouring UAAS; however, it is also stated that "PKC inhibitors reduce the expression of endothelial nitric oxide synthase (eNOS)", which seems to be pretty in contrast to what has been previously explained. Please provide further explanations or address this topic in the Discussion section.

- Please state the aim of the study at the end of Introduction paragraph, before starting describing methods.

- Please review and reformulate the description of animal surgery, as by now it seems more an operative instruction than a method description.

- Page 5, line 27: correct with "stored".

- Page 5, line 31: what kind of tissue debris?

- Methods, Western blot: please review and reformulate, as it seems more an operative instruction than a method description.

- Please correct the 3.1, 3.2, 3.3 and 3.4 paragraph titles with "aorta" or "aortic tissue".

- Page 7, line 7: please correct with "statistical significance".

- Please review the whole 3.3 paragraph, which is currently quite difficult to understand (also because of the lack of Methods description, maybe).

- Page 7, line 58: "End-stage renal disease patients exist high morbidity and high mortality in cardiovascular disease". Please reformulate the sentence.

- Please provide p-values of statistically significant results.
Please confirm that you have included your review in the 'Comments to Author' box?

As a minimum standard, please include a few sentences that outline what you think are the authors' hypothesis/objectives, their main results, and the conclusions drawn. Your report should constrictively instruct authors on how they can strengthen their paper to the point where it may be acceptable for publication, or provide detailed reasons as to why the manuscript does not fulfill our criteria for consideration. Please supply appropriate evidence using examples from the manuscript to substantiate your comments. Please break your comments into two bulleted or numbered sections: major and minor comments.

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Please indicate the quality of language in the manuscript:

Not suitable for publication unless extensively edited

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