Reviewer’s report

Title: The Protective Effect of Activating Nrf2 / HO-1 Signaling Pathway on Cardiomyocyte Apoptosis after Coronary Microembolization in Rats

Version: 0 Date: 19 Jun 2017

Reviewer: Giampaolo Morciano

Reviewer’s report:

1. Please, provide references for i) HBFP staining in assessing micro-infarction method and ii) CME in vivo model establishment.

2. Overall, when describing (pages 5-6) and discussing (pages 6-7) results, please indicate the specific panel of the figure taken into account to illustrate each data, not only and generally the figure.

3. In Fig.1 please add the following information: i) scale bar for each image; ii) a proper quantification of all images analyzed (with explanation in the figure caption and in materials and methods). Why the tissue showed in panel C (and also in D) looks much more damaged than that in panel B?

4. Regarding Fig.2, the authors stated: "The HE staining showed that myocardium nucleic acid decomposition or hypochromiosis with cytochrome staining was observed around the microspheres and we also found peripheral cardiac muscle edema, peripheral inflammatory cell infiltration and erythrocyte effusion (Fig2)”. The reviewer wonders if a single image with a single arrow (Fig.2) could demonstrate all those statements. We suggest providing at least a quantification for each data and more images in support regarding the other experimental conditions.

5. In Fig.3E (the quantification, please insert the letter), the CME method was able to promote only about 12% of apoptotic cell death, is it right? Is this data in line with previous publications? (see again point 1).


7. We recommend to uniform all data presented in Fig.5. In immunoblot analysis we have Sham-AAV Nrf2-CME-CMEcontrol conditions, while in quantification panels Sham-AAV Nrf2-CME-AAVcontrol. Also insert letters to clearly represent each data showed in this figure. We suggest standardizing quantifications placing each sham group equal to 1.

8. We suggest placing Fig.6 before or merged to Fig.1.
9. Please, in the background section provide a bit more references about cardiac dysfunctions in general. For example recent reviews such as 27941300, 27174955 where there are chapters dedicated to microembolization and anything can be useful to the reader.

10. In the light of your results, you can definitively declare what type of apoptosis (intrinsic or extrinsic) is involved in Nrf2-HO1 signaling pathway in CME model? In both case (if yes or not) can you complete the discussion with these information?

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

No

Does the work include the necessary controls?
If not, please specify which controls are required in your comments to the authors.

Yes

Are the conclusions drawn adequately supported by the data shown?
If not, please explain in your comments to the authors.

No

Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

Quality of written English
Please indicate the quality of language in the manuscript:

Acceptable

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None

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