Reviewer’s report

Title: Up-regulating autophagy by targeting the mTOR-4EBP1 pathway: a possible mechanism for improving cardiac function in mice with experimental dilated cardiomyopathy

Version: 1 Date: 09 Dec 2019

Reviewer: Ilia Fishbein

Reviewer's report:

The study by Jin et al investigates the role of autophagy regulation with the inhibitors and activators of mTOR/4EBP1 pathway in the development and progress of dilated cardiomyopathy in mouse model.

Authors present interesting and potentially translatable findings that stimulation of autophagy with rapamycin has therapeutic value in a mouse model, both on the levels of attenuated morphological changes in myocardium and improved hemodynamics.

While the study itself is adequately planned and executed, and the results seem reliable, there are several shortcomings that need to be addressed.

1) It is not clear from the Discussion, whether the induction of autophagy in myocardium of mice immunized with porcine cardiac myosin is the element of DCM pathogenesis or a part of the reparative processes induced to limit DCM progression.

2) DCM in humans is a disease of multifaceted etiology. To what extent does a mouse model reflect the pathogenesis of human disease?

3) The universal nature of autophagy in clinical DCM and a positive correlation of autophagy indices with better outcomes was shown previously by Saito and coauthors (Autophagy, 2016; 12:579-587). Authors missed this crucial reference.

4) Methods section lacks critical information about the starting time and duration of 3-MA and rapamycin administration, and their timing relative to the myosin/adjuvant injections. The total dose of administered myosin for DCM induction is also missing.

5) Fig. 2 - please indicate with arrows the double membrane autophagosomes referred in the text.

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.

Yes

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:

Needs some language corrections before being published

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