

Peer Review File

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First Round of Peer Review comments

First, in the abstract, please indicate why there is a need for this review topic and its potential clinical significance. In the part of methods, please briefly describe how the literature was qualitatively summarized. The conclusion is not informative. Please have summary of the main findings from literature and detailed comments on possible clinical implications.

Reply: We gratefully appreciate for reviewer's comments and have revised the abstract in accordance with your comments. we have modified our text as advised (see Page 2, line 20-40).

Second, in the introduction part, the authors need to have a brief review on known biomarkers associated with diagnosis and treatment of myocarditis, and have comments on their limitations and the strengths of ncRNAs. Please also specify the clinical or translational needs for the current research topic.

Reply: Thank you for reviewer's rigorous consideration advice. We have revised to address the three issues about the introduction in your comments. We have modified our text as advised (see Page 3, line 44-68).

Third, in the main text of the literature view, in addition to describing the findings of identified studies, please also have comments on their methodology. Please have a separated paragraph to describe the literature search, including dates of the search and key terms used.

Reply: Thank you for pointing out this problem in manuscript. We have added comments on their methodology and a separate paragraph describing literature search. we have modified our text as advised (see Page 4, line 72-75) (see Page 12-13, line 289-298) (see Page 15, line 348-353) (see Page 16, line 373-377) (see Page 16-17, line 389-395)

Finally, in the discussion part, please have comments on problems need to be addressed, suggest future search directions, and how to translate existing findings to clinical practice. The authors may consider to use a figure to visually summarize the main findings of ncRNAs mechanisms of myocarditis.

Reply: Considering the reviewer's suggestion, we added a section of " Potential of ncRNAs in the diagnosis and treatment of myocarditis". This chapter analyzed the current problems and future search directions. In addition, we also made corresponding modifications to the discussion section, hoping to reach the level suitable for publication in your journal. we have modified our text as advised (see Page 17-20, line 396-492)(see Page 21, line 494-513). A figure

to visually summarize the main findings of ncRNAs mechanisms has been placed in an appropriate section of the manuscript.

Second Round of Peer Review comments

Reviewer A

Liu's review is topical, timely and suitable in scope for molecular analysis of non-coding RNAs research area, focusing on the role of noncoding RNAs in several types of myocarditis. Authors perform a valuable and very extensive examination about current information about the implications of ncRNAs in viral, autoimmune, Trypanosome cruzi infection-mediated and cancer related myocarditis.

In my opinion, the review is interesting and provides an updated overview and insight into the main findings of the area. However, some minor revisions are needed in order to be acceptable. The manuscript is well organized, but the style must be revised. Redaction is questionable and there are many spelling mistakes as well as too many spaces between words throughout the manuscript.

Abbreviations section is missing but in my opinion is necessary to follow the understanding of the review. In some sections of the text, authors talk about some words without tell the meaning, hindering the interpretation. For example, section 3.1.4 ICI- induced myocarditis models, what is ICI??? Authors has to revise the use of capital letters.

Line 193. Daughter viruses is not adequate, please rephrase.

Line 293 and 295. The expression "lagging behing" is duplicated.

Line 424, please specify what is EMB before using only the acronym.

Reply: We gratefully appreciate for reviewer's comments and have revised the abstract in accordance with your comments.

1. We have revised spelling mistakes and spaces in the manuscript. Please refer to the content changed by using the "Track Changes" function of Word for details.

2. The abbreviation section has been modified as required.

Changes in the text: we have modified our text as advised (see Page 2, line 38).

For other abbreviations, see revised manuscript as well.

3. We have replaced "Daughter viruses" with "Progeny viruses".

Changes in the text: we have modified our text as advised (see Page 9, line 200).

4. We replaced the second "lagging behing" with "are Still trailing Badly".

Changes in the text: we have modified our text as advised (see Page 13, line 303).

5. We've explained what is EMB.

Changes in the text: we have modified our text as advised (see Page 3, line 50).

Reviewer B

The authors provided a comprehensive review of the role of ncRNAs in myocarditis in both human and animal models. The paper is well written and will be this paper will be of interest

to the readers of the journal.

The following are some minor comments regarding this paper.

1. Activation of antigen-presenting cells by stimulation of TLRs is essential for induction of autoimmune myocarditis. Although we believe that adjuvant is always necessary for activation of TLRs in antigen-presenting cells, the author states that EAM can be induced without adjuvant. Please provide the referenced paper and describe the mechanism by which EAM can be induced without adjuvant.

2. Page 6, 3.1.4 ICI-induced myocarditis models, and Table 1. The title is ICI-induced myocarditis models, but the authors introduced spontaneous myocarditis in immune checkpoint molecule knockout mice. I think it would be better to change the title.

Reply: Thank you for reviewer's rigorous consideration advice. We have revised to address the three issues about the introduction in your comments.

1. When we checked the literature again and found the correctness of the reviewer's opinion, we revised our opinion and thanked the reviewer again for pointing out our mistake.

2. We also agree with the reviewer's opinion. We did not choose to directly modify the title, because clinical myocarditis is indeed caused by ICIs, but chose to include a content in the text explaining why we introduced spontaneous myocarditis in immune checkpoint molecule knockout mice.

Changes in the text: we have modified our text as advised (see Page 6, line 133-136).