

Peer Review File

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Review comments—Reviewer A

The paper titled “The molecular mechanism of sepsis-induced diaphragm dysfunction” is interesting. Sepsis-induced diaphragm dysfunction in mice is closely correlated with the activation of TLR signaling pathway, NF- κ B signaling pathway, and TNF signaling pathway and the inhibition of oxidative phosphorylation pathway, cardiac muscle contraction pathway, and citrate cycle pathway. However, there are several minor issues that if addressed would significantly improve the manuscript.

1) Diaphragm dysfunction could be induced by sepsis with subsequent ventilatory pump failure that is associated with local infiltration of inflammatory factors in the diaphragm. Suggest adding the discussion related to inflammation, which may be more meaningful.

Response: Thank you for your valuable comment. We have added corresponding information in the discussion.

2) Figure 1 has no scale bars. Please add relevant information.

Response: Thank you for your kind suggestion. We have added scale bar in revised figure1.

3) Some fonts need to be enlarged, as shown in Figures 2,5,7,9.

Response: Thank you for your kind suggestion. We have enlarged the fonts of the figures.

4) Septic state causes destruction of redox balance in many cell types. How to solve its unbalanced oxidation state? It is recommended to add relevant content.

Response: Thank you for your valuable comment. We have added the corresponding information in the discussion.

5) If the author increases the functional research on the main target genes, it may be more meaningful.

Response: Thank you for your valuable suggestion. We will add functional experiment to verify the finding in our future’s work.

6) The introduction part of this paper is not comprehensive enough, and the similar papers have not been cited, such as “evosimendan protects from sepsis-inducing cardiac dysfunction by suppressing inflammation, oxidative stress and regulating cardiac mitophagy via the PINK-1-Parkin pathway in mice, PMID: 35280364”. It is recommended to quote the article.

Response: Thank you for your kind suggestion. We have added the reference and corresponding information in the instruction.

7) It is suggested to increase the possible mechanism in the discussion section, so as to enrich the information of this paper.

Response: Thank you for your kind suggestion. We have added the corresponding information.

Review comments—Reviewer B

1. Figure 1

For cell map, please indicate the staining method in the figure legend.

Response: Thank you, we have revised the figure legend.

2. Figure 2

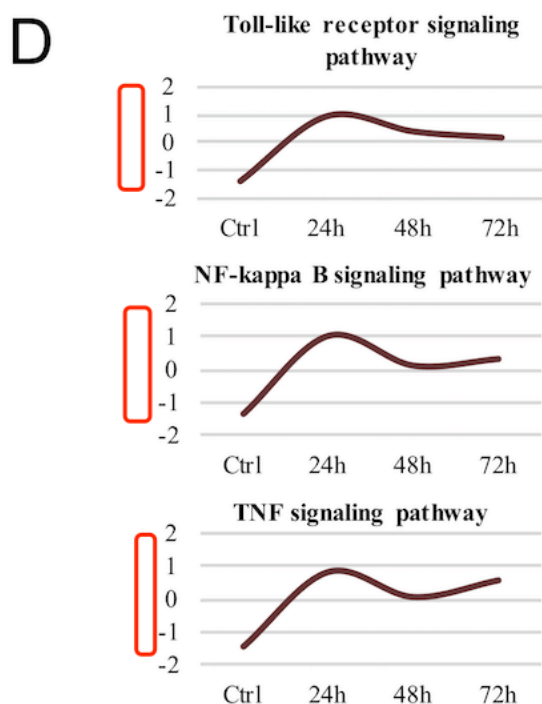
We cannot find this abbreviation in the figure or legend, but you explained it. Please check and revise.

550 diagram analysis of the number of differentially co-expressed genes at different time
531 points after LPS treatment. PC, principal component; ctrl, control; FC, fold change;
532 DEG, differentially expressed gene; LPS, lipopolysaccharide; PCA, principal

Response: Thank you, we have revised the figure legend.

3. Figure 6D and Figure 8D

Please add description for the Y-axis.



Response: Thank you, we have revised the figure.

4. When using **abbreviations** in figure or figure description, please mention the entire expression in a footnote below the corresponding figure. **Please check and revise.** Such as:

