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Fwd: ESCHF: Your manuscript entitled Multiorgan characterization of inflammasome component expression in a rat model of advanced heart failure

Zsófia Onódi <zsofia.onodi@gmail.com>

2025. február 7. 12:21

Címzett: tothartur2000@gmail.com

----- Forwarded message -----

Feladó: **Mihály Ruppert** <ruppertmis@gmail.com>

Date: 2025. febr. 4., K, 15:59

Subject: Fwd: ESCHF: Your manuscript entitled Multiorgan characterization of inflammasome component expression in a rat model of advanced heart failure

To: Dávid Nagy <nagyd1996@gmail.com>, Tamás Radovits <radovitsamas@yahoo.com>, Zoltan Varga <vrgzlt@gmail.com>, Zsófia Onódi <zsofia.onodi@gmail.com>

Dr. Ruppert Mihály, PhD

Egyetemi adjunktus

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----- Továbított levél -----

Feladó: **Zoltán Papp** <em@editorialmanager.com>

Dátum: 2025. febr. 4., K, 12:24

Tárgy: ESCHF: Your manuscript entitled Multiorgan characterization of inflammasome component expression in a rat model of advanced heart failure

Címzett: Mihály Ruppert <ruppertmis@gmail.com>

CC: bakogianniscon@gmail.com

Ref.: Ms. No. ESCHF-24-01487

Multiorgan characterization of inflammasome component expression in a rat model of advanced heart failure

ESC Heart Failure

Dear Dr. Ruppert,

Reviewers have now commented on your paper. You will see that they are advising that you revise your manuscript. We would consider it again if you could respond to the points that have been raised during the review process.

The reviewers' comments can be found at the end of this email or can be accessed by following the provided link.

This is your login information:

Your username is: MihalyRuppert

<https://www.editorialmanager.com/eschf/l.asp?i=317748&l=OMSWSFHT>

To revise your manuscript, go to <https://www.editorialmanager.com/eschf/> and log in as an Author. You will see a menu item called 'Submissions Needing Revision'. You will also find your submission record there.

When revising your work, please submit a list of changes or a rebuttal against each point which is being raised when you submit the revised manuscript. Please make all changes in red and bold font (If you utilize the Track Changes for Word please accept all changes before saving). Please note that you should ensure the revised manuscript is complete, ie. it should include THE FULL TEXT, TITLE PAGE, ABSTRACT, ALL FIGURES, ALL TABLES AND LEGENDS. As this may be the finally accepted version to be sent to the type-setters you should ensure the figures are print quality and you should proof-read and check the quality of all components of the paper after it has been up-loaded.

Your revision is due by 05 Apr 2025.

Please make sure to submit your editable source files (i. e. Word, Text).

Unless we hear from you about this paper before 05 Apr 2025, we will presume you have withdrawn the manuscript from consideration for publication in ESC Heart Failure.

Yours sincerely,

Zoltán Papp
Deputy Editor-in-Chief
ESC Heart Failure

Editorial comments:

The authors are required to pay particular attention to preparing their abstract as this is a reflection of their work and may be the only part that is read by some readers. Abstracts should be prepared in accordance with author guidelines. Authors are encouraged to check their abstract again whether the key messages are presented including important facts and figures, standard deviations and p-values supporting these messages. If in doubt, add more data rather than less. Please omit all "filling words" used for style such as "thus", "therefore", "moreover" and the like. In addition, we ask you to pay particular attention for the abstract to be straight and to the point as well as in a correct English.

Editors will check the abstract quality prior to final acceptance and may ask the authors to adjust according to the above criteria.

Reviewers' comments:

Editorial Comments:

- The abstract is a critical component of an article, often serving as the first point of contact for readers. It should be highly appealing and well-structured, encapsulating the most relevant data and findings. A compelling abstract not only provides a succinct summary of the study but also engages readers, encouraging

them to delve deeper into the full article. Thus, the authors are encouraged to provide key details regarding the methodological approach i.e. number of rats included in the analysis, the results i.e. briefly key histological findings, and the conclusion that should be aligned with one of the objective described in the introduction which is the translation relevance.

- The discussion section should be shortened, while it is suggested to comment on the relevance to human HF. How these findings align with or differ from human studies on inflammasomes in HF?

Reviewer #1: The authors present a study on inflammasome protein expression in different organs in a rat model of advanced heart failure. The topic is important and timely but there are several points to address before the manuscript is suitable for publication. Especially the lack of information on systemic and regional inflammasome activity is of concern.

Major:

- Expression of inflammasome related proteins is mainly dependent on factors like nfkappa, not dependent on typical activators of the respective inflammasome. Have you looked at typical transcription factor activity to explain different expression patterns
- Additionally, expression of inflammasome related proteins does not indicate inflammasome activity. Did you look at Interleukin release or ASC-speck formation? Inflammasome priming alone does not result in relevant inflammation and therefore conclusions have to be drawn cautiously. Additionally, how do you explain the lack of changes in Cleaved caspase expression and Cleaved IL1 β expression in TAC-HF (Fig 2C,3A)?
- How do you explain cleaved Caspases in livers of Sham but not TAC animals (Fig 4A)?
- Why did you not add quantification of cleaved proteins to your figures?
- Did you look at any other inflammatory parameters regarding bacterial translocation from the gut? Did the animals show signs of infection?

Minor:

- The discussion section seems to be very long. You should consider shortening this section of the manuscript.
- Consider using less stars and other symbols for significance in your figures, it makes them look quite messy at times.
- Did you adjust p-values for the number parameters you were looking at?

Reviewer #2: The potential role of inflammation, particularly the NLRP3 inflammasome, in the pathogenesis of HF, is now matter of several preclinical and clinical studies. The clinical trials have mainly targeted IL-1. Overall, the results in these clinical trials with patients with HF support the hypothesis that the NLRP3 inflammasome and its product IL-1 can modulate cardiac function by acting as a soluble cardiodepressant factor. The present study aims to better characterize multiorgan inflammasome components expression in an animal model of HF. The study is of interest, the methodology applied is appropriated and the results are consistent.

I have only few minor issues:

- 1) Authors should explain why they do not include IL-6 in this analysis since its role in HF has been shown (JACC Basic Transl Sci. 2021 Nov 3;7(1):84-98. doi: 10.1016/j.jacbts.2021.08.006)
- 2) I strongly suggest an additional schematic view showing the major findings according the organ in order to help the readers in understanding the differences according the district

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