

ANSWERING REVIEWERS

23,December, 2013



Please find attached our revised manuscript:

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 6898

Article title: Immune dysfunction in cirrhosis

Authors: Nora Sipeki, Peter Antal-Szalmas, Peter L. Lakatos, Maria Papp

We are grateful to the reviewers for their positive opinion, useful recommendations and for suggesting our paper for publication.

Answers to editors' comments:

1. we added running title
2. we added missing postal code
3. we added authors' contribution
4. we added detailed address
5. we revised the manuscript according to the reviewers' requests including language editing as well

Answers to reviewer comments:

Reviewed by 02540706

"Strengths: A very extensive and comprehensive review of this subject. Weaknesses: 1) As English is the language medium for this journal, I have difficulties understanding some of the statements in your manuscript. The manuscript can be improved further if the language is improved to express clearly what the authors meant. 2) In summarizing a particular section, it will be helpful if the authors can string together what the previous works meant and what is the clinical impact on patients with cirrhosis."

Thank you for your comments. 1) We made the requested linguistic edits. 2) In all case of immune system elements, we structured the regarding sections strictly in the same way. At first, we summarized acquired alterations of immune functions related to cirrhosis based on the findings of experimental and clinical studies. We tried emphasizing that depression and overstimulation exists concurrently in the system. Secondly, we demonstrated how immune dysfunction could cause enhanced development of systemic bacterial infections resulting in acute decompensation events in patients with cirrhosis. Thirdly, we demonstrated how immune dysfunction could favor shifting acute inflammation towards its persistence resulting in chronic decompensation and progression of liver fibrosis. Lastly, we showed substantial clinical impact of inherited innate immune dysfunction on acute and chronic inflammatory processes in cirrhosis due to the pre-existing acquired immune dysfunction with limited compensatory mechanisms.

Answers to reviewer comments:

Reviewed by 02540495

"The manuscript highlights in great detail the immunological abnormalities in patients with liver disease. It is a well-written article. I do have some general comments to make: 1. The manuscript requires English editing at several places. 2. In the conclusion of the manuscript, the authors discuss the assessment of immune dysfunction and its clinical implications. They suddenly propose developing a composite score and discuss the cost effectiveness and efficacy of clinical factors and lab markers for predicting the risk of

infection. This discussion may be brought out separately in a paragraph prior to conclusion."

Thank you for your comments. 1) We made linguistic edits. 2) According to the request of the reviewer we created a separate section for the proposed clinical practice of the risk assessment in cirrhosis related infections. Regarding this part of the conclusion, it was transferred into this new section entitled "Risk assessment of cirrhosis related bacterial infections in the clinical practice" (Page 25) and was re-written to some extent.

Answers to reviewer comments:

Reviewed by 02540714

"Manuscript is very well done."

Thank you for the positive opinion.

Answers to reviewer comments:

Reviewed by 00183453

"The manuscript is quite well written. It describes the innate and adaptive mechanisms occurring in cirrhosis. It represents a very comprehensive topic of the field. It would be useful for the readers to include the discussion of PMID: 15242679."

Thank you for the positive opinion. We discussed and included the suggested reference. (Page 22).

Linguistic edits and other changes in the content of the text were highlighted **in red**.

Please find attached **the "highlighted" version of the manuscript with the detailed changes that were made according to the reviewers' comments**.

We would like to thank you again for the helpful comments and for considering our paper. We do hope that the changes that have been made, have improved the quality of the manuscript also with regards to the presentation of the data.

All authors have fulfilled the criteria of authorship and seen and approved the final version of the revised manuscript and they have authorized the first author to grant on behalf of all authors to transfer exclusive copyright to *World Journal of Gastroenterology* in case of acceptance.

We do hope that the new data presented could be of interest to the readers of the *World Journal of Gastroenterology*.

Sincerely yours,
With kind regards,



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The image shows a handwritten signature in black ink. It consists of two distinct parts: a stylized, cursive 'L' on the left and a more complex, looped signature on the right.

Laszlo Peter Lakatos, MD, PhD

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