

## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Immunology*

**Manuscript NO:** 68033

**Title:** The interactions between human microbiome, liver diseases, and immunosuppression after liver transplant

**Reviewer's code:** 05533165

**Position:** Peer Reviewer

**Academic degree:** MD

**Professional title:** Doctor

**Reviewer's Country/Territory:** Canada

**Author's Country/Territory:** Bulgaria

**Manuscript submission date:** 2021-05-09

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2021-05-25 14:02

**Reviewer performed review:** 2021-05-31 20:52

**Review time:** 6 Days and 6 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input checked="" type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## **SPECIFIC COMMENTS TO AUTHORS**

Review of manuscript ID: 68033 Title: The interactions between human microbiome, liver diseases, and immunosuppression after liver transplant Summary: In this review, Peruhova M et al. look at the interaction between the immune system and the microbiome following LT. They further review the impact on microbiome on de novo malignancy Comments to the authors: 1. Focus – I think the authors should focus on the microbiome and LT. After the introduction, you can discuss “Immunosuppressive therapy and microbiota after liver transplant.” You can then discuss “Allograft rejection and microbiome.” You can then have a section on complications following transplant and include de novo/recurrent HCC and if there are enough studies you could include a section on metabolic syndrome. As you note, CVD and malignancy are the most common causes of death post LT. The small section on liver disease should be removed.

2. Introduction – move the 3 paragraph to above the 2nd. This is where you can add dysbiosis/overgrowth may lead to disease. You can also include how the microbiome differs in patients with good health and liver disease. What about microbiome post LT?

3. Human microbiome and liver disease – specify which protective bacteria are decreased (eg. Lachnospiraceae) and which pathogenic bacteria are increased. Include this information in the introduction. I do not think you need to include Sataphaty study.

4. Make a section on HCC and keep the 2nd and 3rd paragraphs of the Human microbiome and liver disease section. 5. Allograft rejection and microbiome - can you expand on how the microbiota and immune system influence each other? Eg. the microbiome helps develop the immune system by providing microbial metabolic products. The immune system affects the microbiome ... 6. Rat models (ref 14) – expand on what changes were seen. How did these changes help predict rejection? 7. Immunosuppressive therapy and microbiota after LT – first sentence; do you mean



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avoidance of rejection after LT depends primarily on IS? Some studies suggest IS may impact PSC recurrence, but there is no clear cut evidence. Similarly NASH recurrence is common, but I do not believe studies have shown impact of IS. 8. Immunosuppressive therapy and microbiota after liver transplant – I think you should remove the 2nd paragraph. It should be in the de novo malignancy/HCC section. 9.

Immunosuppressive therapy and microbiota after liver transplant – add studies on cyclosporine (Liver Transpl. 2003;9:484–488.) and sirolimus (PLoS One. 2012;7:e41584.) to complete the section. Minor comments: 1. Sentence – “In addition, toll-like receptor 4 activation in HCC lines with lipopolysaccharide causes the epithelial-mesenchymal transition.” You are missing the word cell; HCC cell lines. 2. It would be beneficial to get an individual proficient in English to edit the manuscript.

## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Immunology*

**Manuscript NO:** 68033

**Title:** The interactions between human microbiome, liver diseases, and immunosuppression after liver transplant

**Reviewer's code:** 05190007

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**Author's Country/Territory:** Bulgaria

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<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
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<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No
<b>Peer-reviewer statements</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

## **SPECIFIC COMMENTS TO AUTHORS**

Peruhova et al. spotted the interactions between human microbiome, liver diseases, and immunosuppression after liver transplants. The opinion review is well written and highlights an important issue in the field. The title reflects the main subject of the manuscript. The abstract reflects the work described in the manuscript. The keywords reflect the focus of the manuscript. The manuscript appropriately cites the latest and important references. Language is acceptable but needs some revision. Minor points: -

No explicit differentiation between the two terms, microbiome and microbiota was given. Therefore, short definitions should be given. - Some definitions should be given; e.g., dysbiosis -Some language corrections are needed: e.g. Page 5, second paragraph, last line: evaluated..... Correct to evaluate Page 6, second paragraph, last line: maintain..... Correct to maintaining - Page 4, third line: a reference should be added to the data mentioned above