



DIPARTIMENTO DI SCIENZE MEDICHE E CHIRURGICHE

April 8, 2021

Dear Editors,

Thank you very much for giving us the opportunity to resubmit a revised version of the manuscript titled "**Hepatocellular carcinoma in viral and autoimmune liver diseases: role of CD4+ CD25+ Foxp3+ regulatory T cells in the immune microenvironment**".

We thank you for your thoughtful suggestions and insights. The manuscript has benefited from these insightful suggestions. I look forward to working with you and the reviewers to move this manuscript closer to publication in *World Journal of Gastroenterology*.

The manuscript has been rechecked and the necessary changes have been made in accordance with your suggestions.

Please find below a point-to-point reply to the reviewer comments with an explanation of the changes.

We are at full disposal for any other changes that might further improve the quality of our manuscript.

Point by point reply

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: The study revealed that CD4+ CD25+ foxp3 regulatory T cells (Tregs) played a crucial role through their immune suppressive role in the development and progression of HCC. The logic and language of the article are very good.

Author response:

We sincerely thank the reviewer for this evaluation and comment on our manuscript.

We are very much honored.

Reviewer #2:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: In this study, the authors reviewed the role of cd4+cd25+foxp3+ Treg cells in hcc microenvironment rising from viral and autoimmune liver diseases. It's well written. Here is my suggestion. There are many preclinical and clinical studies of ICIs in HCC, a table including these studies especially those studies mention the role of Treg should be listed.

Author response:

We thank the reviewer for this suggestion. Unfortunately, clinical studies that include in their objectives the assessment of immune cell populations, particularly Tregs, are still too scarce. However, clinical study assessing immune cell populations, including Tregs in HCC, as study outcome, have been added in Table 2 (<https://www.clinicaltrials.gov/>).

We hope that our revised manuscript is now acceptable for publication and await your decision.

Please note that this manuscript has not been published or presented elsewhere in part or in entirety and is not under consideration by another journal.

All authors have contributed significantly to the work and have read and understood your journal's policies.

Thank you for your consideration. I look forward to hearing from you.

Sincerely,

Alessandro Granito

A handwritten signature in black ink, appearing to read 'A. Granito'.

Dr. Alessandro Granito

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