Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: Russo et al. have reviewed the immunomodulatory effect of probiotics and prebiotics in hepatocellular carcinoma. Although, there are some concerns which merit discussion in this article.

1 Recently Wan et al. have reviewed extensively the effect of probiotics in HCC (HepatoBiliary Surg Nutr 2018). Therefore, the current review has no novelty. Furthermore, the role of prebiotics in HCC is interesting though the underline mechanism is not adequate. Therefore, the author has to include a mechanistic figure describing the role of prebiotics on immunomodulation in HCC. Also, the recent review has to cite in the current review. (Golonka and Vijay-Kumar. Atypical immunometabolism and metabolic reprogramming in liver cancer: Deciphering the role of gut microbiome. Advances in Cancer Research 2021)

Thank you for the comment, we inserted a mechanistic figure (figure 4) describing the role of prebiotics on immunomodulation in HCC. We also inserted the suggested review as number 17.

2. It would be interesting if the author has included the role of probiotics/prebiotics on tight junction regulation in HCC.

We thank the reviewer for the suggestion; we inserted the role of probiotics/prebiotics on tight junction regulation in HCC

3. Some English inadequacy needs to be improved. Thank you for the suggestion, we have further revised the English (in green in the text)

4. A list of abbreviation should be included. In the abstract, PAMPs should be expanded.

We added a list of abbreviations, however it is not possible to insert in the online revision form:

ABBREVIATIONS

ALT: alanine aminotransferase

AMPK: AMP-activated protein kinase

ANGPT2: Angiopoietin-2

AST: Aspartate transaminase

FLT-1: Fms related receptor tyrosine kinase 1

FOS: Fructo-oligosaccharides

GLA: gut-liver axis

GM: gut microbiota

HCV: hepatitis C virus

HBsAg: HBV surface antigen

HBV: hepatitis B virus

HCC: hepatocellular carcinoma

HDAC: histone deacetylase

IEC: intestinal epithelial cells

KDR: kinase insert domain receptor

KRAS: Kristen rat sarcoma viral oncogene homolog

LPS: lipopolysaccharides

MAMPs: microbiota-associated molecular patterns

MELD: Model for End-Stage Liver

NAFLD: Non-alcoholic fatty liver disease

NASH: Non-alcoholic steatohepatitis

NFK: nuclear factor kappa

NLRs: nod-like receptors

NBNC: non-HBV non-HCV

PAMPs: Pathogen-associated molecular patterns

SCFA: Short-chain fatty acids

(TJ): tight junction

TLR: Tall-like receptor

TNF-α: Tumor Necrosis Factor α

VEGFA: Vascular Endothelial Growth Factor A

and we expanded PAMPs in the abstract

5. The page number should be included.

We inserted the page number

6. Introduction; paragraph 3; line 20: “than” should be deleted.

We deleted “than”

7. Stellate cell wrongly spelt under the heading “the involvement of microbiome in HCC.”

We corrected “stellar” with “stellate”

8. 4th paragraph; under the heading of the involvement of microbiome in HCC: 2nd line may be changed to “due to” instead because to.

Thank you, we corrected it

9. Under the heading “Therapeutic impact of probiotics in HCC: paragraph 4: miR needs to be expanded as microRNA.

We corrected it

10. Under the heading “Prebiotics as a novel therapeutic approach”; paragraph 4; Line2: reference needs to be included as per journal format.

We inserted the reference

11. Under the heading “Prebiotics as a novel therapeutic approach”; paragraph 7; line 3: In fact, is hypothesised – check the sentence

We checked it

Reviewer #2:

Scientific Quality: Grade A (Excellent)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: HCC is the most prevalent primary malignancy in patients suffering chronic liver diseases and cirrhosis. Recent attention has been paid to the involvement of the gut-liver axis in the HCC pathogenesis. The authors reviewed the new therapeutic opportunities that may arise from novel insights into mechanisms by which the microbiota immunomodulation, represented by probiotics, and prebiotics, affects HCC through the gut-liver axis. The data is comprehensive. So I suggest that it would be published in WJH.

We thank the reviewer for the positive comments