Dear editors and reviewers,

First of all, thank you very much for your helpful suggestions and sincere comments, which are of great importance of improving the quality of our article. This review has been revised carefully according to your suggestions.

First, since there are many revisions and modifications, we would like to briefly introduce the structure of the revised article:

1. Introduction

2. Gut Microbiota Alteration in HBV-Related Liver Fibrosis

2.1 HBV persistence

2.2 Acute HBV infection

2.3 Chronic HBV infection and HBV-related liver fibrosis and cirrhosis

2.4 Hepatocellular carcinoma (HCC) and end-stage CHB

3. Gut Microbiota-Related Mechanisms of Liver Fibrosis

3.1 Intestinal barrier impairment

3.2 Gut-derived microbe/antigen translocation and metabolic dysbiosis

3.3 Immune-mediated fibrosis and regression

4. Gut Microbiota Dysfunction in Liver Fibrosis Complications

4.1 Spontaneous bacterial peritonitis (SBP）

4.2 Hepatic encephalopathy (HE)

5. Gut Microbiota-Related Treatment toward HBV-Related Fibrosis and Complications

5.1 Gut microbiota stabilization with antiviral treatment (AVT)

5.2 Rifaximin

5.3 Probiotics and synthetic probiotics

5.4 Fecal microbiota transplantation (FMT)

6. Conclusion

Second, we would like to answer the comments of Reviewer 1:

a) To make this review more organized, the order of different parts has been adjusted. The part “gut microbiota alteration in HBV-related liver fibrosis” has been divided into four parts according to the different phases after HBV infection, including “HBV persistence”, “Acute HBV infection”, “Chronic HBV infection and HBV-related liver fibrosis and cirrhosis” and “Hepatocellular carcinoma (HCC) and end-stage CHB”.

More HBV-related literatures have been added, including newly published literatures of 2022 (PMID: 35233369) and previously missed studies (PMID: 31600845, 31925905, etc.).

b) Though there are many studies on the immunobiology of HBV, few reliable studies are focused on the gut microbiota-related mechanisms. Simultaneously, due to the length limitation, immune-related mechanisms only occupy a small part of the whole text. To better fit the content of the review, the title of Part 3 has been revised to “gut microbiota-related mechanisms of liver fibrosis”.

c) To meet the demand of the journal, this review has been sent for language polishing and the polishing certificate is attached.

d) To make the tables more readable, the former Table 2 has been deleted. The former Table 3 has been divided into two separate tables: Table 2 is focused on studies in mice, and Table 3 is focused on studies in humans.

e) Minor points have been revised: 1) HBV in the title has been replaced by *hepatitis B virus*. 2) HCC has been discussed primarily in the section of “Hepatocellular carcinoma (HCC) and end-stage CHB” as a major outcome of CHB. 3) We cite and apply the definitions of the phases of CHB from EASL. The former Ref. 2 has been replaced by *EASL 2017 Clinical Practice Guidelines on the management of hepatitis B virus infection*. 4) We checked the full text to make sure the spellings of CCl_4 are correct. 5) The description of the former L300 has been corrected. The description has been corrected to “Two main options are nucleoside

analogue (NA) and interferon alfa". 6) The former Table 2 has been deleted. 7) The former Table 3 has been divided into two separate tables: Table 2 is focused on studies in mice, and Table 3 is focused on studies in humans.

Then, we would like to answer the comments of Reviewer 2:

1. The relationship between liver and gut microbiota was mainly through portal vein and biliary system. We added several studies focused on the abnormal metabolism of intestinal bile acids, which is related to the gut microbiota. This part belongs to the new section "Gut-derived microbe/antigen translocation and metabolic dysbiosis".

2. To make this review more organized, the order of different parts has been adjusted. The decompensated stage of cirrhosis was described in the section of "gut microbiota dysfunction in liver fibrosis complications", including SBP and HE.

3. Gut microbiota dysbiosis of HE and the possible mechanisms has been added to the part of "Hepatic encephalopathy (HE)".

4. Minor points have been revised: 1) Table 2 has been deleted. 2) The mentioned two mistakes have been corrected, and we have checked the full text again to avoid spelling mistakes, grammar mistakes and other problems. 3) The part you mentioned has been deleted. To avoid these mistakes, the references were selected and modified carefully, and some expressions were modified to better serve the article.

Thank you very much for your considerations and suggestions!

Yours sincerely,

Zhi-Gang Ren