Reviewer #1: This is a frontier article, authors discussed the evidence of the gut–liver axis in cirrhosis : gut dysbiosis, small intestinal bacterial overgrowth, and intestinal barrier alteration ,bacterial translocation, systemic inflammation,vasodilation, arterial hypotension, and hyperdynamic circulation,and then the development of cirrhosis, then authors proposed a model of the gut–liver axis .In general, authors lists many research results, but the summary and analysis are not enough. Some of the articles need to be revised .

1."Normally, bacterial translocation inhibits the predominance of strict anaerobes (Clostridia and Bacteroidetes) and bacteria without LPS (Firmicutes) or with low-activity LPS (Bacteroidetes) in the gut microbiome as well as low permeability of the intestinal barrier". It is hard to understand.

Authors' response: has been edited:

"Normally, bacterial translocation inhibits by the predominance of strict anaerobes and bacteria without active LPS in the gut microbiome and low permeability of the intestinal barrier."

2."short-chain fatty acids (SCFA) produced by the gut microbiota, especially butyrate, play an important role in maintaining the intestinal barrier". authors may need to discuss how short-chain fatty acids (SCFA) act in maintaining the intestinal barrier

Authors' response: has been added:

Short-chain fatty acids (SCFA) produced by the gut microbiota, especially butyrate, play an important role in maintaining the intestinal barrier[28]. *This effect is possibly associated with an increase in the production of proteins of tight junctions which was observed in the culture of epithelial cells after adding SCFA to it[28]. However, the exact mechanism for this has not yet been established.*

3.”The intestinal mucosal mitotic count was significantly lower in patients with cirrhosis than in the controls, and a trend toward increased apoptosis was recorded. Lipid peroxidation in the intestinal cells increased in decompensated cirrhosis but not in compensated cirrhosis “.authors did not explain the correlation between intestinal mucosal mitotic count, lipid peroxidation in the intestinal cells and intestinal barrier dysfunction.

Authors' response: has been added:

These changes (increased death and decreased renewal of intestinal cells and increased oxidative stress in them) also predispose to a decrease in the gut barrier function.

4.”Patients with cirrhosis had a diminished expression of antibacterial peptides defensins 5 and 6 at the intestinal crypts compared with healthy controls, and this was negatively correlated with the blood LPS levels. In addition, the content of intraepithelial lymphocytes in the duodenal biopsy specimen was lower in patients with decompensated cirrhosis than in healthy controls”authors did not explain the correlation between antibacterial peptides defensins 5 and 6 at the intestinal crypts, intraepithelial lymphocytes in the duodenal biopsy specimen and intestinal barrier dysfunction.

Authors' response: has been added:

Thus, the protective properties of the intestinal epithelium against bacterial invasion are reduced in patients with cirrhosis and this also predisposes to a decrease in the effectiveness of the intestinal barrier.

5.BACTERIAL TRANSLOCATION IN CIRRHOSIS authors discussed a number of evidence of Bacterial translocation in cirrhosis, But the author may need to make a summary of the passage to help the reader understand it better .

Authors' response: has been added at the end of this section:

Thus, bacterial translocation is associated with gut dysbiosis, impaired intestinal barrier function, systemic inflammation, endothelial dysfunction, infectious and non-infectious complications of cirrhosis.

6.SYSTEMIC INFLAMMATION IN CIRRHOSIS authors discussed pro-inflammatory cytokine TNF-a,blood CRP level,anti-inflammatory cytokine, pro-inflammatory cytokine,systemic immune activation biomarkers in cirrhosis, but the author may need to summarize and analyse the evidence

Authors' response: has been added at the end of this section:

Thus, systemic inflammation is associated with SIBO, gut dysbiosis, impaired intestinal barrier function, bacterial translocation, infectious and non-infectious complications of cirrhosis.

7.HEMODYNAMIC CHANGES IN CIRRHOSIS authors discussed the evidence of association between NO and pro-inflammatory cytokines, may still need to discuss the evidence of other molecules, including carbon monoxide. The organization of this passage is not so good.

Authors' response: has been added:

Carbon monoxide (CO) is formed as a by-product of the breakdown of heme by heme oxigenase, the activity of which is increased in the liver with cirrhosis[69,70]. The CO concentration in exhaled air was higher in patients with cirrhosis than in healthy individuals, and it was even higher in patients with ascites than in those without ascites. The level of this biomarker correlated with Child-Pugh score, prothrombin time, serum bilirubin and albumin level[71]. No correlation was found between CO concentration

and blood pressure, heart rate, or plasma renin activity[71]. However, plasma CO levels directly correlated with the serum LPS level, cardiac output, and inversely with systemic vascular resistance and mean arterial pressure[72]. This and other vasodilators are much poorer studied in patients with cirrhosis than nitrogen monoxide.

8.authors may need to discuss the mechanism of pro-inflammatory cytokines promote the release of NO from the vascular wall?

Authors' response: has been added:

Despite the established collerations between the levels of proinflammatory cytokines and vasodilators in cirrhosis, the exact mechanisms of increasing the concentration of the latter remains to be determined[72].