

Name of journal: World Journal of Gastroenterology

Manuscript NO: 46556

Title: Microbial metabolites in nonalcoholic fatty liver disease

Reviewer 1:

Comment 1: However, given the manuscript title, the review is incomplete. Many important metabolites are not represented or are not fully described (including tryptophan metabolites, branched-chain amino acids (BCAAs), endotoxin, etc.). There is a discrepancy between the abstract, the figure and the text: for example, the indole propionic acid (IPA) mentioned in the abstract is not discussed in the text, the indole is presented only in the figure, two other tryptophan metabolites are only discussed.

Response: We thank and agree with the reviewer. We have added the associations of the tryptophan metabolites (including indole-3-acetic acid, indole propionic acid and tryptamine), branched-chain amino acids (BCAAs) and endotoxin with NAFLD in the revised manuscript. We added the underline to the modified place and marked it with red.

Comment 2: The section 'Other microbial metabolites' misleads the reader, since most of the metabolites discussed are not microbial (endogenous metabolite dimethylguanidino valeric acid, endocannabinoid anandamide) or human microbiota products (nonsteroidal fungal metabolite altenusin). In the same section, for some unknown reason, the microbial metabolite deoxycholic acid (DCA) is discussed, although the section 'Bile Acids' is present above.

Response: We thank the Reviewer for this comment. We have deleted these metabolites (endogenous metabolite dimethylguanidino valeric acid, endocannabinoid anandamide and nonsteroidal fungal metabolite altenusin) according to the suggestion. And we removed the discussion of DCA to the section 'Bile Acids'. We added the underline to the modified place and marked it with red.

Comment 3: The microbial origin of metabolites is practically not discussed (specific metabolite-producing taxa are not indicated), it also reduces the value of the manuscript.

Response: We thank the Reviewer for this comment. This is a good point. Due to the complexity of gut microbiota, the precise relationships between gut microbiota and metabolites are still unclear. According to the previous investigations, we added the information about the microbial origin of metabolites in the revised manuscript. And we added the underline to the modified place and marked it with red.

Reviewer 2:

Comment: With exception of type errors, the manuscript entitled “Microbial metabolites in nonalcoholic fatty liver disease” is a well structured and presented review where current knowledge in this topic is adequately presented and given conclusions are of high scientific and clinical value.

Response: We thank the Reviewer for the recognition of our work.