

Dear Editor of *World Journal of Gastroenterology*,

Thank you for your kind recommendations on our manuscript (Manuscript NO.: 76868, Letter to the Editor). On behalf of all co-authors, I would like to take this chance to thank the reviewers. Many thanks for the good evaluation on our manuscript and the good advices. The manuscript has been revised according to the reviewers' suggestions, and we are sending herewith the revised version. The revised points are red-highlighted in the text. We provide here in details our responses to the specific points.

Point-by-point responses to **SCIENTIFIC QUALITY**

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Accept (High priority)

Specific Comments to Authors: The manuscript hypothesis is very interesting and certainly the role of D-amino acids is important in IBS and is certainly worth researching. What I miss in my work is the connection between the metabolism of D-amino acids and the microbiota or microorganisms, at least at the order level. And the Latin names of bacteria should be written in *italic*.

Thank you very much for the good evaluation on our manuscript and the good advices. This is valuable to us for the improvement of the manuscript. According to the suggestion, we have changed to the Latin names of bacteria written in *italic*.

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade C (A great deal of language polishing)

Conclusion: Minor revision

Specific Comments to Authors: Overall, it is a good article with an important message for the readership of the journal. The letter provides new insights into the original article. Minor points to consider: • I advise the authors to focus on the subject of the manuscript (page 3, D-serine and renal diseases). • The authors should provide **clear conclusion** for the manuscript to summarize the data. • The manuscript needs editing for language to improve readability.

This is valuable to us for the improvement of the manuscript. Thanks. According to the suggestion, we have changed and explained the sentences in the text. In addition, we have gone over the text/abstract and amended typos, misspellings and grammatical errors in the previous manuscript as much as possible in order to improve the manuscript more helpful to the readers.

Reviewer #3:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Accept (General priority)

Specific Comments to Authors: IBS is emerging as a new psychosomatic disorder of the intestinal system, and bring much trouble to the patients. IBS is usually thought to be a functional disease that closely associate with emotional change, however, recent studies suggested that low-grade inflammation and intestinal immune response are involved in the development of IBS. Therefore, countering intestinal inflammation present to be a new strategy for IBS treatment, in which modulation of gut microbiota and related metabolites is fundamental. This letter provides the evidence of D-amino acids in improving intestinal inflammation, which is an interesting topic. However, further evidence is needed, such as **whether the alteration in gut microbiota and amino acid metabolites in IBS patients support this finding**, or if IBS-related inflammation will be more severe when endogenous intestinal D-amino acids are specifically reduced, and which **different amino acid types plays a dominant role**.

Thanks for the critical evaluation to our manuscript. This is valuable to us for the improvement of the manuscript. According to the comments, we have amended the manuscript. Because of limited information in literature at present, we think it will be needed in the future study to explore the types of D-amino acid with a dominant role.

Point-by-point responses to EDITORIAL OFFICE'S COMMENTS

(1) Science editor:

Please address the comments of all reviewers accordingly.

Language Quality: Grade B (Minor language polishing)

Scientific Quality: Grade B (Very good)

Thank you very much for the good evaluation on our manuscript.

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Gastroenterology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Please provide decomposable Figures (in which all components are movable and editable), organize them into a single PowerPoint file. Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is 'original', the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2022. Before final acceptance, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript. To this end, authors are

advised to apply a new tool, the Reference Citation Analysis (RCA). RCA is an artificial intelligence technology-based open multidisciplinary citation analysis database. In it, upon obtaining search results from the keywords entered by the author, "Impact Index Per Article" under "Ranked by" should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision. Please visit our RCA database for more information at: <https://www.referencecitationanalysis.com/>.

Thanks. This is valuable to us for the improvement of the manuscript. According to the suggestion, we have changed and explained the sentences in the text. In addition, we have gone over the text/abstract and amended typos, misspellings and grammatical errors in the previous manuscript as much as possible in order to improve the manuscript more helpful to the readers. With the use of RCA database, we improved and added the references including the following. 21. Canteros MG. D-Arginine as a neuroprotective amino acid: promising outcomes for neurological diseases. *Drug Discov Today*. 2014, 19(5):627-636.