April 20, 2021

Science Editor, Editorial Office

Baishideng Publishing Group Inc

Re: **Manuscript NO.:** 63931

Title: "Prospects on Clinical Applications of Butyrate-Producing Bacteria"

Dear Dr. Ji:

Thank you for the careful review of our manuscript. We fully appreciated the constructive comments raised by your expert reviewers and the editor. Changes in the manuscript have been made accordingly. We hope the carefully revised manuscript will meet the standard of the Journal and satisfy reviewers and editors for publication.

The point-by-point response to the comments of the reviewers is enclosed. Please let me know if you need other information.

Sincerely yours,

Jing Lin M.D.
Associate Professor of Pediatrics
Icahn School of Medicine at Mount Sinai
New York, NY10029

The point-by-point response to the comments of the reviewers

Reviewer 1:

According to existing research, intestinal flora and its metabolites are involved in the occurrence and development of many diseases. As one of the main metabolites, short-chain fatty acids include propionic acid, butyric acid and so on. This article reviews the recent studies of butyric acid in gastrointestinal diseases. However, this review lacks a summary and description of the various mechanisms of butyric acid. The above only represents my personal views.

We added a brief description of the possible mechanisms in the summary section. In fact, the true mechanisms underlying the effects of butyrate producing bacteria is still mostly speculative.

Reviewer 2:

The review manuscript written by Libin Zhu et al. summarizes the current understanding of butyrate-producing bacteria in the treatment of various diseases. The review is well written and provides important information to the readers. However, there is a concern that need to be addressed. Minor point 1. There are several reports showing that gut microbiota is associated with the effect of immunotherapy, especially that with immune checkpoint inhibitors. The authors should add the statement on that point.

More recently, a clinical study found that higher fecal SCFA concentrations were associated with the efficacy of immunotherapy in solid cancer tumor patients, indicating that gut microbiota might have wide-ranging impacts on host immune response. This sentence and the reference were added into the section 2, Regulation of Intestinal Immune Response. There are many studies about the role of SCFAs in the tumor biology. The detail discussion or elaboration about this topic is beyond the scope of this mini-review specifically aimed for pediatricians.

LANGUAGE QUALITY

Please resolve all language issues in the manuscript based on the peer review report. Please be sure to have a native-English speaker edit the manuscript for grammar, sentence structure, word usage, spelling, capitalization, punctuation, format, and general readability, so that the manuscript's language will meet our direct publishing needs.

We have performed a further English language editing with the help from Dr. Green.

EDITORIAL OFFICE'S COMMENTS

Authors must revise the manuscript according to the Editorial Office's comments and suggestions, which are listed below:

(1) The "Author Contributions" section is missing. Please provide the author contributions;

It is added.

(2) The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s)

They are provided and loaded.

(3) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor; (4) The authors should add some figures or tables.

A figure was added into the manuscript.