

April 2, 2014

Dear Editor:

I greatly appreciate the completion of reviewing our paper and good comments on it.

**Title:** Intestinal microbiota in the pathophysiology and management of irritable bowel syndrome

**Author:** Lee Kang Nyeong, Lee Oh Young

**Name of Journal:** *World Journal of Gastroenterology*

**ESPS Manuscript NO:** 9351

The manuscript has been improved according to the suggestions of reviewers:

*Suggestions of Reviewer 02442330*

The last paragraph about "anti-inflammatory therapy" should be omitted.

➔ We removed the indicated paragraph and the corresponding references.

*Suggestions of Reviewer 00502973*

In this manuscript, Lees reviewed the current knowledge of intestinal microbiota related to IBS. This is an interesting topic, and deserves further discussion. Before its final acceptance, some minor concerns in this manuscript should be addressed.

1. In Abstract: "The human intestinal microbiota can include any of more than 1,000 different bacterial species..." I suggest change to "The human intestinal microbiota are composed of more than 1,000 different bacterial species..."

➔ The sentence was rewritten as you indicated.

2. Page 4, the 1st paragraph: "...and Bacteroides spp. Increase in formula-fed babies (babies receiving a high-fat diet)[15]." "Increase" should be in low case.

➔ "Increase" was rewritten as "increase".

3. Page 6, the 1st paragraph: "Endocrine pathways in microbiota-gut-brain axis were suggested in in a study showing that..." change to "Endocrine pathways in microbiota-gut-brain axis were suggested in a study showing that..."

➔ We changed the sentence as you indicated.

4. Page 9, last paragraph: "preceipitate" is a typo.

➔ The word was rewritten as "precipitate".

5. Page 13, the 1st sentence: “normalized levels of pro-inflammatory cytokines such as IL10 and...”. It is generally believed that IL10 is an inhibitory cytokine rather than a pro-inflammatory cytokine.

→ I agree with you. The sentence was rewritten: “normalized the ratio of cytokines IL-10/IL-12 in the systemic circulation”.

6. Page 14, the section titled “Anti-inflammatory therapy: This section is not related with intestinal microbiota, and thus should be deleted. 7. Table and figure are ok.

→ The indicated paragraph was deleted.

#### ***Suggestions of Reviewer 00503025***

This review aims to summarize recent data on IBS and its interaction with microbiota. It is well written and the subject has been clearly addressed. I have two questions: one concerns actual microbioma analysis in IBD patients, is there any data that could be added?

→ We added the finding of increased ratios of Firmicutes:Bacteroidetes in IBS patients.

Second, the title and the 1st paragraph should be rewritten: eliminate the abbreviation and add ‘...cannot be fully explained...’ since the role of microbiota could be indirect through biochemical and metabolic changes.

→ The title was rewritten.

We totally agree with the comment, thus added the sentence “cannot be fully explained” in the 1st paragraph.

#### ***Suggestions of Reviewer 00503048***

The review by Kang Nyeong Lee and Oh Young Lee summarizes recent advances in the knowledge of the role of microbiota in controlling the pathophysiology and treatment of IBS. A critical analysis has been done taking into account all aspects of both the mechanism of action of the microbiota on gut and the gut response. Interestingly, a clinical relevance of the importance of the use of microbiota in managing the symptoms of IBS is proposed and discussed. Finally, the figure could be better improved, rather than being a simple scheme.

→ Thank you for your reviewing our manuscript and comments. We resubmitted the figure as a decomposable form according to the editor’s instruction.

#### ***Suggestions of Editor***

The title page carries the title, the authors, the authors’ affiliations, and footnotes. Title: The title must

be informative, specific, and brief (Title should be no more than 10~12 words/60 bytes. Please revise it). Words should be chosen carefully for retrieval purposes. All nonfunctional words should be deleted, such as 'the', 'studies on', 'observations of', and 'roles of', *etc.* The title should not include **Acronyms**. Please modify it. Thank you!

➔ The title was rewritten as "Intestinal microbiota in pathophysiology and management of irritable bowel syndrome".

A decomposable figure is required. It means that the fonts and lines can be edited or moved. The example is attached. The coordinate graphs supplied should be **decomposable** (each part of your figure could be moved so as to easily edited). You can send it as excel, word or powerpoint format so that I can edit them easily.

➔ We resubmitted the figure as powerpoint format.

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,



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