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Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 11563-edited.doc).

**Title:** Bifidobacterium infantis attenuates colitis by regulating T cell subsets responses

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

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

1 Format has been updated

**2 Revision has been made according to the suggestions of the reviewer**

1). How many mice were examined in total?

55 Female BALB/c mice, 6-8 weeks old are used

2). Was B. infantis administered in high dose for the TNBS-induced colitis study?

We found that feeding with high dose of B.infantis could increase higher expressions of Th1, Th17 and Tregs-related cytokines and levels of CD4<sup>+</sup>T cells, Th17 cells and CD4<sup>+</sup>Foxp3<sup>+</sup> Tregs in MLN of normal mice than feeding with low dose of B.infantis. Therefore, we chose high dose B.infantis to be administered for the TNBS-induced colitis study.

3). High dose B. infantis alone induced rather than reduced Th1-Th17 response in mesenteric lymph nodes. How do you reconcile the data with the B. infantis-mediated attenuation of TNBS-induced colitis?

In normal mice, the crosstalk between intestinal microbes and local immune cells represents one of the fundamental features of intestinal homeostasis. These interactions are essential for maintaining normal intestinal homeostasis and for mounting protective immunity to pathogens. In our study, high dose B.infantis indeed elicited some Th1 and Th17 responses in the normal gut environment, though this did not cause pathological inflammation. One reason why B.infantis feeding resulted in a little high immune

response is that *B.infantis*, which is derived from human gut, is regarded as foreign antigen, thereby triggering weak responses. But this immune response did not lead to pathological inflammation, which indicated that there was a proper balance among Th1, Th17 and Tregs in maintaining gut homeostasis. It may be that high dose *B.infantis* also increased the Tregs response, which may in turn weaken the slightly increased Th1 and Th17 responses. Accordingly, we think that *B.infantis* feeding keeps a good balance among Th1, Th17 and Tregs in maintaining gut homeostasis in normal mice. Meantime, a proper increase in Th1 and Th17 response induced by *B.infantis* feeding may enhance the mucosal defense against pathogens and thus be beneficial to the promotion of the host intestinal immunity. However, in TNBS-induced colitis mice, the abnormal Th1 and Th17 responses and an inadequate Tregs response resulted in the excessive intestinal inflammation. under this inflammatory condition, *B.infantis* reshapes development and function of the mucal immune system, driving it to play anti-inflammatory effects. We showed that high dose *B.infantis* feeding reduced the excessive Th1 and Th17 responses and promoted the deficient Tregs responses in colitis mice, finally restoring the intestinal immune homeostasis. Taken together, we think that *B.infantis* has different effects in different gut environment, remaining a balance among immune cell responses.

4 or 5) The English is poor. Please provide a revision of the language by a native speaker.

Or the English is poor. Please provide a revision of the language by a native speaker.

Given that the manuscript has a poor language, we have asked an English professor and a native English speaker with scientific background to edit it thoroughly.

6). The introduction section is too long. Many parts should be moved to discussion section. This suggestion is very important, we feel sorry for not describing them briefly in our previous manuscript. We have rewritten and shorten the introduction section and reorganized discussion sections in the revised manuscript.

7). A table gathering the main characteristics of the study population should be provided.

Table 1 Summary of the study population

Different doses of B.infantis feeding		Colitis induction		B.infantis treating colitis mice	
Control	10 mice	Control	5 mice	PBS-TNBS	5 mice
Low-infantis	10 mice	TNBS-3	5 mice	B.infantis-TNBS	5 mice
High-infantis	10 mice	TNBS-6	5 mice		

8). No multiple regression analysis had been provided.

In our study, the independent variable is considered as the treatment with low dose or high dose B.infantis or PBS in normal model. The levels of cytokine, Th17 cells and regulatory T cells measured in mesenteric lymph nodes in colitis mice are acted as the dependent variable. In colitis model, the independent variable is considered as the treatment with high dose B.infantis or PBS, the dependent variables are considered as various kinds of cytokines. We think that other factors such as mouse age, weight, gender are ignored. We think it is not much meaningful to make multiple regression analysis on our data.

3 References and typesetting were corrected

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

Sincerely yours,



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