

Dear Editor

Thank you for carefully reviewing our manuscript previously titled “Diversity of bacterial lactase genes in intestinal contents of mice with antibiotics-induced diarrhea” for publication in the World Journal of Gastroenterology. We are grateful to you and your reviewers for their constructive critique.

I have been in accordance with the requirements of the Journal changed my manuscript. We have revised the manuscript, highlighting our revisions in red and have attached point-by-point responses detailing how we have revised the manuscript in response to the reviewers’ comments below.

Thank you for your consideration and further review of our manuscript. Please do not hesitate to contact us with any further questions or recommendations.

Yours Sincerely,
Chengxing Long

For Reviewer #1:

a) Why did you choose the Sprague Dawley rats

To ensure the accuracy, sensitivity, and reproducibility of animal experiments. We selected SPF (specific pathogen free animal) mice. SPF has obvious advantages, for example, SPF can effectively control animal diseases, asymptomatic infection and may interfere with animal experimental results of pathogens. It is also applicable to intestinal microbial research and experimental treatment.

b) What age were they when you started the experiment?

One month

c) Did all the model group mice have diarrhea at the time of the study, with or without any other symptom (pain, blood in the stool, etc)? How many days did they have the diarrhea?

All the model group mice had diarrhea without any other symptom. The model group mice began to have diarrhea on the third day, and all the model mice had diarrhea on the fifth day.

d) Did all the control group mice have a normal stool at the time of the study?

Yes

e) Are lactase-forming bacteria at the colon? Are they important in this clinical entity?

In our studies, contents in jejunum to ileum of the mice were collected separately, which are important in clinical research. Because the contents in this segment are numerous, erosive and rich in microbial species, which are beneficial to study the bacterial diversity.

For Reviewer #2:

1, Please explain abbreviations in ‘abstract’ and ‘manuscript’.

SPF (specific pathogen free animal), KM (Kunming), OTUs (operational taxonomic units), Principle Component Analysis (PCA), Principle Coordination Analysis (PCoA), Nonmetric Multidimensional Scaling (NMDS), Phosphate Buffered Saline (PBS), phosphate buffer solution (PBS), hexadecyl trimethyl ammonium bromide (CTAB), sodium dodecyl sulfate (SDS)

2, Please show the direct relationship between the reduction of the diversity of bacterial lactase gene and the clinical outcomes.

The correlation between intestinal lactase and disease is mainly manifested in lactose intolerance. When the diversity of bacterial lactase genes in intestinal contents is decreased, the activity of lactase is inhibited. The unabsorbed lactose remains in the intestine and is decomposed into lactic acid, carbon dioxide or other gases by intestinal bacteria. This increases the osmotic pressure in the intestine, causing flatulence, intestinal cramps, and even diarrhea.

3, Please discuss the clinical relevance and the treatment for antibiotics-induced diarrhea.

Previous studies have shown that antibiotic induced diarrhea was associated with dysfunction of intestinal lactase due to loss of its activity. Antibiotics can destroy or inhabit intestinal lactase activity leading to diarrhea. And various causes of diarrhea can lead to lactase deficiency and then occur secondary lactose intolerance, most of diarrhea can be treated with lactase supplement or enhancing lactase activity.

For Reviewer #3:

There are many abbreviation in abstract - In the Introduction, the results of this study don't must be mentioned - Many sentence start by "and"

Abbreviations in the abstract have been added, the results of this study in the introduction have been deleted, many sentences have been modified.