

Responses to the Reviewers' Comments

Manuscript Number: 55758

Dear Editor,

We greatly appreciated both editor and reviewers' for insightful comments and suggestions, which are extremely valuable for us to improve this manuscript. We agree with all the comments and revised our manuscript accordingly. We have supplied revision notes and provided point-by-point responses to reviewers' comments and hope that this revision will have overcome the identified problems. All modified texts were highlighted in yellow.

Responses to Editorial corrections:

COMMENT: **1.** I found no "Author contribution" section. Please provide the author contributions.

Response: Thank you for these comments. We added "Author contribution" section in the revised manuscript, details as shown on page 1, line 27.

COMMENT: **2.** I found 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).

Response: Thank you for your suggestions. We added the approved grant application form(s). It is shown on page 2, line 34, in the revised manuscript. And we upload the funding agency copy of any approval document(s).

COMMENT: **3.** I found the authors did not provide the original figures. 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 edit.

Response: Thank you for your suggestion! I read your Figure Guidelines and I also provide the original figures using PowerPoint files.

COMMENT: 4. I found the authors did not write the “article highlight” section. Please write the “article highlights” section at the end of the main text.

Response: We have added the “article highlight” section at the end of the main text, the details as shown on page 32, line 735.

COMMENT: 5. please don't include any *, #, †, §, ‡, ¥, @....in your manuscript; Please use superscript numbers for illustration; and for statistical significance, please use superscript letters. Statistical significance is expressed as ^a $P < 0.05$, ^b $P < 0.01$ ($P > 0.05$ usually does not need to be denoted). If there are other series of P values, ^c $P < 0.05$ and ^d $P < 0.01$ are used, and a third series of P values is expressed as ^e $P < 0.05$ and ^f $P < 0.01$.

Response: We have revised all figures and used the superscript letters for illustration.

Responses to Reviewer

COMMENT: 1. I think this is an excellent manuscript. There are very few grammatical errors eg. 'that' used too often;

Response: We check the spelling and grammar. Now the unnecessary “that” and spelling errors are removed. Thank you for this again.

COMMENT: 2. page 3 last sentence needs to be rewritten; page 5, 1st paragraph, last sentence.

Response: Thank you for your suggestion. We rewrote page 3 last sentence and page 5, 1st paragraph, last sentence.

COMMENT: **3.** Clarification on the impact of GM-CSF and biotin levels would be helpful (abstract suggests GM-CSF increases fecal biotin but then states biotin metabolism is reduced as does the text).

Response: I'm sorry for the confusing issue. Actually, the statement is consistent between the abstract and full-text (page.13, line 339). To avoid unnecessary misunderstanding, I modified the sentences.

COMMENT: **4.** Did authors evaluate impact of GM-CSF on fecal bile acid concentration? Would also like authors to discuss limitations.

Response: Thank you for your comments, We have added limitations to the discussion about the impact of GM-CSF on fecal bile acid concentration, please see details on page 18, line 477.