Reviewer’s report

Title: The relationship between bile acid concentration, glucagon-like-peptide 1, fibroblast growth factor 15 and bile acid receptors in rats during progression of glucose intolerance

Version: 0 Date: 17 Apr 2017

Reviewer: Curtis Klassen

Reviewer’s report:

I do not agree with the open peer review policy of the journal. I do not want my name revealed.

This manuscript describes studies in which rats were fed a high-glucose, high fat diet, as well as given STZ. Total bile acids, TGR5, FGF15, glucose, insulin, triglycerides, etc were quantified. The authors correlated these various parameters, especially bile acids, TGR5, and FXR and concluded they contribute to glucose homeostasis.

1. English is not the first language of the authors, and thus many corrections are necessary. I will list some below.

2. The results of these studies are correlations, rather than cause and effect. Thus, this is a descriptive manuscript.

3. It is known that some bile acids are agonists and some are antagonists of FXR. Thus, it would be better to quantify individual bile acids than total bile acids.

4. First 3 lines: bile acids are involved in activation of the G protein---A few researchers have explored changes TGR5.....

5. Abstract line 20: intolerance in rats.....lipid, TBAs, alanine

6. Introduction, line 6: In 1999, bile acids were discovered.

7. Line 11. The FXR pathway... by bile acids synthesized in hepatocytes or ....pathway that suppresses hepatic.....epithelial cells, mainly.....

8. Line 50: in a glucose

9. Page 3, line 1 bile acids on lipid and glucose homeostasis, we hypothesized that an alteration of bile .....glucose intolerance. Little is known in regard to changes TR5....TGR5 and Fxr in intestine.

10. Throughout, whenever a company is given, also indicate city and state.

11. Line 39: Thirty-three four-week old male
12. Throughout: high-fat, high-sugar

13. Page 4, line 1: groups to assess insulin.....blood glucose was measured at ....diabetes. Blood glucose

14. Line 17 considered to have developed type

15. Line 42: at the 5-hour time point were

16. line 50: used for quantifying

17. Line 12: Remove THE at the beginning of the two sentences.

18. Line 17: instructions.....with a DPP4

19. Line 42: Remove THE...

20. Line 56: System (remove s)

21. Line 28: What is RIPA?

22. Page 7, line 11: At the 4th week

23. Line 36. levels

24. No discussion of figure 1 is provided.

25. Page 8 line 1 and 2: Change smaller to less in both lines

26. Page 9, line 31: demonstrated changes.....levels were increased

27. Page 9, last line: to the FGR in

28. Page 11, line 6: studies discovered a relationship

29. In contrast most scientists, the authors have indicated the importance of the large intestine in these correlations. They might want to indicate the first manuscript that suggested the importance of the large intestine of these parameters in germ-free mice—see Selwyn in Drug Metab and Dispos 43: 1544, 2015.

30. Fig 3B: Is the statistics on the right two bars not significant?

Are the methods appropriate and well described?
If not, please specify what is required in your comments to the authors.

Yes
**Does the work include the necessary controls?**
If not, please specify which controls are required in your comments to the authors.

Yes

**Are the conclusions drawn adequately supported by the data shown?**
If not, please explain in your comments to the authors.

Yes

**Are you able to assess any statistics in the manuscript or would you recommend an additional statistical review?**
If an additional statistical review is recommended, please specify what aspects require further assessment in your comments to the editors.

I am able to assess the statistics

**Quality of written English**
Please indicate the quality of language in the manuscript:

Not suitable for publication unless extensively edited

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