

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 30113.

Response to Reviewer(s):

COMMENTS TO AUTHORS :

- The role of butyrate in maintaining intestinal homeostasis is undoubted. (Curr Opin Clin Nutr Metab Care 2012, 15:474–479, Ann N Y Acad Sci. 2012 ;1258:52-9). -As well as, it is known today that the enormous number of gut microorganisms has an indispensable role in the normal development and functioning of the human body. (O'Hara and Shanahan, 2006 EMBO Rep. 7,688–693; Sommer and B?ckhed, 2013 Nat. Rev. Microbiol. 11,227–238). The challenge for the upcoming years will however be to first find out whether these changes in gut microbiota composition are the cause or the consequence of disorder. (Frontiers in Microbiology June 2016, 7, article979). This aspect should be addressed by the authors

We thank and agree with the reviewer. We have added this information in the discussion of revised manuscript.

“the role of butyrate in maintaining intestinal homeostasis is undoubted which is confirmed by our study, meanwhile, gut microbiota has an indispensable role in the human body, and the challenge is to find out whether these changes in gut microbiota composition are the cause or the consequence of disorder. Further resarches on this aspect may uncover the precise relationship between gut microbiota and NAFLD” (Page 26, Para 2).

-page 7- first paragraph- “Studies investigating butyrate in NAFLD are limited in both humans and animal models. Whether this gut metabolite can be useful for the prophylaxis or treatment of NAFLD is controversial. -Previous studies have demonstrated beneficial effects of butyrate on steatohepatites evolution. (Plos one, July 2013, Volume 8 , Issue 7, e68626; Br J Nutr. 2015 Dec 14; 114(11):1745-55). These studies should be addressed by the authors.

Firstly, we thank and agree with the reviewer. We have added this information in the discussion part of our new revised manuscript.

“And previous studies have demonstrated beneficial effects of butyrate on animal models of steatohepatitis” (Page 22, Para 1).

- The authors investigated gut microbiota of NAFLD patients and controls. Maybe these results shouldn't be included in this manuscript. Another manuscript reporting gut dysbiosis and association with biopsy findings should be considered by the authors. - The manuscript should include only the results of the experimental study in mice divided in three groups, normal control, fed standard chow and model group, fed a high-fat diet (HFD) for 16 wk, the intervention group fed HFD for 16 wk and treated with sodium butyrate (NaB) for 8 wk. Where they investigated gut microbiota, liver histology gastrointestinal barrier indicators, serum and liver endotoxin, and inflammation-or metabolism associated genes in the mice subgroups.

We thank and agree with the reviewer. We have deleted all the comparative results of gut microbiota between NAFLD patients and controls, and revised our abstract, core tip, introduction, materials and methods, results and discussion.(Page 5,6,9,10,15,21,22).

Page 7-last line - I think it is bettermay play

We thank and agree with the reviewer. We have revised the introduction part of our manuscript.

“NaB may play an important role in relieving steatohepatitis and may be a useful therapeutic approach in the management of NAFLD” (Page 9,Para 2).

Page 24- Discussion-last paragraph- “and whether it will work on clinical populations remains a significant challenge. However, it opens potential avenues for intervention strategies for the treatment of NAFLD.” - The unpleasant taste and odour of sodic butyrate make extremely difficult the oral administration of butyrate, these difficulties are even more remarkable in children where the administration is complicated. Thus, new formulations of butyrate with a better palatability, which can be easily administered orally, are needed. (Plos one July 2013, Volume 8, Issue 7, e68626). Consider this information and review this part of the manuscript. ,

We thank and agree with the reviewer. We have added this information in the discussion part of our manuscript (Page 27, Para 2).

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