

Format for ANSWERING REVIEWERS

July 24, 2014

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: "Giannelli V Manuscript Microbiota 24 july". NO: 11647).

We appreciate the opportunity to resubmit our manuscript. We have revised the paper and have prepared a point by point response to the comments from the reviewers, that we thank for their thoughtful comments. We believe that the present version is significantly improved and we hope it will be accepted for publication. We are uploading the revised copy of the manuscript, with the new and/or revised text marked in yellow.

Thank you for your ongoing consideration.

Yours sincerely,

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Title: Microbiota and the gut-liver axis: bacterial translocation, inflammation and infection in cirrhosis. New insights into an old relationship

Author: Valerio Giannelli, Vincenza Di Gregorio, Valerio Iebba, Michela Giusto, Serena Schippa, Manuela Merli and Ulrich Thalheimer

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 11647

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

1 Format has been updated, the English form as been corrected by a native English speaker reviser

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

(1) The manuscript is a review very comprehensive and interesting Points: - Revise English. - Add some figure that summarizes the pathophysiology. - Add two tables with the treatments (RCT) applied in the intestinal flora of cirrhotic patients and animals model to prevent complications. For example, probiotics, erythromycin, neomycin, rifaximin, lactobacillus, etc.

Response to comment 1: according to reviewer's suggestion, we have prepared a figure that summarize the pathophysiological consequences of gut dysbiosis. In addition, we prepared 2 table, the first summarize the most relevant study which described the gut flora composition in cirrhosis (on stool and mucosa) and the second regards the treatments applied in the intestinal flora of cirrhotic patients. we also included results from animal models.

(2) Giannelli et al., described the microbiota and the gut-liver axis, i.e., bacterial translocation, inflammation and infection in cirrhosis in this paper. Comments: 1. Contents of the abstract is similar to contents of introduction. Authors had better to described the essence of this paper in abstract. 2. Abbreviation are not

used properly. Full spells and abbreviations of SBP, PCR, BT, MLN etc., were written repeatedly. 3. In the contents of 3. the liver-gut axis, description on HBTs had better to be more simple, because HBT is investigation method

Response to comment 2: To address the reviewer's requests, we totally changed the abstract. It is now more attractive and aimed at describing the relevance of the herein review. We have corrected the use of abbreviation, removing the repetitions which were present in the text before. We have removed some technical explanation of breath test, which were out of our aims.

(3) The current review article should be enriched more for final acceptance. 2) addition of figure should be prerequisite from authors background. Otherwise, not attractive 3) In session 6; Clinical consequence of changes in the intestinal microbiome, though authors introduced two points, dysbiosis and infection, bacterial translocation and infection in cirrhosis, more descriptions should be added from the point of clinical view relevant to microbiota in cirrhosis . 4) SIBO related descriptions should be added more under the different heading subtitle of SIBO in cirrhosis. 5) Abstracts should be enriched more, currently too weak for comprehensive aspect (

Response to comment 2: According to the reviewer's suggestion we added one figure which explain the background of our review. We intended to represent the physiopathological background of the clinical implications of gut dysbiosis (figure 1). To address the request 3 we enriched the clinical point of view of gut dysbiosis. We particularly aimed at describing the consequences of gut flora alteration on the portal hypertension, the risk of bacterial translocation, the pro inflammatory status and the risk of infection. We also mentioned the effects of therapeutic intervention on gut composition in patients with chronic liver disease (see also table 2). Regarding the comment 4 it was not entirely clear to us. We trust that our exposition of SIBO is satisfactory with the corrections we already made. The abstract has been completely revised according to the reviewer's suggestions.

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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