

Answering reviewers

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 28247

Title: *Ex vivo* response to mucosal bacteria and muramyl dipeptide in inflammatory bowel disease

Authors List: Claudia Loganes, Erica Valencic, Alessia Pin, Elisa Marini, Stefano Martelossi, Samuele Naviglio, Luigina De Leo, Tarcisio Not, Lorenzo Monasta, Alberto Tommasini, Annalisa Marcuzzi

Reviewer's code: 03599415

Trieste, August 12, 2016

Dear Editor,

Thank you for accepting our paper and for the reviewer comments concerning our manuscript.

We have taken into account the points raised by the reviewer, and revised the manuscript in order to improve its readability, as suggested. Moreover, we gave the manuscript to a native English speaker for editing. Format, references and typesetting were corrected.

Any change to the text of the edited manuscript has been highlighted in green.

The answers to the reviewer comments are as flowing, highlighted in bold.

We hope that our revision will meet with approval.

Thank you again for publishing our manuscript in the World Journal of Gastroenterology.

Reviewer comment:

The reviewer recommends that (1) apparent typographical errors in the manuscript be fixed;

Author replay:

Thanks for your advices: we apologize for mistakes and inaccuracies.

We carefully proofread the article, checked the grammar and corrected the errors.

Reviewer comment:

(2) consider the statistical methods in order to include corrections for multiple independent analyses (Bonferroni correction);

Author replay:

We do agree with the reviewer that a correction should be applied to adjust for multiple bivariate analyses, both considering the 17 cytokines, chemokines and growth factors, and the outcome groups (CD, UC and healthy controls). However, as specified in the manuscript in the methods section, considering the relatively small sample size, which implied having relatively large p values, we decided not to apply any correction to the p value for statistical significance. However, bivariate analysis was mainly conducted to select variables to be included in the multivariate model. We reported in the discussion that the lack of correction in the bivariate analyses should be considered as a limitation of our study.

Reviewer comment:

(3) add information regarding the enrollment of pediatric patients and especially controls;

Author replay:

Thank you for the suggestion: we have now added to the Materials and methods section information regarding the enrollment of patients.

Reviewer comment:

(4) include a table with characteristics that might represent confounding factors that might raise the levels of inflammatory cytokines in a participants (recent acute illness, chronic illness, BMI, and exc.).

Author replay:

As suggested, we have now added a Supplementary Table reporting the BMI values and the BMI percentiles (Supplementary Table 2). Any other recent acute diseases or chronic inflammatory conditions were found in these patients.

Editor Comment

Step 1. Please revise your manuscript according to the reviewers' comments.

Author replay: We revised our manuscript according to the reviewer and editor comments. We corrected few sentences, as well as added new table in order to make the manuscript more clear and precise. All corrections are highlighted in green in the revised manuscript. Here we reported the major corrections and modifications:

- All reference numbers were changed, as suggested by the editor;
- Grammar mistakes were corrected;
- Further information regarding the enrollment of patients or controls were added in Methods section, as well as a new Supplementary Table reporting the clinical characteristics that might represent confounding factors for the cytokine levels, as suggested by the reviewer;
- The Statistical analysis section was improved and a critical comment was added in the discussion;
- The Multivariate logistic analysis section was enhanced, adding new tables (Table 2, Table 3 and Table 4) reporting the outputs of these analyses;

Step 2. Please update the manuscript according to the Guidelines and Requirements for Manuscript Revision-Basic study.

Author replay: We revised the manuscript according to the provided guidelines.

Step 3. Please provide the scientific research process

Author replay: The scientific research process was provided, as required.

Step 4. Please provide an Audio Core Tip.

Author replay: The audio core tip was recorded and provided as an mp3 format.

Step 5. Please subject the manuscript to CrossCheck analysis and the final title to Google Scholar search, and store screenshot images of the results.

Author replay:

We performed the plagiarism analysis on our manuscript using Turnitin, a plagiarism-prevention service, used in our Institute. Turnitin gave a 31% of similarity, and removing from the analysis the article title page, the percentage of similarity became 14%. Also the Google Scholar search didn't provide a similar title. We reported in the "Google Scholar" and "CrossCheck" documents the screenshot images of the obtained results.

Step 6. Please provide the files related to academic rules and norms.

Author replay: We provided as PDF files the documents related to the academic rules and norms, including Institutional Review Board statement, Institutional Animal Care and Use Committee statement, animal care and use statement, biostatistics statement, conflict-of-interest statement, and data sharing statement.

Step 7. Please provide the approved grant application form(s) or funding agency copy of any approval document(s)/letter(s).

Author replay: the approved grant application form was provided, as requested.

Step 8. Please revise the language of your manuscript.

Author replay: The revised manuscript was carefully checked and corrected by a native English speaker.

Step 9. Please sign the Copyright Assignment form.

Author replay: The copyright assignment form was signed by all the authors and attached as PDF file.

Step10. Submit the revised manuscript and all related documents.

Author replay: We submitted the edited manuscript and all required documents.

Thank you and best regards

Sincerely yours,

Annalisa Marcuzzi, PhD

Department of Medicine, Surgery and Health Sciences,

University of Trieste,

Piazzale Europa 1, Trieste 34128, Italy

Tel/Fax: +39 040 3785422

e-mail: annalisa.marcuzzi@burlo.trieste.it