



November 5, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 6499-revised.doc).

**Title:** The Pathophysiology of Autoimmune Pancreatitis

**Author:** Raffaele Pezzilli, Nico Pagano

**Name of Journal:** *World Journal of Gastrointestinal Pathophysiology*

**ESPS Manuscript NO:** 6499

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

**Reviewer 1**

1. Pezzilli and Pagano wrote a brief review on the pathophysiology of autoimmune pancreatitis focusing on humoral and cellular responses. The humoral part is fairly concise and decent. However, the cellular immune activation part is too short and lashed together. Much more is known on the latter topic. E.g. no detailed analysis of cellular response in type 1 and type 2 AIP is provided.

Answer. We agree with the comment of the reviewer and the paragraph regarding cellular immunological aspects of AIP has been revised and expanded (Page 7, lines 13-30). Ten references have been added (references 46-55).

2. I have some major concerns regarding the figures. Generally, they are of poor quality. Please show scale bars, rather than indicating the original magnification (isn't the magnification 200 instead of 20 for fig. 1?).

Answer. The figures have been deleted according to the reviewer comment.

3. On page 3, line 2 from the bottom, Figure 1 is not actually showing various types of immune cells (at least you can't tell from the histological picture that they are of different types). It would also be nice to indicate alterations such as infiltrates and fibrosis by signs (arrows, stars) on the figure. Additionally, it would be great if you could demonstrate alterations at higher magnification.

Answer. See answer to comment #2.

4. Does figure 2 show a pancreatic section? Is CD20 positivity always so focal in AIP?

Answer. See answer to comment #2.

5. Also, I do not quite understand why there is a separate section on "Animal models for studying the pathophysiology of AIP" just before the conclusions. This is out of place and could be incorporated in the previous sections.

Answer: we believe that due to the no high incidence of AIP, the animal models are important in helping the research to test new pathogenetic hypotheses on AIP and new drugs for treating this disease. Thus, we have added a sentence to the paragraph (page 8, lines 12-14).

6. The conclusions should state the take-home message, so I find it inappropriate that the authors review their own findings in this place (last sentence).

Answer: We do not agree with the comment of the reviewer and the sentence has not been modified.

7. Some minor points: Near the middle of page 2: "B cells with the CD20 antibody" does not make sense

Answer. According to the suggestion of the reviewer, the sentence has been modified (Page 4, lines 1).

8. Near the middle of page 2: regarding instead of egarding

Answer. We apologize for the mistake. Egarding has been changed with regarding (Page 2, line 19).

9. Page 3, line 6 from the bottom. regarding instead of egardingt.

Answer. We apologize for the mistake. Egardingt has been changed with regarding (Page 3, line 28).

10. Throughout the paper: in vivo and in vitro should be written in italics Page 7, line 6 from the bottom:

Answer. Both in vivo and in vitro have been written in italics throughout the manuscript.

11. The same model used model??? Page 7, line 5 from the bottom: It is also possible "to" induce...

Answer. We agree with the reviewer comment and the sentence has been modified (page 8, lines 18-19).

12. In ref. 9, is the publication year 2011 (as indicated after the article title) or 2012?

Answer. Criteria were established in 2011, as reported in the title of the paper, and the article has been published in 2012.

## Reviewer 2

1. Major comments Conclusions; the authors must make comments on future possibilities of research and diagnostic tools in this or these diseases .Are they different diseases or different presentation of the same one.

Answer. We agree with the comment of the reviewer and a sentence has been added to the text (page 8, lines 31-32).

2. Minor comments In Animal models.. The same model used model.

Answer. We agree with the reviewer comment and the sentence has been modified (page 8, lines 18-19).

Thank you again for publishing our manuscript in the *World Journal of Gastrointestinal Pathophysiology*.

Sincerely yours,



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