



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 39250

Title: Hyperglycemia does not aggravate autoimmune pancreatitis and increases the percentage of regulatory T-cells in the spleen

Reviewer's code: 03699916

Reviewer's country: Denmark

Science editor: Xue-Jiao Wang

Date sent for review: 2018-04-22

Date reviewed: 2018-04-24

Review time: 2 Days

| SCIENTIFIC QUALITY | LANGUAGE QUALITY | CONCLUSION | PEER-REVIEWER STATEMENTS |
|--|---|--|---|
| <input type="checkbox"/> Grade A: Excellent | <input type="checkbox"/> Grade A: Priority publishing | <input type="checkbox"/> Accept | Peer-Review: |
| <input checked="" type="checkbox"/> Grade B: Very good | <input checked="" type="checkbox"/> Grade B: Minor language | (High priority) | <input checked="" type="checkbox"/> Anonymous |
| <input type="checkbox"/> Grade C: Good | polishing | <input type="checkbox"/> Accept | <input type="checkbox"/> Onymous |
| <input type="checkbox"/> Grade D: Fair | <input type="checkbox"/> Grade C: A great deal of | (General priority) | Peer-reviewer's expertise on the |
| <input type="checkbox"/> Grade E: Do not | language polishing | <input checked="" type="checkbox"/> Minor revision | topic of the manuscript: |
| publish | <input type="checkbox"/> Grade D: Rejection | <input type="checkbox"/> Major revision | <input type="checkbox"/> Advanced |
| | | <input type="checkbox"/> Rejection | <input checked="" type="checkbox"/> General |
| | | | <input type="checkbox"/> No expertise |
| | | | Conflicts-of-Interest: |
| | | | <input type="checkbox"/> Yes |
| | | | <input checked="" type="checkbox"/> No |

SPECIFIC COMMENTS TO AUTHORS

General comments: It is well known that a frequent and important complication of autoimmune pancreatitis (AIP) is diabetes. However, it is not so well known how the diabetes (hyperglycemia) affect AIP. From the clinical point in relation to treat the



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diabetic patients with AIP, it is important to investigate the effect of hyperglycemia on AIP. At present study, authors induced hyperglycemia in the MRL/Mp mice of AIP animal models by injection of STZ to investigate the effect of hyperglycemia on AIP. They demonstrated that hyperglycemia does not lead to an aggravation, instead may have an improvement of autoimmune pancreatitis. This study indicated that adjusting blood glucose concentration might not have a beneficial influence on the progression of autoimmune pancreatitis in diabetic patients. Specific comments: 1, STZ has been widely used to induce diabetic model in rats and mice as well as other animals because STZ can relatively and selectively destroy cells of pancreatic islet. Therefore the hyperglycemia is prominent in this type-1 diabetic model. However, how authors in this study can exclude the effect of STZ on AIP? This issue may be needed to discussion. 2, In this study, authors only overserved effect of hyperglycemia on AIP for one time point. As indicated by authors, A temporary or sustained hyperglycemia can be observed in AIP patients, therefore is may also important to study how different time periods of hyperglycemia affect AIP. 3, Authors suggested that adjusting blood glucose concentration might not have a beneficial influence on the progression of autoimmune pancreatitis in diabetic patients. However, authors may also have some other good options and suggestions for treating AIP in diabetic patients. Minor comments 1, About groups of animals In the legend of figure 1, authors indicated that 28-40 week old- MRL/Mp mice were i.p.-injected with streptozotocin (STZ) on day 1-5 (group: AIP+STZ), while one age-matched control cohort was i.p.-injected with the appropriate vehicle (group: AIP). However, in Figure 2 to figure 5, authors use STZ and Sham for two different groups. Please be identical! 2, In each figure (Figure 1 to 5), authors repeat "Box plots indicate the median, the 25th and 75th percentiles in the form of a box, and the 10th and 90th percentiles as whiskers." in each legend. It may not be necessary to repeat it in the legend of each figure.



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INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

- The same title
- Duplicate publication
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- No

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- Plagiarism
- No



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 39250

Title: Hyperglycemia does not aggravate autoimmune pancreatitis and increases the percentage of regulatory T-cells in the spleen

Reviewer's code: 00504708

Reviewer's country: United States

Science editor: Xue-Jiao Wang

Date sent for review: 2018-05-10

Date reviewed: 2018-05-10

Review time: 6 Hours

| SCIENTIFIC QUALITY | LANGUAGE QUALITY | CONCLUSION | PEER-REVIEWER STATEMENTS |
|---|--|--|---|
| <input type="checkbox"/> Grade A: Excellent | <input type="checkbox"/> Grade A: Priority publishing | <input type="checkbox"/> Accept | Peer-Review: |
| <input type="checkbox"/> Grade B: Very good | <input type="checkbox"/> Grade B: Minor language | (High priority) | <input type="checkbox"/> Anonymous |
| <input checked="" type="checkbox"/> Grade C: Good | polishing | <input type="checkbox"/> Accept | <input type="checkbox"/> Onymous |
| <input type="checkbox"/> Grade D: Fair | <input checked="" type="checkbox"/> Grade C: A great deal of | (General priority) | Peer-reviewer's expertise on the |
| <input type="checkbox"/> Grade E: Do not | language polishing | <input type="checkbox"/> Minor revision | topic of the manuscript: |
| publish | <input type="checkbox"/> Grade D: Rejection | <input checked="" type="checkbox"/> Major revision | <input type="checkbox"/> Advanced |
| | | <input type="checkbox"/> Rejection | <input checked="" type="checkbox"/> General |
| | | | <input type="checkbox"/> No expertise |
| | | | Conflicts-of-Interest: |
| | | | <input type="checkbox"/> Yes |
| | | | <input checked="" type="checkbox"/> No |

SPECIFIC COMMENTS TO AUTHORS

I acknowledge the authors' track record in exploring the basic pathophysiology of acute pancreatitis, However, the discussion is flawed as to extrapolation to clinical practice. It is virtually dogma that both acute and chronic hyperglycemia are deleterious to every



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organ system including the immune system. The migration and bacteriocidal capacity is hindered by acute hyperglycemia. Diabetics are clearly more prone to infection. The discussion is not fluent in some segments and requires more polishing. I would keep the title and other sections but redo the discussion. Noting esoteric references to support not treating hyperglycemia runs against the grain of clinical practice. What I would conclude is that aggressive therapy of hyperglycemia may not be warranted and hyperglycemia may have a surreptitious effect on the immune correlates of AIP within the pancreas. I would elaborate more on the detriments of the study including species difference and the unclear correlation of the parameters studies and the clinical course of AIP, I take exception with sentence linked to reference 5. Nowadays with EUS-FNA and laparoscopy, less patients with ultimate AIP need pancreas resection.

INITIAL REVIEW OF THE MANUSCRIPT

Google Search:

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- No



PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

Manuscript NO: 39250

Title: Hyperglycemia does not aggravate autoimmune pancreatitis and increases the percentage of regulatory T-cells in the spleen

Reviewer's code: 02549888

Reviewer's country: India

Science editor: Xue-Jiao Wang

Date sent for review: 2018-05-10

Date reviewed: 2018-05-15

Review time: 5 Days

| SCIENTIFIC QUALITY | LANGUAGE QUALITY | CONCLUSION | PEER-REVIEWER STATEMENTS |
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| <input type="checkbox"/> Grade C: Good | | <input checked="" type="checkbox"/> Accept | <input checked="" type="checkbox"/> Onymous |
| <input checked="" type="checkbox"/> Grade D: Fair | <input type="checkbox"/> Grade C: A great deal of language polishing | (General priority) | Peer-reviewer's expertise on the topic of the manuscript: |
| <input type="checkbox"/> Grade E: Do not publish | <input type="checkbox"/> Grade D: Rejection | <input type="checkbox"/> Minor revision | <input type="checkbox"/> Advanced |
| | | <input type="checkbox"/> Major revision | <input checked="" type="checkbox"/> General |
| | | <input type="checkbox"/> Rejection | <input type="checkbox"/> No expertise |
| | | | Conflicts-of-Interest: |
| | | | <input type="checkbox"/> Yes |
| | | | <input checked="" type="checkbox"/> No |

SPECIFIC COMMENTS TO AUTHORS

Comments on individual sections of the manuscript. Title needs to be a little catchy. In fact the title itself gives away the conclusion thereby precluding the interest in reading the article. Statement made in lines 47 to 49 of the abstract needs reframing as it is very



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misleading. What does the author wish to convey is a cause for some confusion. The keywords seem to be satisfactory. The statement made in the core tip that is line 68-72 should be rephrased. The clinical implications need to be stated in brief to develop interest in the mind of the reader. Background of the article is well formulated and gives a fair idea of the whole issue being addressed. Methods section is well planned. However a clear correlation to the patterns of assessment would have added to the quality of this section. The discussion component is too sketchy. Elaborate details of the cytomorphological- pathological correlation should have been elaborated. A brief implication on the clinical outcome should have been given which would have enabled the reader to consider new paradigms for future research. The illustrations, tables and statistical evaluation is quite good. The overall flow of the presentation is quite good. The referencing is adequate with relevant ones being used. All the necessary rules of conformity in basic research have been satisfactorily complied with. Reflections: The important fact highlighted by this research is the immunological basis for the effects of hyperglycemia on disease progression. The startling fact was improvement in the severity of the disease process which is a novel finding. The article provides a thought provoking insight into the effect of hyperglycemia on this not so well understood disease. The conclusions satisfactorily explains the results of the study. The quality of the manuscript is satisfactory. However a few statement are misleading or confusing. The main issue with the study is the way it can be extrapolated with the human disease. The study provides a new avenue for research that is to study the mechanism of improvement of the disease process by hyperglycemia.

INITIAL REVIEW OF THE MANUSCRIPT

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