

December 18, 2013.

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 6274-Review.doc).

**Title:** "*Helicobacter pylori* infection: host immune response, implications on gene expression and miRNAs"

**Authors:** Aline Cristina Targa Cadamuro, Ana Flávia Teixeira Rossi, Nathalia Maciel Maniezzo, Ana Elizabete Silva

**Name of Journal:** World Journal of Gastroenterology

**ESPS Manuscript NO:** 6274

We are very thankful for the comprehensive review performed to our manuscript referred above. We acknowledge that the reviewers' critiques were pertinent and contributed to improve our review article for the special issue celebrating the 20th anniversary of "World Journal of Gastroenterology" (*Helicobacter pylori*: Pathogenesis, prevention, diagnosis, treatment, and evidence-based medicine). In general, we agree with the reviewers that the manuscript was very extensive and needed a revision. The manuscript was reorganized and reduced, as well as the number of references. Also reduced the title and subtitle, and add the Coret tip. Therefore, we are now resubmitting a revised version of the manuscript and our response to the reviewers' comments.

**Reviewer 01559576:**

Many parts of this paper refer to cellular mechanisms of inflammatory response by Hp infection. However, the title indicates gene expression and miRNA by Hp infection in gastric carcinogenesis; thus the title does not correctly reflect this paper. Do the changes of miRNA listed in Table 1 relate specifically with Hp infection? If yes, state more clearly. If no, the table does not coincide with the title.

**Answer:** We agree with the reviewer that the title does not correctly reflect the content of the manuscript. Thus it was changed for "*Helicobacter pylori* infection: host immune response, implications on gene expression and miRNAs". The "Table 1: miRNAs involved in gastric carcinogenesis", presents a list of miRNA involved in precancerous gastric lesions and inflammatory processes induced by *H. pylori*, but also included studies on miRNA in gastric cancer not associated with *H. pylori* infection. Now, the title of Table 1 was corrected for "miRNAs involved in *H. pylori*-induced inflammatory and carcinogenic processes", and are listed only miRNA related with *H. pylori* infection (precancerous gastric lesions and gastric cancer).

**Reviewer 02520242:**

**Answers:**

- 1- The manuscript was reorganized into a more comprehensive and clearer format. The title and some subtitles were changed.
- 2- The part of the manuscript about "**Modulation of *H. pylori*-triggered host immune response**" was reorganized and we believe that is in a better sequence.
- 3- The "Table 1: miRNAs involved in gastric carcinogenesis", presents a list of miRNA involved in precancerous gastric lesions and inflammatory processes induced by *H. pylori*, but also included studies on miRNA in gastric cancer not associated with *H. pylori* infection. Now, the title of Table 1 was corrected for "miRNAs involved in *H. pylori*-induced inflammatory and carcinogenic processes", and are listed only miRNA related with *H. pylori* infection (precancerous gastric lesions and gastric cancer).

**Reviewer 00484021:**

1. The title is not accurately reflects the major topic and contents of the review.

**Answer:** We agree with the reviewer that the title does not correctly reflect the content of the manuscript. Thus it was changed for "*Helicobacter pylori* infection: host immune response, implications on gene expression and miRNAs".

2. In the abstract, there are no contents about the "Bacterial virulence factors" and "Modulation of *H. pylori*-triggered host immune response". Actually, these two sections taken half space of this review.

**Answer:** These two topics were included in the abstract.

3. According to the title, there should be a section about "*Helicobacter pylori* infection". However, the first paragraph of "**Bacterial virulence factors**" is the content of the bacteria infection. This paragraph is not related to the virulence factors and should be several sentences describing the role of virulence factors in the bacterial infection. The authors could put this paragraph to **Intro** or add this section.

**Answer:** We reorganized the introduction with a brief description on the bacteria and relationship with pre-cancerous lesions and gastric cancer. Then we focus on bacterial infection and their virulence factors, as well as the role of virulence factors in the bacterial infection.

4. The last paragraph in "**Bacterial virulence factors**" is not related to and should be focus on the virulence factors. This paragraph could be several sentence summaries the role of bacterial virulence factors played in the course of the bacterial infection.

**Answer:** The last paragraph was included along with the contents of bacterial infection.

5. The first paragraph of "**Modulation of *H. pylori*-triggered host immune response**" is an unrelated forward words, this paragraph is not related to immune response. It seems the authors like to write too much this kind of contents in every section. Please delete or shorten them.

**Answer:** We agree with the reviewer and this first paragraph was withdrawn from the manuscript.

6. The section "**Modulation of *H. pylori*-triggered host immune response**" only summarize the modulation of *H. pylori*-triggered innate immune response/inflammation response, there is only little content of acquired immune response. Please change the title or add the related contents.

**Answer:** This section was also reorganized in a better sequence, but as *H. pylori* triggers mainly the innate immune response, this section focuses in more detail this mechanism and to a lesser extent the adaptive immune response.

7. The first paragraph of page 9 belongs to page 8, last paragraph, before the description of TLR2.

**Answer:** The section "**Modulation of *H. pylori*-triggered host immune response**" was reorganized, so this paragraph was changed.

8. There are some repetitive discussions of the same topic in different section, such as "virulence factors", "microRNAs" in "**Modulation of *H. pylori*-triggered host immune response**"....

**Answer:** We agree with the reviewer and try to eliminate repetition, despite the issues are interconnected.

9. The section "***H. pylori* infection deregulates the expression of genes involved in inflammatory response and cell kinetics**" is too long, and the structure and route was not thoughtful devised, just was discussed ref by ref. Please shorten it in a proper order.

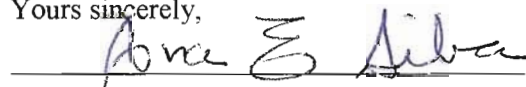
**Answer:** The reviewer is correct. ~~This section was revised and~~ described more broadly.

10. The first 4 paragraphs of "**miRNAs regulating the inflammation induced by *H. pylori***" should be shortened; there is no need to introduce too much background of miRNAs and please focus on the major topic.

**Answer:** We agree with the comment of reviewer and this paragraph was shortened.

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

Yours sincerely,



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