Dear colleagues,

I am pleased to submit the revised version of the manuscript entitled **"Role of non-Helicobacter pylori gastric Helicobacters in H. pylori-negative gastric mucosa-associated lymphoid tissue lymphoma"** (Manuscript NO.: 86046, Minireviews) for consideration for publication in the *World Journal of Gastroenterology*. Please allow me to express my sincere gratitude for your valuable and pertinent suggestions. We resolved all issues in the manuscript based on the peer review report and here we make a point-by-point response to each of the issues raised in the peer review report. The suggested changes are highlighted in the main text.

1. **Reviewer #1 - Specific Comments to Authors:** 该文章选题新颖，阅读文献广泛，评论分析条例清晰，**有良好的**临床指导作用.

   Reply:

   Dear reviewer #1,

   Thank you once again for your valuable review. We have worked diligently to ensure that our research encompasses fresh perspectives and a comprehensive examination of relevant literature. Additionally, we have strived to present our findings in a manner that offers practical and effective clinical guidance. If you have any further suggestions or feedback, please do not hesitate to share them with us.

2. **Reviewer #2 - Specific Comments to Authors:** Dear Authors, thank you for submitting the manuscript entitled, "Role of non-Helicobacter pylori gastric Helicobacters in H. pylori-negative gastric mucosa-associated lymphoid tissue lymphoma" in WJG. The manuscript is well written and compactly summarized, and the topic is interesting and sounds nice. However, some major criticisms should be addressed as below.

   Major) 1. What the reader most wants to know is why NHPH-positive cases of H. pylori-negative gastric MALT lymphoma often occur in patients who respond to eradication therapy. Furthermore, how is NHPH involved in the pathogenesis of MALT lymphoma? You state only that further research is needed to elucidate this, but what specific research and experiments should be done? Please add to your discussion. I appreciate that in the section "Pathogenesis of Gastric MALT Lymphoma" in this paper, you specifically mention the association of H. pylori infection with the development of H. pylori-positive gastric MALT lymphoma, citing recent findings. Can the same be said of NHPH? On the contrary, the NHPH infection rate is low (a few percent), which means that the majority of the remaining patients are not expected to benefit from eradication therapy. However, there are some cases of NHPH-negative gastric MALT lymphoma that do respond to eradication therapy. Why is this, and isn't it possible that NHPH infection is present but just not identified? Or can we not assume that NHPH is just a trigger for carcinogenesis and that there are other multiple major factors in the subsequent sequence that lead to tumorigenesis? Please add your own opinions on this important subject to the section of discussion.

Reply:

Dear reviewer #2,

Thank you for your pertinent suggestions. The comments you made on our manuscript were very important to the improvement of its quality and we are grateful for your crucial help. In our study, we acknowledge that the majority of available information regarding the pathogenesis of NHPH-positive gastric MALT lymphoma is derived from extrapolations of *H. pylori*-positive GML. In this regard, we emphasize the need for future studies to investigate the underlying mechanisms and conduct specific experiments that can provide a more comprehensive understanding of these phenomena. Following your valuable comments, we have incorporated future research directions in the "CLINICAL IMPLICATIONS AND RESEARCH PROSPECTS" section encompassing these aspects (YELLOW). Furthermore, in the main text, we highlighted the current understanding of the role of NHPHs in the pathophysiology of this neoplasia (GREEN). Finally, we have improved the figures that depict the proposed pathogenic model, enhancing their clarity and accuracy. There is currently a lack of comprehensive epidemiological studies to accurately determine the prevalence of NHPHs-positive gastric mucosa-associated lymphoma (GML). Moreover, there is indeed some limitation in the diagnostic tools available for the identification of NHPHs. In light of your valuable comments, we have highlighted these aspects in the main text (BLUE).

3. **Reviewer #3 - Specific Comments to Authors:** In recent years, the role of non-Helicobacter pylori (NHPHs) in the development of Helicobacter pylori negative gastric MALT lymphoma and its response to bacterial eradication therapy have attracted increasing attention from researchers. This review explored the current understanding of the role of NHPHs in Helicobacter pylori-negative gastric MALT lymphoma and proposes future prospects, as well as their potential response to bacterial eradication therapy, which has some novelty and reference value.

Reply:

Dear reviewer #3,

We are pleased to know that you found our work to be novel and of reference value. It is our intention to contribute to the scientific community's understanding of the complex relationship between NHPHs and *H. pylori*-negative gastric MALT lymphoma, and to shed light on potential treatment options. Your feedback is encouraging and motivates us to continue exploring this important field. If you have any further suggestions or areas of interest, we would be grateful to receive them. Thank you once again for your valuable review.

Sincerely,

Fabrício Freire de Melo

Fabrício Freire de Melo, PhD

Professor,

Federal University of Bahia, UFBA