

Dear editors and reviewers:

Thank you for your letter and your comments concerning our manuscript entitled “Clinical Value of Serum Pepsinogen in the Diagnosis and Treatment of Gastric Diseases” (Manuscript ID: 84814). These comments are valuable and very helpful for revising and improving our work, as well as the important guiding significance to our research. We have studied the comments carefully and have made correction which we hope meet with approval. Revised portion is marked in blue in the manuscript. The main corrections in the paper and the responds to the reviewer’s and editor’s comments are as following:

Reviewer #1

- 1. Comment from reviewer:** The authors did not discuss the metabolism of the pepsinogen extruded from the stomach and the complications of the long-term use of PPI. All these matters were focused in the work. Review Pharmacol Res. 2000 Mar;41(3):265-81. doi: 10.1006/phrs.1999.0586. Pepsinogens: physiology, pharmacology pathophysiology and exercise.

Response: Thanks for your kind comments. These contents have been shown in the “PEPSINOGEN AND HELICOBACTER PYLORI (*H. PYLORI*) INFECTION” section in the manuscript.

Reviewer #2

- 1 . Comment from reviewer:** There is an “ABC classification”, a serological screening method that assesses the risk of gastric cancer by assessing pepsinogen and H. pylori antibody titers, which should also be mentioned.

Response: Thank you for your comment and attention to that detail. The relevant content was added in the “PEPSINOGEN AND GASTRIC CANCER” section of this manuscript.

Reviewer #3

- 1. Comment from reviewer:** This review article describes the usefulness of blood pepsinogen measurement for screening diagnosis of Helicobacter pylori infection, gastric ulcer, atrophic gastritis and gastric cancer. A number of review papers have been published on pepsinogen. In addition, there are a number of misstatements, for

example in the journal title, and although it is important to go back to the starting point and discuss the issue, no clinical significance can be found in this paper.

Response: Thank you for your comments. We regret that the manuscript does not meet your requirements. Although there have been some articles summarizing pepsinogen in recent years, they are usually aimed at a certain disease. Our work summarized the application of serum pepsinogen in several major gastric diseases and summarized the latest research progress in recent years. At the same time, according to your comments, we have further added the latest research progress, carefully checked the full text and corrected the mistakes. Serum pepsinogen detection in the diagnosis and treatment of stomach diseases are not uniform enough, and there are still shortcomings. This paper summarized the clinical value of serum pepsinogen 1, pepsinogen 2 and pepsinogen 1/pepsinogen 2 in the diagnosis of *helicobacter pylori* infection, atrophic gastritis and gastric cancer, in order to provide more research ideas for readers. It is hoped that pepsinogen will play a greater role in the prevention, screening and diagnosis of atrophic gastritis and gastric cancer, as well as in the prediction of postoperative recurrence and metastasis of gastric cancer.

Company editor-in-chief

- 1. Comment from editor:** The author must supplement and improve the highlights of the latest cutting-edge research results, thereby further improving the content of the manuscript.

Response: Thank you for your kind comments. According to your comment, we have added and supplemented the highlights of the latest cutting-edge research results in the manuscript.

Looking forward to hearing from you.

Thank you and best regards.

Yours sincerely,

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