

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 5548-review.doc).

Title: *Helicobacter pylori* and interleukin-8 in gastric cancer

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Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 5548

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

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

(1) Reviewer 1 was very favorable to our manuscript without any suggestions.

(2) Reviewer 2 asked us to enhance the accuracy of language used. Per this recommendation, the manuscript was copyedited by a professional English language services company, Harrisco.

(3) Reviewer 3 was very favorable to our manuscript and suggested a small mistake in the “core tip” section. We did edit the problematic sentence in that section.

(4) Reviewer 4 was favorable and requested a new figure illustrating the functions and molecular mechanisms of IL-8 in gastric cancer (angiogenesis, proliferation of cancer cells). We agree with the review’s suggestion and have provided a new figure (Fig. 1) in the revised manuscript.

- (5) Reviewer 5 suggested a number of revisions. i) There were some paragraphs not relevant to the topic in this manuscript. We edited and moved some sentences in "Introduction" and "A role for IL-8 in gastric cancer" sections. ii) IL-8 inhibitors against gastric cancer in poorly introduced. The reviewer is correct that the therapeutic potential of IL-8 against gastric cancer is still unknown. However, considering the small molecules developed for targeting IL-8 signals for prostate and colon cancer, anti-IL-8 therapy is a promising therapeutic approach for gastric cancer. iii) Since CXCR-1 and CXCR-2 are not main topics of this study, we removed the CXCR-1 and CXCR-2 in the "Conclusion" section.
- (6) Reviewer 6 was unfavorable to our paper. While the reviewer was interested in the subject matter presented, he/she indicated that the manuscript lacked novelty and innovation. The revised manuscript is supplemented with a new figure (Fig. 1), and comprehensively reviews key articles related to IL-8 and H pylori in gastric cancer. We believe these changes would help the readers in understanding the topics.

3 References and typesetting were corrected

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

Sincerely yours,

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Reviewer letter from Journal

#1

This is a review of studies exploring the roles of interleukin-8 and *Helicobacter pylori* in gastric cancer development. The manuscript comprehensively reviewed key articles addressed on this issue and well organized them. This review would help the readers efficiently to know current understanding of this issue. This reviewer thinks this manuscript is potentially worth publishing in *World J Gastroenterology*.

#2

The authors should further enhance the accuracy of language used.

#3

Excellent, well written work. I only signal a mistake in the "core tip" section: line 2 lacks of something.

#4

In this paper, Lee et al. review the roles of interleukin (IL)-8 in gastric cancer, signals involved in *Helicobacter pylori*-induced IL-8 expression in gastric cancer, and anti-IL-8 therapies for gastric cancer. The mortality rate of gastric cancer is still high, and the improvement of therapeutic strategies is indispensable. Anti-IL-8 therapy is one of the promising new therapies for gastric cancer, and thus, this paper deals with an important topic. In addition, this paper is generally well written. However, I suggest one point to make this paper more intelligible: The authors should show the functions of IL-8 in gastric cancer (angiogenesis, proliferation of cancer cells, etc) and their molecular mechanisms schematically as a Figure.

#5

This manuscript is composed of many paragraphs not necessarily related to direct interactions between Hp and IL-8, thus sounds redundant. This manuscript should be improved by concise description. The authors presented several IL-8 inhibitors, however, the challenges of these agents on 'gastric cancer' are poorly introduced. Without these information, the therapeutic potential of these agents on gastric carcinogenesis is still unknown. "Mere IL-8 inhibitors" do not necessarily mean therapeutics against gastric cancer development induced by IL-8 and Hp. In conclusions, the authors described that IL-8 receptor CXCR-1 and -2 are up-regulated in gastric cancer and its microenvironment. However, only small number of references is introduced concerning this topic, so that the conclusions do not

reflect the text.

#6

I'm afraid that the novelty and innovation of the research are not achieved... The form of the manuscript requires systematization since it doesn't clearly summarize the current state of knowledge and lacks in producing a focused description of a topic but is mostly a report on some found references. The topic itself, however, is quite interesting.