

September 27, 2013

Editor, *World Journal of Gastroenterology*

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 5059 Membrane bound mucins HO SB FINAL 9-27-13).

Title: Membrane-bound mucins and mucin terminal glycans expression in idiopathic or *Helicobacter pylori*, NSAID associated peptic ulcers.

Author: Yaron Niv, Doron Boltin, Marisa Halpern, Miriam Cohen, Zohar Levi, Alex Vilkin, Sara Morgenstern, Vahig Manugian, Erica St. Lawrence, Pascal Gagneux, Sukhwinder Kaur, Poonam Sharma, Surinder K. Batra, Samuel B. Ho

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 5059

We would like to thank the reviewers for their helpful comments. The manuscript has been improved according to the suggestions of reviewers in that the format has been updated. Revisions have been made according to the suggestions of the reviewers and are highlighted in yellow in the text. A point-by-point response to the Reviewers is as follows:

Reviewer 01002233:

1.Method: The author used many immunohistochemistry staining (such as MUC1, MUC4 MUC17, SNA and ECA) for *H. pylori*-associated or non-steroidal inflammatory drug (NSAID)-associated patients. The author may need to use polyclonal *H. pylori* antibody to analyze the *H. pylori* expression compared to distinct MUC stains in both gland and foveola cells.

Response: We used standard clinical practice for *H. pylori* diagnosis for this study, which used standard clinical criteria based on histology using hematoxylin and eosin staining and rapid urease testing. If available, breath tests for *H. pylori* diagnosis were also used. Furthermore, if hematoxylin staining was equivocal, special stains such as Giemsa and toluidine blue could be used at the discretion of the pathologist. This process has been shown to be highly accurate for *H. pylori* diagnosis in routine clinical practice (*Am J Surg Pathol* 2006;30:357–361). This was clarified in the Methods section. Specific immunostaining for *h. pylori* was not available, and other methods such as multiple biopsies, culture, etc, were not available and would require a prospective study. Given the methods used we believe the addition of *h. pylori*

immunostaining would have changed the results little, if any. This is a limitation of the study that was emphasized in the discussion section.

2.Results: The 1st paragraphs in page 12, “MUC17 protein was strongly expressed on the apical membrane of the mucosal epithelial cells and in some small positive vacuoles within the foveola surface cells”. The English sentence writing of this manuscript is confusing. The author needs to modify the sentence correctly and please provide some references.

Response: This sentence was revised and references made to the appropriate figure for illustration.

3.Discussion: There are some sentences without provide reference. Please support some references.

Response: References were added to several sentences as requested. These include references 24, 10, 25, 26, 27.

4.Figure 1 in page 25, The Figure 1A need to show the error bar and Figure 1B and 1C need to show the some arrows to mark clearly the MUCs and SNA expression.

Response: The standard deviation error bars were added in Figure 1A. In Figure 1B and 1C arrows were used and described in the figure legend.

Reviewer 01804177:

In this search the AA evaluated the pattern of different mucins, as proctetive gastric factors, in different gastric ulcer. The AA reported significant variations of mucin levels in different ulcers and support rationally the results. The search appears of clinical and speculative interest. Although the study is retrospective on small sample of patients, it is able to lead significant speculations about mucosal damage in course of H. pylori infection and NSAID intake. The search is well designed and written. Methods and statistical methods are appropriate. The results are clearly reported. Graphics and figures highly illustrative. The bibliography is complete. Minor criticism In Introduction section in 4 line : minor error must be correct : idopathic ulcer in idiopathic ulce. The study can be accepted without changes.

Response: The error in line 4 was corrected.

Reviewer 00505201:

Your paper is same with <http://www.ncbi.nlm.nih.gov/pubmed/22576713>

Response: We have already indicated that the paper indicated here had been withdrawn due to inadvertent overlap, and the submitted paper represents a completely new and corrected paper.

In addition, the References and typesetting were corrected. Please contact me if there are any further questions. Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely,



Samuel B. Ho, M.D.
Section Chief, Gastroenterology
VA San Diego Healthcare System
Professor of Medicine in Residence
University of California, San Diego