

Dear Editors of "World Journal of Clinical Oncology",

We are sending you the revised manuscript entitled **"GASTRIC CANCER MOLECULAR CLASSIFICATION BASED ON IMMUNOHISTOCHEMISTRY AND IN SITU HYBRIDIZATION: ANALYSIS IN WESTERN PATIENTS AFTER CURATIVE-INTENT SURGERY"** (Manuscript NO: 63296, Retrospective Study).

The manuscript was revised according to the reviewers' comments and responses to each question are provided below. Text modifications are highlighted in red.

We are glad for the opportunity to send the revised manuscript to this renowned journal.

Thank you in advance for your time.

Respectfully,

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Response to the Reviewer(s)' Comments

REVIEWER #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade A (Priority publishing)

Conclusion: Minor revision

Specific Comments to Authors: Finding a cost-effective and easier way to identifying the molecular subtypes of GC is quite important in clinics. In this MS, the authors retrospectively evaluated tumor tissues from 287 patients with GC, and MSI status, E-cadherin and p53 expression were analyzed by IHC, and EBV by ISH. Following by evaluating the clinicopathological characteristics and long-term survival of GC based on the subgroups of molecular classification. There are some shortcomings need to be further noticed.

1. Introduction part, In the third paragraph, the author mentioned 2 common classification method for GC in molecular way. However, in the next paragraph, they said “both molecular classifications are based on 4 major signatures”. Here, from their description, the two classification methods do not share some common signatures, for example EBV? Please make it clear or revise it.

The sentence has been corrected, and the 4 signatures mentioned refer to molecular classifications in general.

2. Give a brief introduction why you choose these 4 markers to make the classification, why not others?

Indeed, immunophenotypic classifications use some markers deriving from the previous molecular classification, such as EBV (for the EBV subtype), MLH1 (for the MSI subtype), p53 (for the CIN subtype), and epithelial cadherin (E-cadherin) (for the GS subtype). So, we added a brief explanation regarding the markers used in the study.

3. Showing some clear and magnifying pictures of your staining, for example, showing the different distribution of E-cadherin in cells.

As requested, we provide an additional figure with images of the IHC and ISH findings.

4. The conclusion that “The IHC/ISH analysis was able to distinguish subtypes of GC with distinct clinicopathological characteristics and prognosis.” is not accurate enough. Prospective study is needed to come to this conclusion. You can only get a possibility from the retrospective study.

As questioned, we adapted the sentence mentioned by the reviewer at the conclusion and included in the study some additional limitations regarding the technique and validation of the results in the revised manuscript.

EDITORIAL OFFICE’S COMMENTS

SCIENCE EDITOR:

1 Scientific quality: The manuscript describes a retrospective study of the gastric cancer molecular classification based on immunohistochemistry and in situ hybridization. The topic is within the scope of the WJCO.

(1) Classification: Grade B;

(2) Summary of the Peer-Review Report: The authors retrospectively evaluated tumor tissues from 287 patients with GC, and MSI status, E-cadherin and p53 expression were analyzed by IHC, and EBV by ISH. Flowing by evaluating the clinicopathological characteristics and long-term survival of GC based on the subgroups of molecular classification. The questions raised by the reviewers should be answered;

(3) Format: There are 2 tables and 3 figures;

(4) References: A total of 34 references are cited, including 8 references published in the last 3 years;

(5) Self-cited references: There are 2 self-cited references. The self-referencing rates should be less than 10%. Please keep the reasonable self-citations (i.e. those that are most closely related to the topic of the manuscript) and remove all other improper self-citations. If the authors fail to address the critical issue of self-citation, the editing process of this manuscript will be terminated; and

(6) References recommendations: The authors have the right to refuse to cite improper references recommended by the peer reviewer(s), especially references published by the peer reviewer(s) him/herself (themselves). If the authors find the peer reviewer(s) request for the authors to cite improper references published by him/herself (themselves), please send the peer reviewer's ID number to editorialoffice@wjgnet.com.

The Editorial Office will close and remove the peer reviewer from the F6Publishing system immediately.

2 Language evaluation: Classification: Grade A.

3 Academic norms and rules: The authors provided the Biostatistics Review Certificate, the Institutional Review Board Approval Form. The Written informed consent was not provided. No academic misconduct was found in the Bing search.

[The informed consent statement was waived by the local Ethics Committee because of the retrospective nature of the study.](#)

4 Supplementary comments: This is an invited manuscript. The study was supported by Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP agency). The topic has not previously been published in the WJCO.

5 Issues raised:

(1) The authors did not provide the approved grant application form(s). Please upload the approved grant application form(s) or funding agency copy of any approval document(s);

[As requested, we have included the approval term for the research grant obtained by FAPESP.](#)

(2) The authors did not provide original pictures. Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor; and (3) The “Article Highlights” section is missing. Please add the “Article Highlights” section at the end of the main text.

The original editable figures in Power Point and Tables were added in the review of the manuscript.

The topic "Article Highlights" was previously included in the manuscript submitted shortly after the conclusion of the article. The item is highlighted in red in the new submission.

6 Recommendation: Conditional acceptance.

Company editor-in-chief: I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Clinical Oncology, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office’s comments and the Criteria for Manuscript Revision by Authors.