Ruo-Yu Ma
Science Editor
World Journal of Gastroenterology

April 2, 2019

RE: **Manuscript 47612 "Recent advances in gastric cancer early diagnosis"** by Necula L. et al.

Dear Editor,

Thank you and the reviewers for the careful evaluation of the above-referenced manuscript. We are very grateful for your comments and suggestions, which were valuable in improving the quality of our manuscript. We have considered them carefully and addressed them in full in the revised manuscript. All the changes made in the revised manuscript are highlighted and explained in an itemized, point-by-point response to the **<u>Reviewers Comments</u>** (see enclosed).

We also completed and formatted the manuscript submission according to WJG guidelines for authors and Editor suggestions and highlighted the corrections in the updated version of the manuscript. Also, the citations were introduced in manuscript using EndNote program (PMID and DOI citation are added and all authors are listed) and there are no repeated references.

We did not add a language verification certificate because three of the reviewers appreciated the Language Quality as "Grade A: Priority publishing". Moreover, we have checked and corrected the entire manuscript for language mistakes with the help of a native speaker of English.

We hope that the revised manuscript is now acceptable for publication in World Journal of Gastroenterology.

We look forward to hearing from you.

Sincerely,

Mihaela Chivu-Economescu.

Response to Reviewers Comments:

Comments: The authors have made a good review of new strategies in gastric cancer early diagnosis. I have the following suggestions. 1. In Figure 1, the "Minimally invasive sampling" should include specimen including peripheral blood, urine or saliva, stomach wash/gastric juice, as described in the ABSTRACT. Meanwhile, Figure Legend of Figure 1 should be revised as "Possible non-invasive diagnostic biomarkers for early-stage gastric cancer". 2. In Tables 1 and 2, "Sensitivity", "Specificity" and "Origin of specimen" of each biomarker should be added.

Response: We are very grateful for your comments and appreciations. We followed your suggestions and modified Figure 1, by including all sample types mentioned in the abstract, and its Legend, as well as completed Tables 1 and 2 with *"Origin of specimen"* and *"Sensitivity / Specificity"* columns.

Comments: "This is a very nice review on molecular biomarkers of gastric cancer. However, there are some limitations of these biomarkers. Most of biomarkers can be found in advanced stage of gastric cancer, not in early stage. So clinical significance of these biomarkers should not be overestimated. This limitation should be clearly described in Conclusion."

Response: We are grateful for your comments and appreciations. We agree with your remark and completed our conclusions (see page 18):
Many of these biomarkers are not specific for the early stages, being detected in advanced stages of GC, and cannot be used for early GC detection. However, some of recently discovered circulating molecules (miRNAs, lncRNAs, circRNA) hold the promise for developing new strategies for early diagnosis of GC, being able to discriminate between early stage of GC and healthy subjects, with a sensitivity more than 77.5%.

Comments: The authors review summarized the recently discovered circulating molecules such as miRNAs, lncRNAs, circRNA, which hold the promise to develop new strategies for early diagnosis of gastric cancer. This review was thought to be significant and useful. And this article was well written in detail.

Response: We thank the reviewer for the comments and appreciations.

Reviewer 03478635:

Comments: *"This study describes about the gastric cancer diagnosis in terms of circulating molecules such as miRNAs, lncRNAs, and circRNA. DNA methylation pattern in gastric cancer is very important for diagnosing the stage of gastric cancer".*

Response: We thank the reviewer for the comments.