

Dear professors,

Thank you very much for your constructive suggestions, which improved our manuscript significantly. And we have made the related revisions according to your suggestions.

Reviewer #1:

Scientific Quality: Grade B (Very good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Specific Comments to Authors: This is an interesting study of novel biomarkers for early detection of gastric cancer. This study suggested that plasma exosomal hsa_circ_0079439 was upregulated in GC patients. It could distinguish EGC and advanced gastric cancer patients from healthy donors, which indicated that plasma exosomal hsa_circ_0079439 might be a potential biomarker for the diagnosis of GC in both the early and late stages. The study is overall well written, and the results are well discussed. Comments: 1. The manuscript requires a minor language editing. 2. Images should be updated. 3. References list should be edited.

Answer: 1. We have revised this manuscript according to suggestions. This manuscript's language has been edited by professional biomedical editing company and the language editing certificate is attached included in the revision files. 2. In order to get high-resolution images, we have improved their resolution ratio and organized them into a single PPT file using original pictures. 3. We have revised the references according to the guidelines.

Reviewer #2:

Scientific Quality: Grade C (Good)

Language Quality: Grade C (A great deal of language polishing)

Conclusion: Minor revision

Specific Comments to Authors: This study explored the plasma exosome hsa_circ_0079439 as a novel GC biomarker. The paper can combine theory with practice, from solving clinical problems, draw a more reliable conclusion, has a certain theoretical significance and practical value. The charts and graphs are complete, but most of them are poor in clarity. In addition, there are questions about the lack of significant differences in expression levels and serum levels of other standard serum biomarkers, including CA19-9, CA72-4, AFP, and CA125, between GC and HD patients.

Answer: 1. We have improved pictures' resolution ratio and organized them into a single PPT file using original pictures. 2. As shown in Figure 6, the serum levels of CEA, CA19-9 and CA125 were apparently higher in AGC patients than in HDs ($p < 0.05$). When comparing the levels of CA72-4 and AFP, there was no significant difference between AGC patients and HDs. However, the serum levels of CEA, CA19-9, CA72-4, AFP and CA125 could not be used to distinguish EGC patients from HDs. These results are consistent with previous study that standard serum biomarkers are lack sensitivity and specificity for early detection of GC. Besides, in our clinical work, many EGC patients

were diagnosed by health examination, and their serum tumor markers are usually within normal range. Therefore, it is necessary to identify novel biomarkers with higher accuracy for the early detection of GC. Based on the results of exosomal whole-transcriptome RNA sequencing, bioinformatic analysis and dd-PCR tests, we found that plasma exosomal hsa_circ_0079439 could serve as a novel biomarker for the early detection of GC.

Thank you again for your help from the editorial department and reviewers. I hope your journal will do better and become a benchmark for the industry of Gastroenterology in the future.