Dear Editor,

Please find point-to-point response to reviewers' comments bellow.

Manuscript Title: **Atrophic gastritis and gastric cancer tissue miRNome analysis reveal hsa-miR-129-1 and hsa-miR-196a as potential early diagnostic biomarkers**

Manuscript ID: 71456

Reviewer 1:

In this article, the authors showed changes in expression level of hsa-miR-196a-5p and hsa-miR-129-1-3p in the gastric carcinogenesis pathway and confirmed these miRNAs as a possible noninvasive biomarker for atrophic gastritis and gastric cancer. These results support the Correa gastric carcinogenesis cascade. The new findings have scientific and practical implications for the prevention of gastric cancer. The manuscript is recommended for publication in the World Journal of Gastroenterology.

Reviewer 2:

1. *Page 26, "Table 1 Demographic characteristics of profiling and validation cohorts Validation cohort", there were too many subjects in the GC group with unknown H. pylori infection status, and in this group, with a limited sample size and so many sample losses, is the statistical conclusion persuasive?*

   Response:

   Authors thank for the comment and are aware of "Unknown" status of H. Pylori in the Validation cohort. The statistical conclusions related to *H. Pylori* infection status (made in the publication) include only Profiling cohort where only 3 out of 20 GC patients have the missing status.

2. *Tissue analysis in the profiling (n = 60) cohort revealed that hsa-miR-196a-5p expression in tissue could be significant for discrimination between CON and AG or GC. But, no significant expression changes about hsa-miR196a-5p were observed in validation (n = 65) cohort in plasma samples by using RT-qPCR. It is unreasonable to make inferences that thsa-miR-196a-5p expression in tissue could be significant for discrimination between CON and AG or GC. This inference should be verified in at least one cohort.*

   Response:

   Authors appreciate the comment. However, our results regarding the tissue hsa-miR-196a-5p does not contradict with the validation results, while the Validation cohort includes the plasma and not tissue samples, suggesting that maybe this miRNA is not excreted into the blood circulation. In the Discussion we added that discrimination "analysis suggests great potential of hsa-miR-196a-5p expression in

tissue for discrimination of AG and GC in contrast to CON" and "Therefore, further studies are needed to confirm this finding". Thereby we agree that it is not a final conclusion and rather a tendency. Moreover, as this result is not final therefore it is not described in the Conclusion section.

Re-reviewer:

Agree with the author's reply and agree to publish.

Response:

Thanks for your comments.