

**Manuscript NO:** 51569

**Updated title:** miR-96-5p silence induces cell apoptosis in gastric adenocarcinoma

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Dear editor,

Thank you for your letter with regard to our manuscript (51569). We greatly appreciate for your time in editing our manuscript and the valuable comments and suggestions from reviewers. Accordingly, we have revised the manuscript and highlighted in the updated version of the manuscript (In purple). The point-by-point answers to the comments are listed as below. We would like to re-submit this revised manuscript to *World Journal of Gastroenterology* and hope it is acceptable for publication in the journal.

**Reviewer #1**

**(Comment 1)** There are few errors that should be corrected before publishing. In statistics section > “mean  $\pm$  standard derivation” should be corrected as “deviation” Distal metastasis should be “distant metastasis” P value should be “p value” miRNA-96-5p also inhibits the proliferation, migration and epithelial mesenchymal transition (EMT) of gastric cancer cell by down-regulation of FoxQ1 and few other (Casp..) pathways could be mentioned. Adjacent normal tissue should be detailed as distance in cm. 3-4 centimeters?

**(Response)** Thanks for your comment. According to your suggestions, we have revised the incorrect description, including “mean  $\pm$  standard derivation”, distal metastasis and P value. In addition, we supplemented the discussion of miRNA-96-5p as following: “Notably, previous study has shown that miR-96-5p exerts the inhibiting role in cell proliferation and migration by down-regulation of FoxQ1 in gastric cancer cells<sup>[31]</sup>. Contradictorily, a recent study has demonstrated that miR-96-5p exerts the promoting effect on cell progression by directly targeting FOXO3 in gastric cancer<sup>[32]</sup>. Consistent with this recent study<sup>[32]</sup>, this study found that miR-96-5p inhibitor induced cell apoptosis in MGC-803 cells.” Furthermore, adjacent

normal tissue has been detailed as following: “ adjacent normal tissues (distance in 3-4 cm from the tumor tissue)”.

## **Reviewer #2**

**(Comment 1)** Methods: first line: "level 3" needs explanation.

**(Response)** Thanks for your comment. The level 3 miRNA expression profile data mean that the data have been processed and standardized.

**(Comment 2)** Download date and time is missing.

**(Response)** Thanks for your comment. We have added the download date and time. The miRNA expression profile data (level 3, processed and standardized data) and the corresponding clinical information of GAC were downloaded from TCGA (<https://portal.gdc.cancer.gov/>) on February 11, 2019.

**(Comment 3)** There is no explanation about changing the numbers from 452 to 299. Based on which selective criteria (first line on results)? There is no such criteria in method section.

**(Response)** Thanks for your comment. The number 452 means that a total of 452 samples were obtained from this dataset, including 410 GAC tumor samples and 42 normal control samples. However, the number 299 means that a total of 299 differently expressed miRNAs (DEMs) were identified between GAC and normal control samples, including 225 upregulated and 74 downregulated miRNAs. The number 452 represents samples, while the number 299 represents differently expressed miRNAs.

**(Comment 4)** "... identified between GAC and normal control samples, including 225 upregulated and 74 downregulated miRNAs. ..." The number of

normal control sample was 42. It is not known if these figures belong to which group.

**(Response)** Thanks for your comment. The numbers you mentioned represent different meanings. As mentioned above, the number “225” and “74” represents differently expressed miRNAs, while the number 42 represents samples. It means that a total of 299 differently expressed miRNAs (DEMs) were identified between 410 GAC tumor samples and 42 normal control samples, including 225 upregulated and 74 downregulated miRNAs.

**(Comment 5)** "A total of 20 GAC patients and 20 healthy subjects were included in this study. " What does it mean? There is no explanation in this regard in method section. Table 1 is for 40. Why 299 in abstract and results?

**(Response)** Thanks for your comment. The number 299 means that a total of 299 differently expressed miRNAs (DEMs) were identified between GAC and normal control samples, and the GAC and normal control samples were obtained from TCGA. However, the number 40 means that the sum of paired tumor tissues and adjacent normal tissues, and a total of 20 paired tumor tissues and adjacent normal tissues were collected from GAC patients who underwent surgery in our hospital between October 2017 to October 2018. Sample source is different.

Thank you once again for considering the publication of our manuscript. Should there be any questions, please do not hesitate to contact us.

Yours sincerely,

En-Xu Bi