

Dear editor and reviewers,

Thank you very much for your comments and professional advice. These opinions help to improve academic rigor of our article. Based on your suggestion and request, we have made corrected modifications on the revised manuscript. Meanwhile, the manuscript had be reviewed and edited by language services company. We hope that our work can be improved again. Furthermore, we would like to show some important details as follows, other details of the specific changes are in the manuscript.

**Point-by-point response to the reviewers' comments.**

**Comments for the Authors:**

**Reviewer #1**

**Comment 1:** *How was the sample size calculated?*

**Response 1:** We appreciate your comments. Which are valuable for improving the accuracy of the manuscript. We used the PASS software to calculate the sample size for the logrank test for survival analysis. Of course, our study sample size is relatively small, as retrospective collection of sample sizes is indeed limited, so we also recognize that our sample size is inadequate, but this may not affect the reliability of our conclusions. Thank you again for your comments. We hope you will be satisfied with our response.

**Comment 2:** *The title: "circular clock gene" must be replaced with "circadian clock gene". Moreover, the population selected must be made explicit. The study refers to a multicentric analysis of gastric cancer patients in China. Please modify the title.*

**Response 2:** We are very grateful for your comments. We have made modifications based on your suggestion to circadian clock gene in the manuscript. Also, our patients were collected from one hospital, the Second Hospital of Lanzhou University, and it was not a multicenter study. Thank you for your valuable comments again, and our title could perhaps be revised to read: High expression of circadian clock gene NPAS2

is associated with progression and poor prognosis of gastric cancer: A single-center study

**Comment 3:** *The abstract: “circular clock gene” must be replaced with “circadian clock gene” moreover, the authors should give some background before the objective.*

**Response 3:** Thanks for your kind suggestions. We have revised the related part of the manuscript and abstract to ensure the statement is accurate. We added some research background before the objectives, the revision is as follows: The prognostic assessment of patients after surgical resection of gastric cancer patients is very important. However, the role of NPAS2 expression in gastric cancer remains unknown.

**Comment 4:** *Line 82 Core tip: first line, please delete “in this study”.*

**Response 4:** Thanks for your suggestions. We have made the deletion.

**Comment 5:** *Was the ethnicity homogeneous in the selected sample?*

**Response 5:** Thanks for your suggestions. The ethnicity is homogeneous in the selected sample.

**Comment 6:** *Line 143 “all specimens were anonymous” please refer to “pseudonymous” or “deidentified” because in the anonymization process, there is no possibility to link the specimen to the id of the patient.*

**Response 6:** Thanks for your suggestions. We have changed the anonymity to pseudonymous.

**Comment 7:** *Table 1: please refer to sex not gender. Sex is biological while gender is socio-cultural.*

**Response 7:** We modified gender to sex. Thank you!

## **Reviewer 2#**

**Comment 1:** *Biostatistics is good. I would only like to comment about considering to use Bonferroni correction due to multiple comparisons?*

**Response 1:** We appreciate your comments. Our comparisons between two groups were performed using Pearson chi-square test and have been continuously corrected, Bonferroni correction is generally used for correction of multiple comparisons and may not be suitable for our study. Thank you very much for your comments, which made us re-learn Bonferroni correction, which will be very important for our future studies.

## **Reviewer 3#**

**Comment 1:** *The authors should supply the whole image of IHC staining (such as strong, middle, weak) in GC tissues and normal stomach tissues.*

**Response 1:** We appreciate your comments. We have provided ICH images of NPAS2 expression in three typical patients.

**Comment 2:** *The authors need investigate the role of NPAS2 in GC in vitro and in vivo.*

**Response 2:** We are very grateful for your comments. We plan to continue to explore the role of NPAS2 in vivo and in vitro in our next studies.

We sincerely hope that this revised manuscript has addressed all your comments and suggestions. We appreciated for reviewers' warm work earnestly, and hope that the correction will meet with approval. Once again, thank you very much for your comments and suggestions.