

Editors-in-Chief

*World Journal of Gastrointestinal Oncology*

### **Covering Letter**

Dear Editors and Reviewers,

Thank you very much for your painstaking work and thank you for your letter and comments. Accordingly, we have revised the manuscript entitled **“Identification of a Nine-Gene Prognostic Signature for Gastric Carcinoma Using Integrated Bioinformatics Analyses” (Manuscript NO: 55848)**, and would like to resubmit it for your consideration. We have addressed the instructive comments raised by the reviewers, and the amendments are marked by single underlining in the revised manuscript. Point by point responses to the reviewers’ comments are listed for your consideration. We would like to express our sincere thanks to the editors and reviewers for their constructive and meaningful comments. We are so grateful that you have offered us this opportunity to resubmit our manuscript. We hope that the revised version of the manuscript is now acceptable for publication in *World Journal of Gastrointestinal Oncology*.

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We look forward to hearing from you at your earliest convenience.

Yours sincerely,  
Jin-Lan Jiang

## Response to the Reviewers

### # Major comments:

Q1: The current state of the art literature on gene expression risk models in GC must be included in the introduction. So far only references from other tumor entities have been mentioned (add e.g. Cho JY et al., Clin Cancer Res 2011; Kim HK et al., Pharmacogenomics J 2012; Bauer et al., Ann. Oncol., 2017).

**Response:** Thank you very much for your constructive comment. We fully agree with this suggestion. Accordingly, we have added additional literature on gene expression risk models in GC in the revised manuscript (see: "Introduction" section).

Q2: There is an error on page 5: .....For example, Yin et al constructed a five-gene signature based on data from TCGA and GEO databases that accurately predicted GC prognosis[6]..... Yin et al report about glioblastoma and not about GC!

**Response:** Thank you very much for this comment. We apologize for this mistake and have now changed the original reference to Zhao L et al., J Cell Physiol 2019. We hope this will address your concerns (see: "Introduction" section).

Q3. Hence, the added value of the present work in comparison to the previous works (mentioned above) in GC must be addressed in the discussion

**Response:** We thank the reviewer for this constructive comment, with which we fully agree. Accordingly, we have added a discussion on the value of the present work in comparison to previous GC research according to your suggestion (see: "Discussion" section).

Q4. The number of patients in the test collective should be mentioned in the M&M section, not only in the corresponding chart.

**Response:** Thank you very much for your constructive comment. We fully agree with your point. Accordingly, we have now included the number of patients in the test collective in the revised manuscript (see: "Materials and Methods" section).

Q5. Fig6: The images are not convincing. The tissue is even for an experienced pathologist difficult to identify /analyze. In 6D and H the dots show the same tissue. There is probably no cancerous tissue included. Others seem swapped (C and G)

**Response:** We thank the reviewer for this comment. We completely agree that Figure 6 is not convincing and have now removed it and the corresponding text in the revised manuscript. We hope this will address your concerns.

Q6: Fig8: This is a nice-looking figure. However, in the context of this paper it provides no further information. I recommend the omitting of this figure.

**Response:** We really appreciate your positive comment. Accordingly, we have now moved the figure to supplementary materials (Supplementary Figure 1). We hope the revised version of the manuscript is now acceptable.

Q7: Further limitations that have to be mentioned in the discussion: The efficiency of the nine-gene signature should be confirmed in a larger number of GC patients. Only a very limited amount of normal samples was included in the differential expression analyses. In multivariate Cox regression, one variable per minimal five events should be included. Comparison: Conventional prognostic factors; other multi-gene assays?

**Response:** Thank you so much for your comment. Accordingly, these limitations are now discussed in detail in the revised manuscript. We hope the revised version of the manuscript is now acceptable.