

Cover Letter

Dear Editors and Reviewers,

Thank you very much for taking the time to review this manuscript. We truly appreciate all your valuable comments and suggestions. We hereby submit the revised manuscript to be considered for publication in the World Journal of Clinical Cases. We have addressed all the questions and provided a point-by-point reply, which is attached to the end of this letter.

Here, I confirm that all authors who contributed significantly to the work have read and approved the manuscript, and the manuscript has not been published and is not being considered for publication elsewhere. Thank you again for your consideration. I look forward to your reply.

Sincerely,

Shukun Yao

Email: shukunyao@126.com

Replies to Editors' Comments

#Company editor-in-chief:

I have reviewed the Peer-Review Report, the full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Clinical Cases, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors. Before final acceptance, uniform presentation should be used for figures showing the same or similar contents; for example, "Figure 1 Pathological changes of atrophic gastritis after treatment. A: ...; B: ...; C: ...; D: ...; E: ...; F: ...; G: ...". Please provide the original figure documents. Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor. In order to respect and protect the author's intellectual property rights and prevent others from misappropriating figures without the author's authorization or abusing figures without indicating the source, we will indicate the author's copyright for figures originally generated by the author, and if the author has used a figure published elsewhere or that is copyrighted, the author needs to be authorized by the previous publisher or the copyright holder and/or indicate the reference source and copyrights. Please check and confirm whether the figures are original (i.e. generated de novo by the author(s) for this paper). If the picture is 'original', the author needs to add the following copyright information to the bottom right-hand side of the picture in PowerPoint (PPT): Copyright ©The Author(s) 2022. Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical

lines and do not segment cell content. Please upload the approved grant application form(s) or funding agency copy of any approval document(s).

Reply: Thank you very much for your helpful suggestions. In the revised manuscript, we have revised the abstract, main text, tables and figures according to the revision requirements.

#Science editor:

The authors present a study on the proteomics of colorectal cancer, highlighting the role of CDKN2A as a potential prognostic biomarker. The study is well-written, correctly designed and both methods and results are described in great details. Considering the increasing role of proteomics in oncology treatment, this study is of significant scientific interest.

Reply: We truly appreciate your kind comments, thank you very much.

Replies to Reviewers' Comments

#Reviewer 1:

Q1. Several words throughout the manuscript appear to be merged. Please correct it.

R1. Thank you very much for your helpful suggestion. The merged words have been corrected. For details, please refer to the revised manuscript with tracked changes.

Q2. Major vocabulary and grammar revision (including the figure legends).

R2. Thank you. We apologize for the vocabulary and grammar errors. We have performed a detailed revision and further polished the revised manuscript. Please refer to the revised manuscript with tracked changes and the new language certificate by a professional English language editing company.

Q3. CDKN2A gene mutation should be further explained in the introduction (not in the discussion).

R3. Thank you very much for your valuable suggestion. We have further explained the CDKN2A gene mutation in the introduction as suggested:

- Introduction: "On the basis of the biological central dogma, gene mutation plays an important role in the occurrence and development of malignant tumors, including CRC. Previous studies have revealed possible gene mutations in patients with CRC; however, their effects are not completely consistent. For example, Pearlman et al^[4] proposed that cyclin-dependent kinase inhibitor 2A (CDKN2A) mutation had nothing to do with CRC risk; in contrast, Lee et al^[5] found that CDKN2A was a tumor suppressor, and Li et al^[6] insisted that CDKN2A was an oncogenic gene that was significantly correlated with poor prognosis. Therefore, gene mutation alone could not fully explain the occurrence and metastasis of tumors: the

perspective of proteins, the executors of function, were also needed.”

#Reviewer 2: None.

Reply: Thank you very much for taking the time to review this manuscript, and we really appreciate your kind comment.