

Ms. Ref. No.: 70444

Title: Clinical and prognostic significance of PGAM5 and Parkin in advanced colorectal cancer

World Journal of Clinical Cases

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Dear Editor,

Thank you very much for your attention and the reviewers' comments on our paper *Clinical and prognostic significance of PGAM5 and Parkin in advanced colorectal cancer*.

We have revised the manuscript according to your kind advices and the reviewers' detailed suggestions. Enclosed please find the responses to the reviewers. We sincerely hope this manuscript will be finally acceptable to be published on *World Journal of Clinical Cases*. Thank you very much for all your help and looking forward to hearing from you soon.

Here blow is our description on revision according to the reviewers' comments.

Response to Reviewer:

Thank you for your appreciation to this article and the kind advices.

The reviewer's general comment:

The manuscript "Clinical and prognostic significance of PGAM5 and Parkin in advanced colorectal cancer and its correlation" aimed to assess protein expression of PGAM5 and Parkin as a diagnosis and predictive biomarker for colorectal (CRC). They used immunohistochemistry on 100 CRC tissues from patients to determine the expression of these two proteins. The authors found that PGAM5 and Parkin were higher in cancerous than in adjacent non-cancerous tissues. These two proteins were both cytoplasmic and positively correlated within advanced CRC tissues. The authors suggest PGAM5 and Parkin as new clinical biomarkers for CRC. However, future studies are needed to clarify the contradictory role of these two proteins in CRC.

Major comments: 1. The authors used immunohistochemistry to determine protein expression in CRC tissues. The findings in the paper could be supported with gene expression and protein levels of PGMA5 and Parkin using other methods such as western blot.

The author's Answer: Thanks for your kind advice and we revised it according to the comment. We measured the protein levels of GMA5 and Parkin using western blot.

2. The findings that PGAM5 and Parkin are higher in CRC tissues contradict the role of PGAM5 and Parking in improving mitochondrial function and cellular health. In addition, other studies, including the one cited by the authors and others (Turk J Gastroenterol. 2020 Mar;31(3):211-220), found lower protein levels of parkin in advanced CRC tissues from patients. Many altered proteins in cancers display this dichotomous role (tumor suppressor and tumor promoter). The discussion could be more concise and focused on helping clarify this dichotomy in the role of PGAM5 and Parkin in CRC. Further studies are needed to reconcile the contradictory findings.

The author's Answer: Thanks for your kind advice and we revised it according to the comment.

3. The authors mentioned that PGAM5 might promote CRC development through other mechanisms like energy and/or lipid metabolism. Could the authors expand on this with specific examples?

The author's Answer: Thanks for your kind advice and we revised it according to the comment.

Minor comments. 1. The "and correlation" might be omitted from the title.

The author's Answer: Thanks for your attention and kind suggestion. And we revised it according to the comments (title).

2. Many typos and grammatical issues are present throughout the paper need attention.

The author's Answer: Thanks for your attention and kind suggestion. And we improved the English grammar with the help of an English speaker.

Thank you and all the reviewers for the kind advice.

Sincerely yours,

Mingjun Sun