May 6, 2020

Dear editor,
Please find attached files of revised manuscript in word format

Title: Clinical Significance of SQSTM1/P62 and NF-κB expressions in pancreatic carcinoma

Author: Zhao-yang Zhang 1, Sen Guo 2, Rui Zhao 3, Zhi-peng Ji 4, Zhuo-nan Zhuang 5

Name of Journal: World Journal of Gastrointestinal Oncology

Manuscript NO: 55256

First of all, thank you for your careful guidance of this article. Revision has been made according to the suggestions of the reviewer:

Reviewer: 02856362

Interesting study. I recommend to accept this manuscript after a minor editing.

Reply:

Thank you for your advice.

We have done the minor editing to this manuscript according to the journal's guideline.

Reviewer: 02855134

Overall, the study of SQSTM1/P62 and NF-κB expressions in pancreatic carcinoma is very well designed and the results are very interesting. How about the limit of the study? Please discuss it. Manuscript requires a minor language editing.

Reply:

Thank you for your advice.

After receiving the comments, we read the article carefully and found some small loopholes in the language of the article and made modifications.

We have added the limit of this study on page 10, lines 6 to 8.

Reviewer: 02857752

High expression of p62 was found in small cell lung cancer, breast cancer, liver cancer and other malignant tumor cells. As a scaffold and adaptor protein in signal transduction pathway, P62 participates in the regulation of multiple signal transduction pathways, including Ras/Raf/MAPK and NF-κB pathway, which can enhance the proliferation, migration and invasion of tumor cells. The over accumulation of p62 and the imbalance of NF-κB signal make mice more likely to produce tumors. It has been confirmed that KRAS mutation can induce the overexpression of p62, which promote the growth of pancreatic ductal adenocarcinoma. This study of SQSTM1/P62 and NF-κB expressions in pancreatic carcinoma is very interesting. The rising of AP-1 caused by P62 can lead to the expression of NF-κB in pancreatic cancer cells. P62 expression was also found decreased when NF-κB activity was inhibited. It is thus proved there is a circular relationship between p62 and

NF-κB, which leads to a continuous activation of NF-κB pathway. In this study, the authors explored the expression of p62 in pancreatic cancer and the relationship between its clinicopathological features. Their correlations with clinicopathological features and recurrences were also evaluated to determine whether P62 expression levels could be used to predict the prognosis in patients with follicular thyroid cancer. The manuscript overall is well written. The study design is good, sample are acceptable. Methods of immunohistochemistry are reasonable, and in detail. Minor comments: 1. The manuscript requires an editing according to the journal's guideline. 2. Figures are too small, please provide the images in high resolution. 3. Data in tables are very interesting. However, the tables require editing.

Reply:

Thank you for your advice.

We have edited the manuscript according to the journal's guideline.

We have uploaded the original pictures within PowerPoint.

We have edited the tables according to the journal's guideline.

Science Editor

(1) The authors did not provide original pictures. 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; and (2) The "Article Highlights" section is missing. Please add the "Article Highlights" section at the end of the main text.

Reply:

Thank you for your advice.

We have uploaded the original pictures within PowerPoint. And we have added the "Article Highlights" section at the end of the main text on page 10, lines 15 to page 11, 18.

Thank you again for publishing our manuscript in the World Journal of Gastrointestinal Oncology.

Sincerely Yours,

Zhuonan Zhuang, MD,PhD.