Name of journal: World Journal of Gastroenterology

Manuscript NO.: 31706

Column: Basic Study

Title: Role of Δ133p53 isoform in NF-κB inhibitor PDTC-mediated growth inhibition of MKN45 gastric cancer cells

Authors: Hongmei Zhang, Xiaoguang Sang, Yanze Wang, Can Cui, Li Zhang and Wansheng Ji

Dear Prof. Jing Yu and Reviewers,

Thank you very much for your efforts on our work. According to your and reviewers' constructive comments, we have carefully checked and revised the relevant contents. The detailed revisions have been highlighted in the revised manuscript, and we hope that the improved manuscript can be reconsidered in the journal. Many thanks for your continued attention again.

Yours sincerely,

Wansheng Ji

Reply to the reviewers' comments

Reviewer 1

Comments 1: Please write a summary of less than 100 words to outline the most innovative and important arguments and core contents in your paper to attract readers.

Reply: We add the summary (core tip) as follows: "Intestinal-type of gastric cancer develops from chronic gastritis. Δ133p53 isoform has been recently identified as an oncogenic actor that is pivotal in *Hp*-driven progression of chronic gastritis to gastric cancerogenesis. These results suggest that Δ133p53 isoform is required in PDTC-induced inhibition of MKN45 gastric cancer cells, and disturbance in the cross-talk between p53 and NF-κB pathways is a promising target in pharmaceutical research for the development of treatment strategies against intestinal-type gastric cancer." Thanks.

Comments 2: about audio core tip (In order to attract readers to read your full-text article, we request that the author make an audio file describing your final core tip, it is necessary for final acceptance. Please refer to Instruction to authors on our website or attached Format for detailed information)**.**

Reply: According to the request, we make and upload the qualified audio file. Thanks.

Reviewer 2

Comments 1: Please provide the "Highlighted contents" here, which is a necessary content. See the requirements as follows.

Reply: We provide supplementary contents as follows according to your kind suggestion. Thanks.

The updated contents:

COMMENTS

Background

Accumulating evidence suggests that some p53 isoforms function as p53 co-activators (e.g., p53β); others, its antagonists that possess oncogenic characteristics (e.g., Δ133p53α). Results obtained by our research group and others demonstrate a clear link between *Hp* infection, gastritis, and gastric cancerogenesis, with Δ133p53 isoform being essential in the process. Thus, changes in the cross-talk between inflammatory and apoptotic pathways likely play an important role in gastric cancerogenesis, especially in cases of the intestinal type.

Research frontiers

Expression patterns of p53 isoforms instead of mutant p53 are significant for various malignant diseases. Δ133p53α has been proven to be a good indicator that could be used for the diagnosis and prognosis of breast and ovarian cancers. Moreover, Δ133p53α is also essential in *Hp*-driven gastritis and cancerogenesis.

Innovations and breakthroughs

Disturbed cross-talk between p53 and NF-κB pathways is possibly involved in the progression of chronic gastritis to cancerogenesis. Δ133p53, among other p53 isoforms, is key to the association of *Hp* infection with gastritis and cancerogenesis. These results indicate that Δ133p53 is an important aspect of the NF-κB inhibitor PDTC-mediated biological effect.

Applications

Δ133p53 could serve as a promising target for diagnosis, treatment, and prognosis of gastric cancer.

Terminology

p53 isoforms are produced by alternative splicing of *TP53*. At least twelve isoforms have been identified. Existence of these isoforms results in the regulation of p53 function. Disturbance in the pattern of these p53 isoforms has been observed to be involved in cancerogenesis in various tissues.

Peer review

This is a very significant study that involved investigation of the role of delta133p53 isoform in nuclear factor-kappa B inhibitor pyrrolidine dithiocarbamate-mediated growth inhibition of MKN45 gastric cancer cells. However, I recommend some modifications. In the results section, they mentioned the association between p65 and delta133p53 mRNA expression in MKN45 cells.

However, this result indicates that delta133p53 and p65 are correlated with each other, and does not mean that decreasing mRNA expression of p65 results from that of delta133p53. Therefore, to support these results further, they should prove that these results do not appear after treatment with delta133p53 inhibitors.

Reviewer 3

Comments 1: Please use [a, b, c,] *etc* instead of [*, #,] *etc*.

Reply: We replace "* or #" by "a, b or c" in figure 1 and 2. Many thanks for your conditioned attention again.

Reply to Editor's comments:

Comments 1: A FINAL REMINDER: The following is a list of all required documents that authors have to submit. Please confirm that all these documents are properly prepared before submitting the revision.

Reply: According to your kind suggestion, all of these relevant files have been prepared and uploaded. Many thanks for your continued attention again.

Reviewer 02569136

Comments 1: This is a very good study that investigated the role of the delta133p53 isoform in the nuclear factor-kappa B inhibitor pyrrolidine dithiocarbamate-mediated growth inhibition of MKN45 gastric cancer cells. However, I recommend some modifications. In the results section, they mentioned the corelation of p65 and delta133p53 mRNA expression in MKN45 cells. However, this result means that delta133p53 and p65 are correlated with each other, which does not mean that decreasing mRNA expression of p65 results from that of delta133p53. So, to further support these results, they should prove that these results do not appear when you treat the inhibitors to delta133p53.

Reply: Firstly, thank you very much for your efforts and positive comments on our work. According to your kind suggestion, the relevant contents have been carefully checked and revised, and all of these relevant revised contents have been highlighted in the revised manuscript. Many thanks for your kind suggestion again.