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20707-Answering reviewers

COMMENTS TO AUTHORS

The manuscript, ESPS #20707, reports the results of studies on the expression of p-STAT3 and VEGF in gastric mucosa of rats subjected to MNNG administration for up to 40 days. Using a large number of animals (120), the authors concluded that the mucosal expression of STAT3 as well as VEGF shows significant increase in animals with dysplasia and gastric tumor, and that the VEGF expression exhibits a positive correlation with p-STAT3.

Q: While the authors claim that the obtained data are of major significance, the fact is that the work is mainly confirmatory, and provides no new evidence as to the role of STAT3 in the up-regulation in VEGF expression and the etiology of MNNG-induced gastric precancerous lesion formation and gastric cancer. Hence, the exaggerated claims made in the "Discussion" should be tempered.

R: we agree with you about the relationship between STAT3 and VEGF.

In this study, we found that expressions of p-STAT3、VEGF in model groups measured by immunohistochemistry and Western Blot were increased significantly compared with control groups (Fig. 3); the expression of p-STAT3 and VEGF in tissue with dysplasia was higher than in tissue with gastritis and tissue with atrophy and the expression of p-STAT3 and VEGF in tissue with tumor was substantially higher than tissue in control group ($P<0.001$, $P<0.001$, respectively). We did the correlation analysis and found that there was a strong correlation between them, so in our study, we just found that the there was high expression of p-STAT3 and VEGF in MNNG-induced gastric precancerous lesion formation and gastric cancer and the strong correlation between them. So further research is needed to show whether STAT3 can up-regulate VEGF expression in MNNG-induced gastric precancerous lesion formation and gastric cancer. So we have deleted some sentences about the claim about the relationship between p-STAT3 and VEGF in the first paragraph of "Discussion" which is showed as followings:

We performed this study to examine the significance of p-STAT3 and VEGF expression in the process of gastric cancer from gastritis, atrophy gastritis and dysplasia induced by administration of MNNG in rats. The results from this study showed that STAT3 is partially responsible for the process from chronic gastritis to gastric carcinoma induced by MNNG and is significantly related the expression of VEGF in the process. Although overexpression of p-STAT3 in primary tumor sites has been recognized as a predictor of poorer survival in many malignancies, including gastric cancer [25, 26], to best of our knowledge, this is the first time to report that p-STAT3 is also persistently activated from chronic gastritis to gastritis carcinoma induced by administration of MNNG in rats, which is positively associated with the expression of VEGF.

Q: Moreover, the entire manuscript needs thorough language editing, including spelling, composition, and wedding out "newly created words, i.e., damagement ?

R: We are sorry for some mistakes in language spelling and composition. we did the language editing carefully. Thank you very much for your comments.

Q: The method section does not provide the basis and description of how and who conducted the reported morphological assessment. Same applies to "Extraction of gastric tissue samples for Western Blot analysis. Which stomach segments were used and how the tissue was acquired ? Also, see the last sentence on page 4, 2000og ???

R: Thanks for your questions, we improved the method section according your comments which is as followings:

1. Provide the basis and description of how and who conducted the reported morphological assessment.

Measurement of morphological changes

The rats were terminated respectively in the end of 15th week, 25th week and 40th week. Stomaches were separeated immediately and were opened along long axis to record the conditions as follows: edema, hyperemia, erosion, ulcer or mass, and took photoes by two pathologies who were unaware of the groupings of animals. Then the stomoach tissue was divided into two parts, one was stored in -80℃ low temperature refrigerator and another was put into tubes with 4% paraformaldehyde (PFA).

2. Which stomach segments were used and how the tissue was acquired?

R. We used the whole layer stomach segments in this study because we found that some tumors were occurred in inherent muscular of stomach. We added the information in the page 6.

3. The last sentence on page 4, 2000og ???

R: we are sorry for this mistake, it should be 2000 rpm…… Thanks a lot.