ANSWERING REVIEWERS

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 2429-review.doc).

Title: Expression of zinc finger protein 139 in gastric cancer and its clinical significance

Author: Yong Li, Qun Zhao, Li-Qiao Fan, Li-Li Wang, Bi-Bo Tan, Yan-Li Leng, Yu Liu, Dong Wang

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 10574

Reviewer No. 2559655

The manscript titled "Expression of ZNF139 in gastric cancer and its clinical significance" by Li et al describes the clinical significance of ZNF139 expression in gastric cancer and its prognosis. Although the observations are interesting, the manuscript is ill-prepared for the Publikation and needs to be revised significantly. Major concerns:

1. there seems to me several kinds of GC, hence, it would be meaningful to give details in the kind/type of GC.

Answer:

In present study, there were 34 well-differentiated adenocarcinoma cases, 32 moderately-differentiated adenocarcinoma cases, and 42 poorly-differentiated adenocarcinoma cases according to pathological types.

We have provided this into paper.

2. fig1: the images B and F appears to be non-cancerous and lymphatic tissue. Hence, representation of images containing tumor in gastric units/ tubular structures would be helpful to strengthen the arguments of the authors.

Answer:

We are so sorry for this mistake. Now we have changed the images.

3. there are several concerns regarding the statistical analysis performed:

a) please provide the exact p-values.

Answer:

We have provided exact p-values in paper.

b) which statistical test has been used to correlate the ZNF139 expression and clinical parameters in table 1?

Answer:

The chi-square(X^2) test was applied in table 1.

c) what does that negative line indicates in figure 2? Is this just ZNF negative cells or does this also include weakly positive cells, 1-2?

Answer:

In figure 2, negative line indicated negatively expressed ZNF139 in GC tissues. Weakly positive tissues was not included in it.

d) was the statistical analysis performed by professional stastistician?

Answer:

Yes. Professional statistician of Hebei Medical University has checked statistical analysis of this paper.

4. legends to figure 2 and 3 are missing.

Answer:

We have provided the legends in paper.

5. how many independent times the IHC for all analyzed proteins was performed? And is there any second independent observer who prrformed the scoring?

Answer:

The IHC test in this study repeated 3 independent times.

2 pathology physician performed the scoring independently.

6. on what basis the authors suggest ZNF as an oncogene, when there is GC without ZNF expression?

Answer:

There are so many oncogenes involved in carcinogenesis and development of GC, and till now researchers haven't found an oncogenes which could 100% positive expressed in GC. So we consider that oncogenes other than ZNF139 may be play a role in carcinogenesis and development of GC.

7. i am not quite sure, but i would call ZNF as a TNM-dependent prognosis marker but not an independent! Please clarify with a statistician.

Answer:

Thanks for the reviewer's suggestion. There was relationship between ZNF139 and TNM of gastric cancer. However, we consider that ZNF139 is a prognosis marker, and we have revised this content in paper.

8. the introduction and results parts can be expanded appropriately.

Answer:

We have done some revision according to suggestion of reviewer.

9. there are several grammatical and spelling mistakes throughout the manuscript.

Answer:

We are so sorry for this mistake. Now we have corrected them.

2.

Reviewer No. 289648

In this manuscript, the authors demonstrated that expression level of ZNF139 in GC cells was correlated to GC patient survival rate as well as the expressions of Bcl2 and

Bax. The correlations among ZNF139 expression and caspase-3 activation and cell apoptosis were also shown. The data is convincing and the manuscript is clear written. The significance of the manuscript would be improved if the authors could show that reduce expression (siRNA etc) or overexpression ZNF139 could have an impact on Bcl2 and BAX expression in GC cells as well as apoptosis of GC cells.

Answer:

Thanks for the suggestion of reviewer No. 289648. This paper is part of our a series of studies from National Natural Science Foundation of China. In another study, we used ZNF139-siRNA to inhibit ZNF139 in gastric cancer cell line MKN28, and we found that after ZNF139 was inhibited, expression of Bcl-2 decreased, whereas Bax increased simultaneously(Yong Li *et al*. Regulatory mechanism of ZNF139 in multi-drug resistance of gastric cancer cells. Mol Biol Rep. 2014 Feb 11. PMID: 24515389). In present paper, we want to explore the clinical significance of ZNF139 in gastric cancer tissues. If we add RNA interference experiment, the content of this paper will be too complex. We'll elaborate mechanism of ZNF139 in gastric cancer cells in the future.

3.

Reviewer No. 2446647

Anti-TNF-a agents, such as infliximab, adalimumab, gomumuab, oral tofacitinib, and vedolizumab, for ulcerative colitis are described in this paper. The effects of these drugs on other types of inflammatory diseases other than UC should be described.

Answer:

We have added some relevant content in the part of Discussion.