

August 15, 2017

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 34921-Revised manuscript.doc).

**Title:** Nuclear heat shock protein 110 expression is associated with poor prognosis and hyperthermo-chemotherapy resistance in gastric cancer with peritoneal metastasis

**Author:** Akiharu Kimura, Kyoichi Ogata, Bolag Altan, Takehiko Yokobori, Erito Mochiki, Mitsuhiro Yanai, Norimichi Kogure, Toru Yanoma, Masaki Suzuki, Tuya Bai and Hiroyuki Kuwano

**Name of Journal:** *World Journal of Gastroenterology*

**ESPS Manuscript NO:** 34921

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

(1) Response to Reviewer No. 01850720

We wish to express our appreciation to the Reviewer for his or her insightful comments, which have helped us significantly improve the paper.

Comment:

*Interesting and well written paper describing the role of HSP110 in gastric cancer with peritoneal metastasis.*

Response:

We thank the Reviewer for this pertinent comment.

In this article, we could show that nuclear HSP110 expression in gastric cancer patients with peritoneal metastasis might be a new sensitivity marker and a therapeutic target for patients with tolerance to existing hyperthermo-chemotherapies.

(2) Response to Reviewer No. 00503460

We wish to express our appreciation to the Reviewer for his or her insightful comments, which have helped us significantly improve the paper.

Comment:

*The figures are jam-packed with data.*

Response:

We thank the Reviewer for this pertinent comment.

As you pointed out, Figure 3 seems to be jam-packed with data. Therefore, we explained the detail of this figure in the figure legends.

(3) Response to Reviewer 02941657

We wish to express our appreciation to the Reviewer for his or her insightful comments, which have helped us significantly improve the paper.

Comment 1: *The author did the study with 14 gastric cancer patients with specific treatment and experimented on one specific type heat shock protein expression as a prognostic biomarker.*

Response 1:

We thank the Reviewer for this pertinent comment.

In this article, we could show that nuclear HSP110 expression in gastric cancer patients with peritoneal metastasis might be a new sensitivity marker.

*Comment 2: For the result in table 1, the author should not use word "relationship" on the heading of table. This table only showed characteristic of 2 group- populations and the similarity.*

Response 2:

We thank the Reviewer for this pertinent comment.

We assessed statistically the relationship of nuclear HSP110 expression with clinicopathological factors of 14 gastric cancer patients in Table 1. Therefore, we used the word "relationship" on the heading of Table 1. As a result, there were no significant relationships observed between nuclear HSP110 expression and clinicopathological factors in gastric cancer tissue.

*Comment 3: The author showed risk analysis table 2 that showed remarkable progress free survival rate relative to all risk factors. The result should be more explained in text.*

Response 3:

We thank the Reviewer for this pertinent comment.

We have therefore added the following text (p.14, lines 6-9):

**Univariate analyses of clinicopathological factors affecting progression free survival rates after surgery is shown in Table 2. Relative risk of all factors including HSP110 expression was more than 1. However, they were not statistically significant.**

*Comment 4: For conclusion and discussion, the drug resistance of cisplatin is showed but not for TS-one. Some confounding factors should effect the progress free survival, not only heat shock protein expression. The author should put additional comment*

Response 4:

We thank the Reviewer for this pertinent comment.

We have therefore added the following text (p.17, lines 11-12):

**Thirdly, we assessed only drug resistance of cisplatin. Indeed, drug resistance of S-1 also might affect the progress free survival in gastric cancer patients.**

*Comment 5: I agree with conclusion that the author may test on more drugs those use in clinical practice or compare between drugs.*

Response 5:

We thank the Reviewer for this pertinent comment.

In the future, we need to evaluate more drugs and compare between drugs.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

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