Format for ANSWERING REVIEWERS

June 3, 2015

Dear Editor:

Thank you very much for sending us the Reviewers' reports on our manuscript (**ESPS Manuscript NO:** 18117). **Title:** "Overexpression of Chaperonin Containing TCP1, Subunit 3 Predicts Poor Prognosis in Hepatocellular Carcinoma ". Particularly, we would like to thank the Reviewers and Editors for their valuable comments and criticisms. Please find enclosed the edited manuscript in Word format (file name: 18117reviewed.doc). According to the Reviewers and Editors' recommendations, we have revised carefully our manuscript with colored text (Red).

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Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 18117

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 No. 03015689 reviewer

(1) Question: The control sample should be larger.

Answer: At first, we have enrolled 143 patients with HCC who had undergone hepatecotmy, and acquired fresh-frozen specimens in recent years. The follow-up periods for these deleting 39 patients were no more than 3 years, which could possibly affected the reliability for prognosis, although patients with CCT3 high expression in nuclei of HCC cells also have lower overall survival rate comparing to the low expression group in these 143 patients. All 104 patients enrolled in our study had detailed medical records and complete follow-up records, Which including HCC patients with

viral hepatitis (HBV and HCV) and patients without viral hepatitis. The patients with HBV-associated HCC take the most part in the total, which was similar to ediology distribution in our country. This study tried to explored the possibility of applying CCT3 in predicting the prognosis in a number of patients and possible mechanisms for this phenomenon. Some similar studies in HCC such as (1,*TLR3 expression correlates with apoptosis, proliferation and angiogenesis in hepatocellular carcinoma and predicts prognosis. BMC Cancer. 2015 Apr 9;15(1):245.* 2, *Neoangiogenesis-related genes are hallmarks of fast-growing hepatocellular carcinomas and worst survival. Results from a prospective study. Gut. 2015 Feb 9.* 3, *The aberrant expression of MEG3 regulated by UHRF1 predicts the prognosis of hepatocellular carcinoma. Mol Carcinog. 2015 Jan 16.* 4, *TIMP-3 expression associates with malignant behaviors and predicts favorable survival in HCC. PLoS One. 2014 Aug 29;9(8):e106161*) had enrolled around one hundred of or less patients for survival analysis in their studying. Your suggestions is very valuable. We must concede that the number of patients in our study is not big enough. It is indeed the drawback in our study. We have set out to make a larger scale study which enrolled more patients with HCC to further confirm our findings in clinical.

(2) Question: Important prognostic variables as BCLC stage, Type of treatment and others are missing.

Answer: 1), Thank you very much! Yes, BCLC stage classification is very important criteria for HCC, which had not been adopted in our study. In our country, most widely accepted criteria for HCC pathological classification at present is TNM classification(UICC 2010), which was also widely taken in many HCC studies (1, *Sox12, a direct target of FoxQ1, promotes hepatocellular carcinoma metastasis through up-regulating Twist1 and FGFBP1. Hepatology. 2015 Jun; 61(6):1920-33.* 2, *Overexpression of CXCL5 mediates neutrophil infiltration and indicates poor prognosis for hepatocellular carcinoma. Hepatology. 2012 Dec;56(6):2242-54.*) in the world. In Asia (not including Japan and Indonesia), great differences have been presented in etiologies, biological behaviors, tumor stages, clinical practice guidelines of HCC between Asia and western countries. BCLC stage classification is not wildly used as the first choice for evaluating HCC in clinical work in our country. 2), Your suggestions are extremely valuable. A few treatments had been included in our research. For example in Table 1 and Table 3, type of surgical intervention: radical resction/ palliative resection and postoperative TACE had been taken account for the prognosis and clinicopathological features of these patients. We must admit that if more clinicopathological features could be brought into, the result would be more reliable. Furthermore, we just tried to report an clinical phenomenon, and find associations and differences among these clinicpathology factors in a small scale. The exploration in mechanism only covered one direction

which was not deep enough. A lot of work in this study is need to complete for perfect in future.

Revision has been made according to the suggestions of the No. 02992560 reviewer

Question: Some minor revisions of the language are needed.

Answer: Yes, it is very critical. Language revisions have been taken following you suggestions.

Revision has been made according to the suggestions of the No. 00069797 reviewer

Question: (1) some minor language polishing should be corrected. (2) Figure 2 is very small and not clear. Please check it. (3) Some abbreviations in the text should be explained

Answer: Yes, they are very significant to enhance the quality of our manuscript, thank you very much. According to your advices, we have corrected these mistakes。

3 References and typesetting were corrected。

If any question arises, please let us know. Thank you again for publishing our manuscript in the *World Journal of Gastroenterology*.

Sincerely yours,

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