

5th of August 2012

Dear Editor,

Please find enclosed the edited manuscript and a CD disk containing an electronic copy of the full-text manuscript in Word format (file name WJG27 .doc).

Title: Expression and clinical significance of CD73 and HIF-1 α in gastric carcinoma

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

1. Format has been updated

2. The following is my point-by-point response to the reviewers:

(1) We have carefully revised the spelling and grammar in this manuscript.

(2) We numbered the figures in this manuscript. Yellow or brown granules showed in the cytoplasm are positive immunoreaction which has been described in the article, so we didn't mark it in the figure.

(3) In this manuscript we discussed that hypoxia could induce upregulation of CD73 expression in brain microvessel endothelial cells and in intestinal epithelial cells and one of the mechanisms involved HIF-1. Unfortunately, there were no study explore the correlation between the two moleculars in tumor and the mechanisms. We put forward a hypothesis that HIF-1 α could transcriptionally regulate CD73 expression in tumor cells.

(4) We agree completely with the reviewer's fourth advice and the description "This study was approved by the Institutional Review Board (IRB), and informed consent was obtained from each patient." is added in the article.

(5) According to the reviewer's opinion about the description of CD73 expression in different histological types, the data on statistical analysis is shown in Table1. We analyses the data with one-way ANOVA test again, and find that there is obvious difference between CD73 expression in Tubular adenocarcinoma and in poorly differentiated adenocarcinoma ($P=0.001$). But there are no statistical significance between other each two histological types ($P>0.05$). So we delete this part and Figure2.

(6) About the title of the figure legend 1, we change it as "Expression of CD73 and HIF-1 α in gastric carcinoma ($\times 400$)."

(7) Thanks for the reviewer to point out the errors in Table1. We check the data carefully, find out the errors and correct the mistakes.

(8) We analysed the data again using ROC curve analysis and get a new figure which is added in the manuscript instead of the previous one. The answers for the reviewer's questions are as follows:

① The test result variables were age, gender, size, differentiation, node status, metastasis Borrmann type, AJCC stage, histological type, CD73, HIF-1 α and CD73/HIF-1 α .

② We used semi-quantitative method to evaluate the expression level of CD73 and HIF-1 α , which was described in the article (5th page, 2nd paragraph). We got scores for the two molecules, so they were continuous variables.

③ The best cutoff points for each protein were 5 for CD73 and 3.5 for HIF-1 α .

④ We classified the patients into four groups stratified according to CD73/ HIF-1 α expression, which included CD73+/ HIF-1 α + group, CD73+/ HIF-1 α - group, CD73-/ HIF-1 α + group, and CD73-/ HIF-1 α - group.

(9) About the description that both of the two molecules could be potential targets for combinational therapy of gastric carcinoma, we agree completely with the reviewer's advice and remove this part from the article.

(10) On the suggestion of the reviewer, we add a new Figure 2, in which the start point of the Kaplan Meier curve is set at zero and point of survival time is set at 100% point of the cumulative survival instead of the previous one.

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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