ANSWERING REVIEWERS

April 15, 2013

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 2549-review.doc).

Title: Hugl-1 induces apoptosis in esophageal carcinoma cells both in *vitro* and *vivo*

Author: Jia Song, Xiulan Peng, Mengyao Ji, Minghua Ai, Jixiang Zhang, Weiguo Dong

Name of Journal: *World Journal of Gastroenterology*

ESPS Manuscript NO: 2549

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

1. We have updated the format.

2. Comments: 1- Authors should check the effect of Hugl-1 overexpression in some other esophageal cell line also. 2- Authors nowhere mentioned the transfection efficiency of their plasmids. It should be mentioned in methods. They should also provide a supplementary figure of transfection efficiency. 3- Authors have shown that p21 level get increased during overexpression of Higl-1, they should also check the p53 level as p21 is downstream target of p53. 4- In Figure 2C, difference between Cyclin D1 level is not very clear, authors should provide densitometry analysis along with immunoblot. 5- Authors have shown significant reduction of c-Myc proteion, which is very important regulator of growth and proliferation. They should check the effect of Hugl-1 expression on some expression of downstream targets of c-Myc. 6- In Figure 3C, seprate GAPDH blots should be provided for each panel. 7- Authors should also monitor the molecular changes (lile p21, c-Myc, Cyclin D1 level) in tumor tissues overexpressing Hugl-1 along with control.

(1) We have tested the expression of Hugl-1 in the esophageal tissues. The expression of Hugl-1 in esophageal carcinoma is obviously lower than in normal tissues. The data was shown in the *Chinese Journal of Digestion.* We have tested another esophageal cell line EC9706. The protein level of Hugl-1 was as same as Eca109 cells.
(2) We have checked and updated each figures in our article. We have added a figure to show the transfection efficiency. We also added a figure to show the densitometry of cyclinD1.
(3) We agree with the opinion of reviewers. The protein of c-myc is very important regular of growth. Our results have shown that Hugl-1 down-regulated c-myc expression. Obviously, it point out that the Hugl-1 protein can mediate cell proliferation. In the coming research, we'll check the expression of other downstream targets of c-myc.

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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