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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 2549
Title: Hugl-1 induces apoptosis in esophageal carcinoma cells both in vitro and vivo
Reviewer code: 02462251
Science editor: Gou, Su-Xin
Date sent for review: 2013-03-01 09:50
Date reviewed: 2013-03-13 10:54

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[Y] Grade A: Priority Publishing	Google Search:	[ ] Accept
[Y] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[ ]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[Y] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS

In present manuscript authors studied the effect of Hugl-1 expression on cell survival and apoptosis in esophageal cancer cell line. They have shown that ectopic expression of Hugl-1 in Eca109 esophageal cancer cell line leads to cell cycle arrest and apoptosis. Authors have also shown Hugl-1 induced repression of tumor growth and enhanced apoptosis in xenograft model. Study supports the tumor suppressor role of Hugl-1 in esophageal cancer. 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.

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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 2549
Title: Hugl-1 induces apoptosis in esophageal carcinoma cells both in vitro and vivo
Reviewer code: 00068809
Science editor: Gou, Su-Xin
Date sent for review: 2013-03-01 09:50
Date reviewed: 2013-04-19 15:15

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[Y] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[Y] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[ ]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[ ] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[Y] Major revision
		[ ] No records	

COMMENTS TO AUTHORS

Hugl-1 is a gene which functions as a tumor suppressor gene in various cancer types. However, the effect of Hugl-1 on tumor progression and prognosis of esophageal squamous cell carcinoma has not been reported. This study conducted both in vitro and in vivo experiments and found that Hugl-1 induces growth suppression and apoptosis in a human esophageal squamous cell carcinoma cell line, which is a novel finding. This study is important as it shows that Hugl-1 may provide a novel target for treatment of esophageal cancer patients. The manuscript is generally well written. Use of English language is satisfactory. The study is well designed and carried out. The results are clearly organized and easy to understand. And the experimental procedures are performed in accordance with animal welfare guidelines. The statistical analysis section needs to be revised. The author just said that 'Data were presented as means ± SD and comparisons were made using Student's t test'. But this is actually not all the statistical job in this study. Student's t test is used to compare the means of 2 groups, but there are some comparisons among 3 groups in this study. I believe that univariate analysis of variance is the more suitable statistical method in this circumstance. And how is the sensitivity and specificity in Fig 1 calculated? It seems to me that the manuscript has been read by WJG editorial staffs before, as there are some revision suggestions in red color beside the abstract, results, discussion and references sections. If so, I'm afraid that the authors did not fully revise their manuscript according to these suggestions. The abstract is not so long as it is required and there are no P value and relevant data in the results section of the abstract as well. The first paragraph in the discussion section needs to be revised again. The authors mainly recapitulate the results in this paragraph, which is suggested NOT to do in the revision suggestions beside it. It is more important to highlight the scientific significance of the findings of this study in this paragraph. What are the

novelties of this study? Why are the results important? I would suggest the authors to write something more about these questions in the first paragraph. It is suggested that at least 36 references should be cited, but I'm afraid there are only 26 references included. Also, the majority of the references are too old. There are only 9 out of the 26 references which are published within the past 5 years (2008 and after). I would suggest the authors to renew the references and use articles published within the past 3 years if possible. In conclusion, I think this study is pretty good as it shows some novel and significant findings. But the manuscript is still not ready to be accepted for publication, as major revision is needed for above reasons.

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ESPS Peer-review Report
Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 2549
Title: Hugl-1 induces apoptosis in esophageal carcinoma cells both in vitro and vivo
Reviewer code: 01179998
Science editor: Gou, Su-Xin
Date sent for review: 2013-03-01 09:50
Date reviewed: 2013-04-19 23:59

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[Y] Grade B (Very good)	[Y] Grade B: minor language polishing	[ ] Existed	[Y] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	
[ ] Grade D (Fair)		BPG Search:	[ ]Rejection
[ ] Grade E (Poor)	[ ] Grade D: rejected	[ ] Existed	[ ] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS

Comments 1. In the abstract section, the authors need to briefly describe the study rationale [why you are going to study this gene in esophageal cancer. What implication (conclusion) you will like to reach]. 2. In the introduction section, the authors discussed background information for esophageal cancer (incidence, risk factors, treatment, prognosis and so on) but need to raise a study question to introduce this gene and provide a rationale for this study. 3. The methods section is good and the authors described methodologies used in this study. 4. In the results section, the authors will first report this gene expression in multiple esophageal cancer cell lines and then chose one for gene manipulation. After that, show data on this cell line. 5. In the discussion section, you may first summarize what you did, what you found, and what implication is. After that, discuss your data with literature, agree, disagree, and why. Next, discuss or explain why you data could happen mechanistically. The authors may also discuss the limitation of this study and future research direction or clinical guidance of this study. Overall, the submitted manuscript is an unfinished draft, for example, lots of editing comments. There were four figure legends, but five figures. The data are good, but didn't provide any mechanistic data. The authors did provide rationale why to have manipulated this gene in esophageal cancer. For xenograft assay, the authors will show xenografts or animals with tumor mass.

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Name of Journal: World Journal of Gastroenterology
ESPS Manuscript NO: 2549
Title: Hugl-1 induces apoptosis in esophageal carcinoma cells both in vitro and vivo
Reviewer code: 00053417
Science editor: Gou, Su-Xin
Date sent for review: 2013-03-01 09:50
Date reviewed: 2013-04-23 16:26

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
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[ ] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS
Hugl-1 gene has been reported to be involved in some carcinoma, but little data is present in the field of esophageal carcinoma. This manuscript adds new information in vitro and vivo to the existing knowledge. However, the English writing skill needs improvement.