

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 23403

Title: Auphen and dibutyryl cAMP suppress growth of hepatocellular carcinoma by regulating expression of aquaporin 3 and 9 in tumor-bearing nude mice

Reviewer's code: 02860895

Reviewer's country: Japan

Science editor: Yuan Qi

Date sent for review: 2015-11-16 08:46

Date reviewed: 2015-11-24 07:44

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

This is a comprehensive study using human and animal experimental data to disclose a relationship between high-AQP3/low-AQP9 expression and highly malignant natures of HCC and to demonstrate possibility of a new drug therapy for HCC. I congratulate the authors of this perfect work. Regarding the clinical investigation, I would like to ask whether there was a relationship between background (non-tumorous portion) AQP3/AQP9 expressions and the patients' prognoses. Probably many readers are also interested in this point.

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Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 23403

Title: Auphen and dibutyryl cAMP suppress growth of hepatocellular carcinoma by regulating expression of aquaporin 3 and 9 in tumor-bearing nude mice

Reviewer's code: 02860871

Reviewer's country: Netherlands

Science editor: Yuan Qi

Date sent for review: 2015-11-16 08:46

Date reviewed: 2015-11-19 15:18

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

This article entitled "Auphen and dibutyryl cAMP suppress growth of hepatocellular carcinoma by regulating expression of aquaporin 3 and 9 in tumor-bearing nude mice" by Rui Peng et al is interesting in its field. The authors concluded that the regulation of the expression of AQP3 and AQP9 by Auphen and dbcAMP could suppress growth of HCC. This article is well written with few typos inside. Here some comments: 1. Several point mutations have been identified in human aquaporins (Hum. Mutat. 2008;29:1108-1117). Does expression of AQP3 and AQP9 protein in HCC associate with their gene mutation? 2. Author mentioned that high AQP3 and low AQP9 expression predicts poor survival in HCC patients in separate analysis, what if the result if the analysis is combined for high AQP3 and low AQP9. Authors also mentioned that patients with high AQP3/low AQP9 expression showed increased metastasis formation (page 12). This statement should be corrected because authors did not perform metastasis/ migration assay. Otherwise, authors can also provide the migration data since AQPs are involved in the cell migration and proliferation. Minor points : a) The immunohistochemistry protocol mentioned only for tumor tissues? Provide a clear

method. b) In Fig 1C, it is best to provide the IHC with a matched HCC and normal (adjacent) liver tissue and measure their protein expression level. c) In all figures, for statistical results, it is best to mentioned the P value, odds ratio or the mean in the legend. d) The legend of fig 3 and 4 is the other way around. It is a bit confusing by mentioning nude mouse survival. It is not appropriate to link the mouse survival and the treatment in this mouse model. It is better to remove / separate the mouse image in the figure, do not mix with the tumor mouse in one image/figure. The number of mice that authors use was not stated in the method. How did the authors measure the tumor inhibition rates? e) The Tunnel assay for in vivo model was not clear in the method.

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Name of journal: World Journal of Gastroenterology

ESPS manuscript NO: 23403

Title: Auphen and dibutyryl cAMP suppress growth of hepatocellular carcinoma by regulating expression of aquaporin 3 and 9 in tumor-bearing nude mice

Reviewer's code: 02860590

Reviewer's country: Brazil

Science editor: Yuan Qi

Date sent for review: 2015-11-16 08:46

Date reviewed: 2015-12-08 17:57

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input checked="" type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

COMMENTS TO AUTHORS

Auphen and dibutyryl cAMP suppress growth of hepatocellular carcinoma by regulating expression of aquaporin 3 and 9 in tumor-bearing nude mice. This study evaluated the impacts of decrease of AQP3 and increase of AQP9 induced by Auphen and dbcAMP on hepatic tumor growth. My specific queries and comments are below: 1. Design: Page 10 line 214-220 - "Terminal deoxynucleotidyl transferase-mediated dUTP nick end labeling (TUNEL) assay The tumor tissues were fixed with 10% formalin for 4 h and embedded in paraffin. The slices were deparaffinized in water and placed in 3% H₂O₂ for 10 min at room temperature. The TUNEL assay was carried out according to the manufacturer's instructions (KGI Biotechnology, Nanjing, China). A positive result was brown staining in the nucleus". Can the authors clarify this methodology in more details? 2. Statistical analysis: Page 10 -11 - Were the data distributed normally? If not, then perhaps medians would be better than means. Can the authors clarify this point? 3. Results: The results section and material and methods section are conflated. Results should be reported in the results section and a description of the methodology should be presented in the material and methods section. The data



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were not deeply analysed. 4. The legends of the figures should be reviewed. ? Reviewer conclusion: Accept but needs minor and major revision.