

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 16391

**Title:** Ursodeoxycholic acid induces apoptosis in hepatocellular carcinoma xenografts in mice

**Reviewer's code:** 02936804

**Reviewer's country:** China

**Science editor:** Jing Yu

**Date sent for review:** 2015-01-16 10:32

**Date reviewed:** 2015-04-16 21:04

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 checked="" 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

The manuscript submitted by Hui Liu et al. is To evaluate the potential efficacy of UDCA as hepatoma-preventive agent by using BALB/c Nude Mice bearing s.c. xenografts of hepatoma cell line BEL7402. the study is important and valuable. All the experimental data were collected properly and the analysis were done following the standard. the writing needs further improvement. My concerns are as following: 1.Why did you use "BEL7402" instead of "HepG2 or Hu-H7 et al" in your experiment? 2.Materials and methods:why use 30, 50 and 70 mg/kg UDCA?What were your evidence? 3.References:Please select more reference in recent 5 years. 4. Fig.1 and Fig.3: "P<0.01", Please explain in the statistical analysis part.

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 16391

**Title:** Ursodeoxycholic acid induces apoptosis in hepatocellular carcinoma xenografts in mice

**Reviewer's code:** 03087259

**Reviewer's country:** Greece

**Science editor:** Jing Yu

**Date sent for review:** 2015-01-16 10:32

**Date reviewed:** 2015-03-13 16:13

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 type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input checked="" 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 type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

In this manuscript, Liu H and co-workers present data on the use of ursodeoxycholic acid (UDCA) as an anti-cancer agent in a hepatoma BEL7402 xenograft model in mice. Overall, the research findings are of interest to the scientific community as this form of cancer is clearly in the need of new treatments. The data presented are clear and the conclusions are supported by the evidence. Despite a lot of English language related problems that could be corrected in a revised form, the points raised are easily understood by the reader. However, for reasons that will be analyzed in detail below, the manuscript cannot be published in its current form and needs considerable revision. Major comments 1. Despite a good overall presentation of the data and appropriate statistic tools and analyses, all conclusions in this paper are based on a single xenograft experiment. Although the authors utilize a significant number of mice per group (10 mice per group), drawing conclusions from a single experiment in the lack of additional data is not an optimal scientific practice. As such, the authors are invited to present additional evidence on the action of UDCA in hepatoma cells. Results to be submitted could include a 2nd (smaller) xenograft experiment confirming findings of the

current experiment and/or in vitro growth inhibitory data in the same or other hepatoma lines. As the authors have already published in vitro work in the same cell line, it would be advised to explore additional testing aspects i.e. experiments in non-tested hepatoma cell lines or experiments in combination with other agents used in this indication. 2. Xenograft experiments allow monitor of tumor growth over time (using volume measurements via calipers). As such, the authors are invited to submit tumor volume curves for the complete 21-days period of the experiment (3 time points plus baseline as per the experiment description). The terminal analysis prior to sacrifice (volume measurements) and the representation of the weights of the tumors upon excision in grams should both be included in the analysis. The current figure incorrectly presents excised tumor data using volumes; this is not according to standard practice in the field. 3. Effects of treatments on body weights should be clearly mentioned in results (now mentioned in one line in discussion) or shown in a separate figure panel within figure 1 throughout the different time points (3 weeks plus baseline. 4. There are 6 figures in addition to the xenograft figure in this manuscript. Fr the sake of space, we propose that these 6 figures are pooled in 2-3 figures to save space. 5. Extensive corrections on the English language should be introduced in the manuscript; the authors are advised to seek editing by a native speaker

Minor comments: 1. Introduction. The opening statements on hepatoma are not correct. If hepatoma is second in prevalence in China and 3rd in the world, it cannot be the most devastating cancer worldwide (it will be at least second!) 2. Material and methods: the authors should include a basic description on what the hepatoma cell line they are using is (genetic mutation, origin etc). 3. Results a. The 1st paragraph needs shrinking; the analysis on how tumors are measured is already included in the materials and methods. b. A testing rationale for the UDCA doses used should be presented; why use 30, 50 and 70 mg/kg and not something else? Are these related to the maximul tolerated dose of UDCA? Were the doses chosen arbitrarily? What does that mean in terms of future treatment? The authors need to include some language. Relevant brief language should be included in the discussion c. As mentioned above, the language needs revision by a native speaker. It is also advised that repetition of the dose unit (mg/kg) for each dose should be avoided (e.g. no need to write 30 mg/kg, 50 mg/kg and 70 mg/kg; rather 30, 50 and 70 mg/kg).