

## ESPS PEER-REVIEW REPORT

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

**ESPS manuscript NO:** 14687

**Title:** The proportion of acetyl-histone-positive hepatocytes indicates the function status and prognosis of cirrhotic patients

**Reviewer's code:** 02992609

**Reviewer's country:** Spain

**Science editor:** Jing Yu

**Date sent for review:** 2014-10-20 19:08

**Date reviewed:** 2014-12-15 04:00

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	PubMed 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 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 checked="" type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input checked="" type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

## COMMENTS TO AUTHORS

The idea of finding tissular prognostic markers in patients with chronic liver disease is interesting. However, because of methodological errors, this work fails to provide clear evidence. The assumptions and objectives are not clearly drawn and this makes the methodology and the results are ill-defined and presented erratically. The study is based on analysis of a cohort of patients with liver cirrhosis Hepatitis B Virus, however there is no data in the study on whether patients were or not on antiviral treatment. Patients with hepatocellular carcinoma should be excluded from the analysis because they are a special subset of patients that alters the interpretation of the findings.

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**Title:** The proportion of acetyl-histone-positive hepatocytes indicates the function status and prognosis of cirrhotic patients

**Reviewer's code:** 02995389

**Reviewer's country:** Egypt

**Science editor:** Jing Yu

**Date sent for review:** 2014-10-20 19:08

**Date reviewed:** 2014-12-10 16:10

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	PubMed 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"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input checked="" 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 checked="" type="checkbox"/> Minor revision
	<input type="checkbox"/> Grade D: Rejected	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

First of all, I would like to state that this study is a very interesting one with a clear aim. The study methods and results successfully answered the question raised by the authors. However, there are some comments, to be revised by the authors before considering this article for publication. 1. English is poor with many grammatical and spelling mistakes. 2. In the introduction section, you stated that HBV is the major cause of chronic liver disease in developing countries. I think that you should emphasize the role of HCV as well, as a very important cause of chronic liver disease. Exposure to Aflatoxins is also another important cause of chronic liver disease in developing countries. 3. In the last paragraph of the introduction, you presented your results! that you should postpone to the results section. Instead, you should emphasize the aim of your research work. 4. In the material and methods, you do not need to explain the cause of chronic liver disease in the excluded cases specially that you did not specify a cause for the majority of the excluded cases. 5. Under the TMA and the immunohistochemistry section, you wrote H&E and PBS without explaining these abbreviations previously in the manuscript. 6. Under the TMA and the immunohistochemistry

section, you said that antibody details are available on request. I believe that you should present these details. 7. In page 6, references [21-22] should be written like this [21,22]. Please revise others. 8.8. In the first paragraph of the results section, you stated: "During the 15 years, 3280 cases (88.6%) of liver cirrhosis induced by hepatitis B were screened from 3701 cases of liver cirrhosis". However, this is not matching with what is written in the material and methods section: "Among the 3090 excluded cases, 421 cases were non-hepatitis B associated cirrhosis (including alcoholic abuse, cholestatic diseases and blood fluke infection), 1982 cases were core-needle biopsy tissue with rare available tissues for investigation, and 687 cases were lack of integrate clinical data". 9. In the second paragraph of page 8, please mention the duration of the follow up period and the number of patients that died during follow up. 10. In the second row of table 1, you only put the P value without putting any data about the CTP grades in the total and the follow up cases. 11. In page 9, you stated that: "Among the 611 patients, the proportions of H2AK5ac+, H3K9/K14ac+ and H3K27ac+ hepatocytes were positively associated with the values of TBIL, PT and LDH, and negatively associated with ALB. The proportions of H2AK5ac+ and H3K27ac+ hepatocytes were also positively associated with both ALT and AST. Meanwhile, the proportions of H2AK5ac+, H3K9/K14ac+ and H3K27ac+ hepatocytes were positively associated with AFP, GGT and CK, respectively (Fig.3)". Please put the P value or clarify that this positive association was a significant one. 12. Also put the P value in the last paragraph of page 9. 13. In page 12, you stated that: "Our work demonstrates an unprecedented mechanism to explain the compensatory capability of the liver, however, it is still unknown whether this is the same case in chronic liver damage". Didn't you consider liver cirrhosis as chronic liver damage?! 14. In page 12, you stated that: "In order to keep the consistence of the cases, in this study we excluded the HBV-negative patients." I believe you should state this in the material and methods and re- put in the discussion to explain the shortcoming of not including other causes of chronic liver disease in your study. I believe that including HBV cases only is considered one of the shortcoming of the study, because it is important to investigate if there is any correlation between different causes of chronic liver disease and the extent of acetyl histone positive hepatocytes. I think that you may consider this in further studies.

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

**ESPS manuscript NO:** 14687

**Title:** The proportion of acetyl-histone-positive hepatocytes indicates the function status and prognosis of cirrhotic patients

**Reviewer's code:** 00037668

**Reviewer's country:** United States

**Science editor:** Jing Yu

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	PubMed Search:	<input type="checkbox"/> [Y] 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"/> 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"/> [Y] No	<input 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"/> [Y] No	

## COMMENTS TO AUTHORS

This study investigates whether the proportion of acetyl-histon positive hepatocytes can be used as a marker of the deterioration of liver function in the context of cirrhosis. For the study, liver biopsies from 611 cirrhotic patients were used. The proportion of positive hepatocytes were recorded and correlated with clinical and laboratory indicators. The results indicated that the proportions of H2AK5ac+, H3K9/K14ac+, and H3K27ac+ hepatocytes increase proportionally with the deterioration of liver functions and the increase in circulating levels of markers of liver injury. The follow-up of patients with >70% acetyl-histon positive hepatocytes present lower rates of survival. The conclusion of the study is that the prportions of aceytl-histone positive hepatocytes closely associated with liver functions and survivial prognosis of cirrhotic patients. A few typos and missing words (e.g. 1st line of abstract) are noticed throughout the manuscript