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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 17600

Title: Blood DNA methylation markers in prospectively identified hepatocellular carcinoma from a case-control study at Taiwan

Reviewer's code: 02444752

Reviewer's country: China

Science editor: Yue-Li Tian

Date sent for review: 2015-03-16 08:36

Date reviewed: 2015-03-26 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 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 type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		[Y] No	[Y] Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

The authors demonstrated that three possible biomarkers in WBC including high methylation of cg10272601, cg12680131, and cg22511877 were associated with hepatocellular carcinoma (HCC). This finding is interesting and maybe can be used to develop a non-invasive method for identifying people at high risk of HCC. In my opinion, this manuscript is suitable for publication in World Journal of Hepatology after addressing the following issues. 1. The sum of the number of female and male in case and control group isn't equal to 159 and 312, respectively in table 1. Why? 2. In table 2, the differences of mean methylation values between cases and controls were analyzed. But, why did authors use median (not mean) as cutoff value in table 3? Were the values passed the normality test? 3. There are some spelling errors in the text (page 3, "ca be used" should be instead of "can be used", page 8, "cg1272601 methylation above" should be instead of "cg10272601 methylation above", for instance). Please check.



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 17600

Title: Blood DNA methylation markers in prospectively identified hepatocellular carcinoma from a case-control study at Taiwan

Reviewer's code: 02444960

Reviewer's country: Spain

Science editor: Yue-Li Tian

Date sent for review: 2015-03-16 08:36

Date reviewed: 2015-03-27 19:51

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 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 type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		[Y] No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

DNA methylation is involved in cancer etiology by silencing tumor suppressor genes through hypermethylation or activating oncogenes through hypomethylation. Recently Wu HC and coauthors have identified DNA methylation pattern between HCC tumor and adjacent nontumor tissues. Thus, in the present work, they have tried to elucidate whether the dysregulation of DNA methylation patterns observed in tumor tissues from HCC patients can be detected in white blood cells DNA. For this purpose the authors have measured methylation levels in 96 loci using baseline WBC DNA from 159 HCCs and 312 matched controls who participated in a community-based cancer screening cohort. They have found that hypermethylation of WNK2 (cg10272601) was associated with high risk to develop HCC and on the contrary, that hypermethylation of TPO and MYT1L was associated with a decreased risk to develop HCC. This study provides evidences that it could be possible to develop a non-invasive blood test to measure DNA methylation in order to help to identify people at high risk of HCC.



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 17600

Title: Blood DNA methylation markers in prospectively identified hepatocellular carcinoma from a case-control study at Taiwan

Reviewer's code: 00071717

Reviewer's country: Turkey

Science editor: Yue-Li Tian

Date sent for review: 2015-03-16 08:36

Date reviewed: 2015-04-08 16:26

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" 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 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

Authors studied the dysregulation of DNA methylation patterns observed in tumor tissues in WBC DNA. They found that alterations in methylation of cg10272601, cg12680131, and cg22511877 were associated with HCC risk later in life. Minor concern occur; 1- At methods, Loci selection and Methylation measurement section the number of selected CpG sites (96) is not consisted with the sum of hypermethylation (65) and CpG sites with hypomethylation (32). Check and correct.



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 17600

Title: Blood DNA methylation markers in prospectively identified hepatocellular carcinoma from a case-control study at Taiwan

Reviewer's code: 00069262

Reviewer's country: Mexico

Science editor: Yue-Li Tian

Date sent for review: 2015-03-16 08:36

Date reviewed: 2015-04-02 01:21

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" 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 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

It's an excellent job, well presented. Meets the standards of a publication. Congratulations.

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Hepatology

ESPS manuscript NO: 17600

Title: Blood DNA methylation markers in prospectively identified hepatocellular carcinoma from a case-control study at Taiwan

Reviewer's code: 00742516

Reviewer's country: China

Science editor: Yue-Li Tian

Date sent for review: 2015-03-16 08:36

Date reviewed: 2015-03-22 21:56

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> [Y] Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> [Y] Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> [] High priority for publication
<input type="checkbox"/> [Y] 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 type="checkbox"/> Plagiarism	<input type="checkbox"/> [] Minor revision
<input type="checkbox"/> Grade E: Poor		[Y] No	<input type="checkbox"/> [] Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

This is a very interesting paper which measured methylation levels in ninety-six loci that were aberrant in DNA methylation in HCC tumor tissues using baseline WBC DNA from 159 HCC cases and 312 matched controls. The authors found that high methylation level in cg10272601 in WNK2 was associated with increased risk of HCC; High methylation levels in both cg12680131 in TPO and cg22511877 in MYT1L; however, were associated with decreased risk. There are several minor concerns about this paper: 1. Did the authors acquired any approve from government of Taiwan before they bring the samples to USA? or there is no need for such kind of approve from the government? 2. Familial clustering of HBV infection is one of the major concerns worldwide especially in Chinese population. Therefore we often observed HCC occurring in several members from one family. It is interesting to know whether the authors observed HCC patients from one families? if yes, do they show similar DNA methylation in those patients? are there any differences in the DNA methylation between HCC patients from different families and those from one family? 3. there are still some spelling/typing error in the paper, please correct them.