



# BAISHIDENG PUBLISHING GROUP INC

8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

http://www.wjgnet.com

## ESPS PEER REVIEW REPORT

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

**ESPS manuscript NO:** 13834

**Title:** Methylation of interleukin-1 receptor-associated kinase 3 (IRAK3) is a novel prognostic marker in hepatocellular carcinoma

**Reviewer code:** 00503404

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2014-09-04 16:19

**Date reviewed:** 2014-09-18 00:03

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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"/> Existing	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

### COMMENTS TO AUTHORS

The paper is investigating the importance of the methylation of the IRAK3 during the progression of HCC and was associated with tumor stage and poor prognosis of patients. Comments; 1. the technique and cohort size was appropriate. 2. A question would be if authors could further digest the stage/causative agent association, in other words was there the same trend in different HCCs, for the stage IRAK association? Please analyse the HCV-HBV-negative patients separately. 3. Authors could/should calculate HRs for the time dependent models by using COX regression



**ESPS PEER REVIEW REPORT**

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

**ESPS manuscript NO:** 13834

**Title:** Methylation of interleukin-1 receptor-associated kinase 3 (IRAK3) is a novel prognostic marker in hepatocellular carcinoma

**Reviewer code:** 01943107

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2014-09-04 16:19

**Date reviewed:** 2014-09-19 15:59

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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"/> Existing	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

**COMMENTS TO AUTHORS**

In this study the authors demonstrated that IRAK3 and GLOXD1 gene expression was down-regulated in HCC cell lines and that it was partially restored after treatment with 5DAC. Importantly, they also found that IRAK3 methylation was statistically associated with tumor stage and with a trend of poor 3-year disease-free survival in HCC samples. Data are very interesting; however there are some critical points. 1. HCC cell lines experiments: in my opinion the addition of ChIP methylation assay could reinforce data obtained in cells lines. Moreover, more deatails than Refs 16 should be provided about methods. 2. HCC liver samples experiments: data on the Real-Time PCR expression of IRAK3 and GLOXD1 in HCC and non-HCC samples should be reported and correlated with methylation status and clinical features by adequate statistical analysis. 3. Methods section should be presented as in order of results. 4. Editing English revision is required. 5. Check abbreviations and reference format as requested by the Journal.



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## ESPS PEER REVIEW REPORT

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

**ESPS manuscript NO:** 13834

**Title:** Methylation of interleukin-1 receptor-associated kinase 3 (IRAK3) is a novel prognostic marker in hepatocellular carcinoma

**Reviewer code:** 00069618

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2014-09-04 16:19

**Date reviewed:** 2014-09-21 21:03

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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"/> Existing	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	BPG Search:	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> Existing	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

### COMMENTS TO AUTHORS

Due to the lack of reliable biological markers for prognosis of HCC, the role of IRAK3 is promising. However the authors should better describe how they think to translate this research in clinical practice. Minor point: in the first line of abstract correct hepatocellular to hepatocellular