

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 8686

Title: Epigenetics in Hepatocellular Carcinoma: An Update and Future Therapy Perspectives

Reviewer code: 02458123

Science editor: Wang, Jin-Lei

Date sent for review: 2013-05-02 14:40

Date reviewed: 2013-05-12 22:05

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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"/> Existed	<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	<input type="checkbox"/> Existed	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

Thank you very much for sending the manuscript entitled "Epigenetics in Hepatocellular Carcinoma: An Update and Future Therapy Perspectives". This is a good paper on epigenetics in hepatocellular carcinoma.

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO:8686

Title: Epigenetics in Hepatocellular Carcinoma: An Update and Future Therapy Perspectives

Reviewer code: 02462028

Science editor: Wang, Jin-Lei

Date sent for review: 2013-05-02 14:40

Date reviewed: 2013-05-13 23:30

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 checked="" type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	language polishing	BPG Search:	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

In this nice review, the authors discuss the role of epigenetics in Hepatocellular Carcinoma (HCC). Certain factors such as HBV were considered to play a role in HHC development; however, other factors (such as NAFLD, NASH, dietary, HCV) were not discussed. Regarding epigenetics, the authors describe summary the role of hypomethylation of CpG, the DNA methylation of two tumor suppressor factors, APC and CDKN2, and the variability of H3K27M3. The authors also describe the role of several miRNAs involved in HCC. Very nice review of a nice topic. Comments: 1. The authors do not discuss the mechanisms associated with hypermethylated genes such as NAT2, CSPG2, DCC with HBV-related HCC. 2. Please discuss why overexpression of Ezh2 is found in advanced HCC. 3. The Authors state that miR-26 expression is correlated to the response to interferon. Is there any evidence for this?

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 8686

Title: Epigenetics in Hepatocellular Carcinoma: An Update and Future Therapy Perspectives

Reviewer code: 00068533

Science editor: Wang, Jin-Lei

Date sent for review: 2013-05-02 14:40

Date reviewed: 2013-05-14 02:01

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"/> Existed	<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"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

The paper has some typographical and grammatical errors as follows: 1. The first sentence of abstract (lines 1 and 2) should be rewritten. 2. Page 2, the second sentence "Epigenetic regulation encompasses a number of different modifications to chromatin, including methylation of the DNA cytosine bases, as well as chemical modifications of histone tails" Should be corrected. 3. Page 2, second paragraph, needs the references for the data presented. In a study where HBV- and HCV-associated HCC cases were employed, average promoter methylation was increased relative to the surrounding tissues (Ref). Furthermore, panels of gene methylation signatures were proposed for clinical outcome prediction. Specifically, a panel of hypermethylated gene promoters (APC, RASSF1A, CDKN2A, FZD7) were able to discriminate tumor from surrounding tissues (Ref). 4. The sentence "Significantly, promoter methylation of DNMT1 correlated with poor tumor differentiation." should be re-written. 5. What is transcribed by RNA polymerase II is called Pri-miRNAs not pre-miRNA. The pri-miRNA is cleaved by an RNase III endonuclease to form a 60-70-nucleotide precursor miRNA or pre-miRNA. This should be corrected in the last paragraph of page 5. Finally, a brief description of the techniques mentioned in this review article like Methylation450 BeadChip and TLDA would make the subject more understandable especially for novice.

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 8686

Title: Epigenetics in Hepatocellular Carcinoma: An Update and Future Therapy Perspectives

Reviewer code: 00069394

Science editor: Wang, Jin-Lei

Date sent for review: 2013-05-02 14:40

Date reviewed: 2013-05-15 11:22

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"/> Existed	<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"/> 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"/> Existed	<input checked="" type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

The author has reviewed epigenetics in terms of DNA methylation, histone modifications and miRNAs in general and in hepatocellular carcinoma (HCC) as well as the use of epigenetic drugs for effective treatment of HCC. This review has covered all major aspects of epigenetics. However, I have several comments. The author should include the recent article "Exploring genome-wide DNA methylation profiles altered in hepatocellular carcinoma using Infinium HumanMethylation 450 BeadChips" by Shen J, et al, Epigenetics 2013;8:34-43. This article provides the information of novel genome-wide aberrant DNA methylation patterns in HCC predominantly associated with HCV infection. There are no references coded under the sections "miRNA treatment of liver cancer" (page 9) and "DNA methylation inhibitor drugs in treating HCC" (page 10) since the author assigned {ref}, not sure whether the author forgot to cite the references or not. The English language should be edited by the native English speaker regarding grammar and punctuation. Abbreviation; HDACi (page 10, second paragraph) should have the full form before since the author provided full form later under the section "HDAC inhibitor (HDACi) drugs in treating HCC" (page 11).