

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Experimental Medicine

**ESPS manuscript NO:** 21879

**Title:** HEPATOCELLULAR CARCINOMA:WHERE ARE WE?

**Reviewer's code:** 00504156

**Reviewer's country:** Greece

**Science editor:** Yue-Li Tian

**Date sent for review:** 2015-07-31 09:16

**Date reviewed:** 2015-08-12 02:52

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"/> 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

The manuscript is suitable for publication. Minor remarks are highlighted in the attached text.

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Experimental Medicine

**ESPS manuscript NO:** 21879

**Title:** HEPATOCELLULAR CARCINOMA:WHERE ARE WE?

**Reviewer's code:** 00007076

**Reviewer's country:** Italy

**Science editor:** Yue-Li Tian

**Date sent for review:** 2015-07-31 09:16

**Date reviewed:** 2015-08-12 21:51

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 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"/> 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 review article addresses the current knowledge and the future perspectives in the biology and treatment of HCC. However there are several points the authors must address before the Ms can be further evaluated. Specific Critiques 1. The review lacks of focus in some of its portions, particularly in the biological section. The different pathways shown or suggested to be involved in the development of HCC are listed consequentially without any critical hierarchy. One or two cartoons will help providing the message in a much clearer and catching form. 2. Also lacking is the role of cancer stem cells. This topic is now rather flourishing and a review on HCC with clinical perspectives cannot disregard this issue. This must be inserted and the relevance for diagnosis, prognosis and treatment critically discussed. 3. The section dealing with the treatment also lacks of critical revision and as for the biologicals section is a list of options with no outcome. A much stringent comparison among the different treatment regimens is needed.

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Experimental Medicine

**ESPS manuscript NO:** 21879

**Title:** HEPATOCELLULAR CARCINOMA:WHERE ARE WE?

**Reviewer's code:** 03015689

**Reviewer's country:** Spain

**Science editor:** Yue-Li Tian

**Date sent for review:** 2015-07-31 09:16

**Date reviewed:** 2015-08-14 05:30

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"/> 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 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

The text is so comprehensive and up to date in the many aspects of hepatocellular carcinoma that transpires the great undertaking achieved in the compilation of the information it provides. If I may offer any feedback, in my opinion the article would greatly benefit from reviewing the following points: 1. Throughout the whole article a certain lack of hierarchy of the abundant information provided is present, not being clear what is the consensus on which resources / techniques are most indicated in all occasions 2. The invasive diagnosis by biopsy, of great value for both the clinic and in order to know more about HCC, isn't usually performed and is substituted by the non invasive diagnosis, this being supported by different well respected scientific societies. The authors' opinion in favour of the biopsy (page 11) is highly valued, especially when many researchers are asking for verified information in order to develop different carcinogenesis models, treatments efficacy, etc; hence the article would benefit from adding bibliographic support for that option. 3. The non invasive diagnostic criterion is used in both the EASL (2012) and USA (2013) so they should also be added to the references 4. The use of the Milan criteria for liver transplantation is supported by several scientific societies but there also is an unstoppable trend since 2001 (Yeo, Duvoux, Tosso...) that



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should also be included given that in all guidelines is currently accepted that reality of being too strict 5. The unique case of very early cancer is hardly dealt with and there are some particularities in the treatment that should also be named In my opinion the article could greatly benefit from adding some of the points previously named. Regarding readability, it has a very reader friendly approach. I have thoroughly enjoyed reviewing your article and I am looking forward to reading the revision

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Experimental Medicine

**ESPS manuscript NO:** 21879

**Title:** HEPATOCELLULAR CARCINOMA:WHERE ARE WE?

**Reviewer's code:** 03016694

**Reviewer's country:** Turkey

**Science editor:** Yue-Li Tian

**Date sent for review:** 2015-07-31 09:16

**Date reviewed:** 2015-08-16 04:54

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
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<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
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		<input type="checkbox"/> No	

## COMMENTS TO AUTHORS

This is a well-organized and written review article about an important issue. Biological features and treatment options are the attractive discussions at the literature nowadays. The sections before the "Potentially Curative Treatments" were discussed as well as needed but "Potentially Curative Treatments" section needs to be discussed around the new literature findings. 1-) The knowledge given at this review article about HCV antiviral treatment must be discussed again according to the new data at the literature. Especially with new HCV antiviral treatment option the antiviral treatment resistance is very low. 2-) Liver Transplantation (LT) option for the treatment must be clarified. Especially the questions; -Timing of the LT? -Which stage of the chronic liver disease is suitable for LT or resection? - What about Living Donor LT option? - What are the new discussions about the HCC cases Beyond the Milan Criteria? must be answered. 3-) The factors effecting the prognosis also must be review again. Especially pathological differentiation which is very important for the prognosis and also deciding for the treatment option must be discussed. 4-) The value of the PEI treatment and microsphere treatment must be discussed according to the new literature data. 5-) What about the value of sorafenib? How long survival benefit does sorafenib



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have ? Some abbreviation ( PEI, NMR,TACE, TAE etc.) are used directly without explanation. Better to use them after the explanation of the abbreviations.