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# ESPS PEER REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology
**ESPS manuscript NO:** 5884
**Title:** Implications of biomarkers in human hepatocellular carcinoma pathogenesis and therapy
**Reviewer code:** 00070803
**Science editor:** Su-Xin Gou
**Date sent for review:** 2013-09-29 15:20
**Date reviewed:** 2013-09-30 01:09

| CLASSIFICATION | LANGUAGE EVALUATION | RECOMMENDATION | CONCLUSION |
|---|---|---|---|
| [ ] Grade A: Excellent | [ ] Grade A: Priority publishing | Google Search: | [ ] Accept |
| [ ] Grade B: Very good | [Y] Grade B: Minor language polishing | [ ] Existing | [ ] High priority for publication |
| [Y] Grade C: Good | [ ] Grade C: A great deal of language polishing | [ ] No records | |
| [ ] Grade D: Fair | [ ] Grade D: Rejected | BPG Search: | [ ] Rejection |
| [ ] Grade E: Poor | | [ ] Existing | [ ] Minor revision |
| | | [ ] No records | [Y] Major revision |

## COMMENTS TO AUTHORS

This article is of interest but need and could be largely improved.

1. Introduction: is too long. Please reduce it.
2. Several sections can be reduced.
3. Specially the authors need to eliminate some preclinical data focusing on clinical trials.
4. EGFR section needs to be reduces. Poor activity with these agents.
5. Update with ASCO and ESMO 2013 meetings.
6. Update new references.

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# ESPS PEER REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology
**ESPS manuscript NO:** 5884
**Title:** Implications of biomarkers in human hepatocellular carcinoma pathogenesis and therapy
**Reviewer code:** 00068252
**Science editor:** Su-Xin Gou
**Date sent for review:** 2013-09-29 15:20
**Date reviewed:** 2013-09-30 08:17

| CLASSIFICATION | LANGUAGE EVALUATION | RECOMMENDATION | CONCLUSION |
|---|---|---|---|
| [ ] Grade A: Excellent | [ ] Grade A: Priority publishing | Google Search: | [ ] Accept |
| [ ] Grade B: Very good | [Y] Grade B: Minor language polishing | [ ] Existing | [ ] High priority for publication |
| [Y] Grade C: Good | [ ] Grade C: A great deal of language polishing | [ ] No records | |
| [ ] Grade D: Fair | [ ] Grade D: Rejected | BPG Search: | [ ] Rejection |
| [ ] Grade E: Poor | | [ ] Existing | [ ] Minor revision |
| | | [ ] No records | [Y] Major revision |

## COMMENTS TO AUTHORS

So many tumor markers have provided useful clinical information not only in prognosis but also in pathogenesis and treatment efficacy. Considerable progress has been made recently in HCC at the molecular level increasing the potential of molecular targeted therapy. A number of molecular targets have been identified that have been showing promising results in treatment of HCC. 1. Authors should stress in specific biomarkers for pathogenesis and therapy of HCC. 2. new references in last 3 years. 3. new markers such as MiRNAs, mRNA.

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# ESPS PEER REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology
**ESPS manuscript NO:** 5884
**Title:** Implications of biomarkers in human hepatocellular carcinoma pathogenesis and therapy
**Reviewer code:** 00227487
**Science editor:** Su-Xin Gou
**Date sent for review:** 2013-09-29 15:20
**Date reviewed:** 2013-11-06 15:13

| CLASSIFICATION | LANGUAGE EVALUATION | RECOMMENDATION | CONCLUSION |
|---|---|---|---|
| [ ] Grade A: Excellent | [ ] Grade A: Priority publishing | Google Search: | [ ] Accept |
| [ ] Grade B: Very good | [Y] Grade B: Minor language polishing | [ ] Existing | [ ] High priority for publication |
| [Y] Grade C: Good | [ ] Grade C: A great deal of language polishing | [ ] No records | |
| [ ] Grade D: Fair | [ ] Grade D: Rejected | BPG Search: | [ ] Rejection |
| [ ] Grade E: Poor | | [ ] Existing | [ ] Minor revision |
| | | [ ] No records | [Y] Major revision |

## COMMENTS TO AUTHORS

This review article by Han et al. describes several biomarkers (mainly miRNA) in the pathogenesis and therapy of HCC. The topic is important for clinicians who are treating with liver cell cancer and the manuscript is well-written. However, several points listed below should be considered. 1) Page 8-10: Biological therapy for HCC should be written with biomarkers in a new paragraph. 2) Ref. nos. 118 and 122 are same. Carefully check the references. 3) Table(s) and/or Figure(s) can be provided for readers.

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# ESPS PEER REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology
**ESPS manuscript NO:** 5884
**Title:** Implications of biomarkers in human hepatocellular carcinoma pathogenesis and therapy
**Reviewer code:** 02454001
**Science editor:** Su-Xin Gou
**Date sent for review:** 2013-09-29 15:20
**Date reviewed:** 2013-12-19 11:28

| CLASSIFICATION | LANGUAGE EVALUATION | RECOMMENDATION | CONCLUSION |
|---|---|---|---|
| [ ] Grade A: Excellent | [ ] Grade A: Priority publishing | Google Search: | [ ] Accept |
| [Y] Grade B: Very good | [Y] Grade B: Minor language polishing | [ ] Existing | [ ] High priority for publication |
| [ ] Grade C: Good | [ ] Grade C: A great deal of language polishing | [ ] No records | |
| [ ] Grade D: Fair | | BPG Search: | [ ] Rejection |
| [ ] Grade E: Poor | [ ] Grade D: Rejected | [ ] Existing | [Y] Minor revision |
| | | [ ] No records | [ ] Major revision |

## COMMENTS TO AUTHORS

The authors have scanned 142 publications and reviewed the potential of Biomarkers for HCC. While discussing a few (4) serum biomarkers, their attention turned to Drugs to target VEGF (a potential biomarker for many cancers) and they have listed six drugs which target this BM. Then they list a number of microRNAs and discuss their mode of regulation – upregulation or down regulation in HCC. Information here is updated and informative. After reviewing the serum biomarkers and microRNAs they conclude that "mRNA" may be potential new targets for HCC. One aspect which is missing is the SNPs as Biomarkers. This is a good review – but a few lines on the limitations of this report will be useful as most of the biomarkers listed here are not specific to HCC, they are found in other cancers like cervical cancer, breast cancer etc. Reference included- Rama Mani , Kaiser Jamil and M. Ch Vamsy (2007) :Specificity of serum tumor Markers (CA125,CEA, AFP, Beta HCG) in Ovarian Malignancies. Trends in Medical Research , 2, (3), 128-134.

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# ESPS PEER REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology
**ESPS manuscript NO:** 5884
**Title:** Implications of biomarkers in human hepatocellular carcinoma pathogenesis and therapy
**Reviewer code:** 01564820
**Science editor:** Su-Xin Gou
**Date sent for review:** 2013-09-29 15:20
**Date reviewed:** 2013-12-23 23:03

| CLASSIFICATION | LANGUAGE EVALUATION | RECOMMENDATION | CONCLUSION |
|---|---|---|---|
| [ ] Grade A: Excellent | [ ] Grade A: Priority publishing | Google Search: | [ ] Accept |
| [ ] Grade B: Very good | [Y] Grade B: Minor language polishing | [ ] Existing | [ ] High priority for publication |
| [Y] Grade C: Good | [ ] Grade C: A great deal of language polishing | [ ] No records | |
| [ ] Grade D: Fair | [ ] Grade D: Rejected | BPG Search: | [ ] Rejection |
| [ ] Grade E: Poor | | [ ] Existing | [Y] Minor revision |
| | | [ ] No records | [ ] Major revision |

## COMMENTS TO AUTHORS

The review article by Han and colleagues focused on the role of several specific biomarkers implicated in the pathogenesis of HCC and several promising molecular-targeted drugs which target the biomarkers of HCC. This is an important clinical and research topic in the field of hepato-gastroenterology. The article is well written and concise. I have some comments that the authors should address. - in the glypican-3 section, provide a reference for the "International Consensus Group" - Given the fact that it is the only approved chemotherapy for HCC, the authors may want to provide more details about clinical characteristics of sorafenib, including safety of the drug and main side effects. This section should be expanded. - typo error in the bevacizumab section in lines 1-2 - in Table 1, please add a column with main side effects of the drugs and their prevalence; this is an important clinical information in medical pratice. - if it is true that the new molecules, miRNA have a more clear pathophysiologic association with HCC and a better diagnostic accuracy for HCC, it is also true that aFP is widely available and a relatively cheap biomarker for screening. The authors should comment on this. The new biomarkers/molecules may not be easily available in all clinical settings (especially primary and secondary clinical settings) and accessibility may not be straightforward everywhere.

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# ESPS PEER REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology
**ESPS manuscript NO:** 5884
**Title:** Implications of biomarkers in human hepatocellular carcinoma pathogenesis and therapy
**Reviewer code:** 02521070
**Science editor:** Su-Xin Gou
**Date sent for review:** 2013-09-29 15:20
**Date reviewed:** 2014-01-07 16:04

| CLASSIFICATION | LANGUAGE EVALUATION | RECOMMENDATION | CONCLUSION |
|---|---|---|---|
| [ ] Grade A: Excellent | [ ] Grade A: Priority publishing | Google Search: | [ ] Accept |
| [ ] Grade B: Very good | [Y] Grade B: Minor language polishing | [ ] Existing | [ ] High priority for publication |
| [ ] Grade C: Good | [ ] Grade C: A great deal of language polishing | [ ] No records | |
| [Y] Grade D: Fair | [ ] Grade D: Rejected | BPG Search: | [ ] Rejection |
| [ ] Grade E: Poor | | [ ] Existing | [ ] Minor revision |
| | | [ ] No records | [Y] Major revision |

## COMMENTS TO AUTHORS

Comments for the author: In this review, Han LL et al. show the importance of tumor markers and options for future HCC treatment. Interestingly, they extensively review both currently available biomarkers in clinical practice and research-based biomarkers. And also, they review theses possible useful data in clinical practice. Major concerns: 1. The author should provide the sensitivity, specificity, PPV and NPV for all traditional biomarkers including references. 2. This journal is commonly read by physicians who are not well understanding basic science. The author should provide the diagrams or pictures to explain the mechanism of these markers. 3. Regarding to clinical trials that they mention(i.e. anti-VEGF), they show only the survival rate and benefit of these drugs without clinical background data. 4. The original article about miR-122 that recently published in "New England Journal of Medicine" must be cited (NEJM 2013;368:1685-1694). Minor concerns The topic of Sorafenib is missing.