

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: World Journal of Gastrointestinal Oncology

Manuscript NO: 61866

Title: Biomarkers for hepatocellular carcinoma based on body fluids and feces

Reviewer's code: 03742333

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Doctor, Full Professor, Professor, Surgeon

Reviewer's Country/Territory: Brazil

Author's Country/Territory: China

Manuscript submission date: 2020-12-21

Reviewer chosen by: Chen-Chen Gao

Reviewer accepted review: 2021-02-24 10:06

Reviewer performed review: 2021-03-12 12:08

Review time: 16 Days and 2 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input checked="" type="checkbox"/> Grade A: Priority publishing <input type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

I have read with great interest the manuscript entitled 'Biomarkers for hepatocellular

carcinoma based on body fluids and feces', submitted to the World Journal of Gastrointestinal Oncology. In this minireview article, the current evidence on the role of molecular biomarkers detected in body fluids and faeces for diagnosing and managing hepatocellular carcinoma (HCC) is summarised. While the article comprehensively reports several molecular biomarkers under investigation, it acknowledges in the conclusion of the manuscript this may be a promising future application (not currently widely used). The manuscript is written well, and the topic is of clinical interest. MAJOR COMMENTS - While the manuscript mention in the Conclusion that most of the molecular biomarkers cited may improve diagnosis and management of HCC in the future, it would be necessary also to include this comment in the Abstract. This is because despite promising, most of these biomarkers are not currently used on a daily basis. Alternatively, it would be interesting to make clearer in the manuscript the centres where they are routinely used in clinical practice. - Page 12, In the phrase 'hepatitis C virus (HCV) information', the word 'information' is likely to be misplaced. It seems the word 'infection' is more appropriated. - Legends for Figure 1 could be expanded and include a slightly more detailed explanation about the figure.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: World Journal of Gastrointestinal Oncology

Manuscript NO: 61866

Title: Biomarkers for hepatocellular carcinoma based on body fluids and feces

Reviewer's code: 00058381

Position: Editorial Board

Academic degree: MD

Professional title: Professor

Reviewer's Country/Territory: Austria

Author's Country/Territory: China

Manuscript submission date: 2020-12-21

Reviewer chosen by: Chen-Chen Gao

Reviewer accepted review: 2021-03-13 13:27

Reviewer performed review: 2021-03-14 14:28

Review time: 1 Day and 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input checked="" type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This manuscript provides an enumeration of plenty of biomarkers and studies that

leaves the reader quite unsatisfied: A more explicit critical appraisal from the clinical point of view would be expected; the final conclusion ("In conclusion, testing body fluids and feces has a role to play in serving as a minimally-invasive and effective tool in improving diagnosis and management of HCC in the future") is vague. Figure 1 should be omitted; it does not yield substantial information. Stylistic/linguistic improvement is required (e.g., "A multicenter retrospective study reported that a decrease in perioperative serum AFP to be an independent risk factor for prognosis in HCC patients after liver resection", "The detection of CTC with stem-like phenotypes can used for diagnosis, prognosis and therapeutic response evaluation in HBV-related HCC", "In addition, use of probiotics in murine HCC models inhibited HCC development, suggesting this strategy to have a potential to be used as a therapeutic option for HCC patients in the future, provided that further studies can show alterations of gut microbiota by certain probiotics can also be observed in human", etc.). Page 12/35: What is meant by "patients with chronic hepatitis C virus (HCV) information"? Table 2 and Page 13/35: "Nacetylated" -> N-acetylated.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: World Journal of Gastrointestinal Oncology

Manuscript NO: 61866

Title: Biomarkers for hepatocellular carcinoma based on body fluids and feces

Reviewer's code: 00073640

Position: Editorial Board

Academic degree: PhD

Professional title: Associate Research Scientist

Reviewer's Country/Territory: Slovenia

Author's Country/Territory: China

Manuscript submission date: 2020-12-21

Reviewer chosen by: Chen-Chen Gao

Reviewer accepted review: 2021-03-12 10:55

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Review time: 3 Days and 21 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input checked="" type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
Conclusion	<input type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The subject of the manuscript is topical and interesting. Author summarize numerous

potential molecules of agents that might be interesting to evaluate as a potential biomarker for hepatocellular carcinoma (HCC). Author nicely explain in the introduction section that at present, diagnosis of HCC is mainly based either by histopathological studies or imaging findings and that there is still a high but an unmet need for a safe, effective, and non-invasive approach for diagnosing early HCC, predicting responses to specific therapies, evaluating prognoses before or after therapies. However, in the manuscript authors mostly summarize the literature without any critical opinion or discussion about limitations or advantages. In the manuscript there is numerous biomarkers – which are appropriate to use? Can they be used in the clinic or should they be evaluated in the future? The fact is, that they are not accepted as suitable in the diagnostic purposes. Thus, all above mentioned questions need to be properly and critically discussed in the manuscript.