



## PEER-REVIEW REPORT

**Name of journal:** *World Journal of Gastrointestinal Oncology*

**Manuscript NO:** 76514

**Title:** Liquid biopsy to detect resistance mutations to anti-EGFR therapy in metastatic colorectal cancer

**Provenance and peer review:** Invited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 05387405

**Position:** Peer Reviewer

**Academic degree:** MSc, PhD

**Professional title:** Research Scientist

**Reviewer's Country/Territory:** Hungary

**Author's Country/Territory:** Chile

**Manuscript submission date:** 2022-03-19

**Reviewer chosen by:** AI Technique

**Reviewer accepted review:** 2022-04-02 07:28

**Reviewer performed review:** 2022-04-10 07:11

**Review time:** 7 Days and 23 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<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
<b>Conclusion</b>	<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
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No



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<b>Peer-reviewer statements</b>	Peer-Review: [ <input checked="" type="checkbox"/> ] Anonymous [ <input type="checkbox"/> ] Onymous Conflicts-of-Interest: [ <input type="checkbox"/> ] Yes [ <input checked="" type="checkbox"/> ] No
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### **SPECIFIC COMMENTS TO AUTHORS**

The minireview of Valenzuela et al. is well written, easy to follow, with good English.

Major issue: Due to some error, the uploaded file completely lacks the list of References.

Prior to any decision, authors must update the manuscript with the References. Minor

issue: "In contrast, the Japanese Society of Medical Oncology clinical guidelines recommend the use of anti-EGFR for the usefulness and monitoring of this therapy[62]."

-> "In contrast, the Japanese Society of Medical Oncology clinical guidelines recommend the use of anti-EGFR antibodies (???) for the usefulness and monitoring of this therapy[62]."



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**Peer-review model:** Single blind

**Reviewer's code:** 05402068

**Position:** Peer Reviewer

**Academic degree:** MD, MSc

**Professional title:** Doctor

**Reviewer's Country/Territory:** United States

**Author's Country/Territory:** Chile

**Manuscript submission date:** 2022-03-19

**Reviewer chosen by:** Dong-Mei Wang

**Reviewer accepted review:** 2022-04-29 21:34

**Reviewer performed review:** 2022-04-30 01:41

**Review time:** 4 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<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
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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**SPECIFIC COMMENTS TO AUTHORS**

This is an overall well-written min-review, and is suitable for publication.



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**Provenance and peer review:** Invited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 05775860

**Position:** Editorial Board

**Academic degree:** PhD

**Professional title:** Assistant Professor

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** Chile

**Manuscript submission date:** 2022-03-19

**Reviewer chosen by:** Dong-Mei Wang

**Reviewer accepted review:** 2022-04-30 00:05

**Reviewer performed review:** 2022-05-01 04:36

**Review time:** 1 Day and 4 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<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
<b>Conclusion</b>	<input checked="" type="checkbox"/> Accept (High priority) <input type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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<b>Peer-reviewer statements</b>	Peer-Review: [ <input checked="" type="checkbox"/> ] Anonymous [ <input type="checkbox"/> ] Onymous Conflicts-of-Interest: [ <input type="checkbox"/> ] Yes [ <input checked="" type="checkbox"/> ] No
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### **SPECIFIC COMMENTS TO AUTHORS**

The manuscript entitled “Liquid biopsy to detect resistance mutations to anti-EGFR therapy in metastatic colorectal cancer” reports a mini review on clinical studies of liquid biopsy for early detection of resistance mutations in CRC patients with cetuximab or panitumumab therapy. The manuscript is well written. I recommend publication of the manuscript.



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**Provenance and peer review:** Invited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 05224033

**Position:** Editorial Board

**Academic degree:** PhD

**Professional title:** Director

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** Chile

**Manuscript submission date:** 2022-03-19

**Reviewer chosen by:** Dong-Mei Wang

**Reviewer accepted review:** 2022-05-03 16:44

**Reviewer performed review:** 2022-05-03 17:10

**Review time:** 1 Hour

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<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
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No



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<b>Peer-reviewer statements</b>	Peer-Review: [ <input checked="" type="checkbox"/> ] Anonymous [ <input type="checkbox"/> ] Onymous Conflicts-of-Interest: [ <input type="checkbox"/> ] Yes [ <input checked="" type="checkbox"/> ] No
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### **SPECIFIC COMMENTS TO AUTHORS**

In this study, the author reviewed liquid biopsy in metastatic colorectal cancer. This is a comprehensive review and provided the latest research advances in liquid biopsy of mCRC. However, the mutation spectrum of KRAS, NRAS and BRAF shall be showed in Figure or Table. Moreover, the other mutation shall be showed in the Figure. The third, the progression of detection technology in this field shall also be described in this review.



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**Provenance and peer review:** Invited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 05448343

**Position:** Editorial Board

**Academic degree:** MD

**Professional title:** Professor

**Reviewer's Country/Territory:** China

**Author's Country/Territory:** Chile

**Manuscript submission date:** 2022-03-19

**Reviewer chosen by:** Dong-Mei Wang

**Reviewer accepted review:** 2022-04-30 02:21

**Reviewer performed review:** 2022-05-06 13:48

**Review time:** 6 Days and 11 Hours

<b>Scientific quality</b>	<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
<b>Language quality</b>	<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
<b>Conclusion</b>	<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
<b>Re-review</b>	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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### **SPECIFIC COMMENTS TO AUTHORS**

The objective of this review is to evaluate the role of liquid biopsy in the early identification of resistance mutations for therapy with cetuximab or panitumumab. They have pointed out liquid biopsy has a promising future as an innovative tool for the management of mCRC patients who are being treated with anti-EGFR therapies. My concern is that except of CTCs and ctDNA, tumor-derived exosomes could be detected by liquid biopsy , however, this part is missing. I suggest the author add this part in revised MS.



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**Provenance and peer review:** Invited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 05774721

**Position:** Peer Reviewer

**Academic degree:** PhD

**Professional title:** Research Assistant

**Reviewer's Country/Territory:** Argentina

**Author's Country/Territory:** Chile

**Manuscript submission date:** 2022-03-19

**Reviewer chosen by:** Dong-Mei Wang

**Reviewer accepted review:** 2022-04-29 03:49

**Reviewer performed review:** 2022-05-09 15:23

**Review time:** 10 Days and 11 Hours

<b>Scientific quality</b>	<input checked="" type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<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
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Re-review</b>	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No



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<b>Peer-reviewer statements</b>	Peer-Review: [ <input checked="" type="checkbox"/> ] Anonymous [ <input type="checkbox"/> ] Onymous Conflicts-of-Interest: [ <input type="checkbox"/> ] Yes [ <input checked="" type="checkbox"/> ] No
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### **SPECIFIC COMMENTS TO AUTHORS**

Revision: I have read with great interest the contribution entitled “Liquid biopsy to detect resistance mutations to anti-EGFR therapy in metastatic colorectal cancer” by Valenzuela G et al. It is a very well elaborated Minireview on the subject treated by the authors. I only have a few minor concerns before I consider this paper fully acceptable:

1- Some references should be updated. 2- Some abbreviations should be defined the first time they appear in the text: FOLFOX, FOLFIRI, FIRE-3. This is important for basic scientists who are not very into the latest clinical approaches, but are interested in these topics. 3- Several typing errors are found, for instance “utilises”, “harbouring”, “characterise”, “analised”. I recommend Grammarly free software to quickly screen and correct these simple mistakes. 4- I recommend to include a short description of anti-EGFR therapy in the Introduction 5- Is there any relevance in CTNNB1 gene mutations related to resistance to anti-EGFR therapy that could be detected through liquid biopsy? 6- An illustrative figure of the key pathways involved in CRC resistance to anti-EGFR that could be detected through liquid biopsy, as well as the involved drugs in this processes, could be included. This would allow readers to have a general overview of the content of the work



## RE-REVIEW REPORT OF REVISED MANUSCRIPT

**Name of journal:** *World Journal of Gastrointestinal Oncology*

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**Provenance and peer review:** Invited Manuscript; Externally peer reviewed

**Peer-review model:** Single blind

**Reviewer's code:** 05387405

**Position:** Peer Reviewer

**Academic degree:** MSc, PhD

**Professional title:** Research Scientist

**Reviewer's Country/Territory:** Hungary

**Author's Country/Territory:** Chile

**Manuscript submission date:** 2022-03-19

**Reviewer chosen by:** Jia-Ru Fan

**Reviewer accepted review:** 2022-06-15 14:16

**Reviewer performed review:** 2022-06-16 16:35

**Review time:** 1 Day and 2 Hours

<b>Scientific quality</b>	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
<b>Language quality</b>	<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
<b>Conclusion</b>	<input type="checkbox"/> Accept (High priority) <input checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
<b>Peer-reviewer</b>	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous



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statements

Conflicts-of-Interest: [ ] Yes [ **Y** ] No

#### **SPECIFIC COMMENTS TO AUTHORS**

The manuscript improved significantly. All my concerns had been solved. I recommend the publication of the manuscript.