

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

Scientific quality	<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 Grade E: Do not publish
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 type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

Peer-reviewer statements	Peer-Review: [<input checked="" type="radio"/>] Anonymous [<input type="radio"/>] Onymous Conflicts-of-Interest: [<input type="radio"/>] Yes [<input checked="" type="radio"/>] 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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Manuscript NO: 76514

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Provenance and peer review: Invited Manuscript; Externally peer reviewed

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

Scientific quality	<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
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 checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No



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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
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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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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: 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

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



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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
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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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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: 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

Scientific quality	<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
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 checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

Peer-reviewer statements	Peer-Review: [<input checked="" type="radio"/>] Anonymous [<input type="radio"/>] Onymous Conflicts-of-Interest: [<input type="radio"/>] Yes [<input checked="" type="radio"/>] 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

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 type="checkbox"/> Minor revision <input checked="" type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

Peer-reviewer statements	Peer-Review: [<input checked="" type="radio"/>] Anonymous [<input type="radio"/>] Onymous Conflicts-of-Interest: [<input type="radio"/>] Yes [<input checked="" type="radio"/>] 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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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: 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

Scientific quality	<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
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 checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Re-review	<input checked="" type="checkbox"/> Yes <input type="checkbox"/> No

Peer-reviewer statements	Peer-Review: [<input checked="" type="radio"/>] Anonymous [<input type="radio"/>] Onymous Conflicts-of-Interest: [<input type="radio"/>] Yes [<input checked="" type="radio"/>] 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”, “analysed”. 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*

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: 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

Scientific quality	<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
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 checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer	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.