



PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Cases

Manuscript NO: 41852

Title: Biomarkers in colorectal cancer: current clinical utility and future perspectives

Reviewer's code: 00070916

Reviewer's country: Germany

Science editor: Jin-Lei Wang

Date sent for review: 2018-09-07

Date reviewed: 2018-09-14

Review time: 7 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input type="checkbox"/> Anonymous
<input checked="" type="checkbox"/> Grade C: Good	polishing	<input checked="" type="checkbox"/> Accept	<input checked="" type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This systematic review by Vacante et al. gives an overview of the current use of the different genetic and epigenetic biomarkers - mostly from a clinical point of view. I have only minor comments which can be considered suggestions for the most part. If introducing abbreviations, use them consequently thereafter. In the CIMP paragraph,



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Group**

7901 Stoneridge Drive, Suite 501,
Pleasanton, CA 94588, USA
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Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
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there is one mistake: "Interestingly, in stage II and II CRC patients ..." must be II and III. The Figure is the weakest part of the manuscript. The question is, if it is at all necessary. At least, I would not have "mutated KRAS" and "mutated BRAF" together - they are not observed together unless a selective pressure is applied. Since fact that this is not the first review of his kind must still be considered when judging the scientific quality.

INITIAL REVIEW OF THE MANUSCRIPT

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PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Cases

Manuscript NO: 41852

Title: Biomarkers in colorectal cancer: current clinical utility and future perspectives

Reviewer’s code: 00227433

Reviewer’s country: United Kingdom

Science editor: Jin-Lei Wang

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Date reviewed: 2018-09-16

Review time: 15 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer’s expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

This review article outlines biomarkers in colorectal cancer, and has been structured by specific mutations and/or epigenetic changes, such as BRAF, KRAS, APC or methylation. I appreciate that the authors have attempted to provide an overview in this way, however further work could be done to improve the presentation and summary of



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evidence, and to discuss more novel work relating to these. Comments on the article are below: 1. There has been little discussion or focus on whether these biomarkers are being studied in the context of being predictive or prognostic. 2. In general, there has been very little critical appraisal of study designs, sample sizes or strength of evidence conveyed throughout the article. Quite rightly, there is a concentration on meta-analyses, but are these meta-analyses of single centre studies with high selection bias, for example? Was there heterogeneity in the pooled estimates identified? 3. Although I appreciate that molecular subtypes are not biomarkers per se, it seems remiss to not have a section on the overarching Consensus Molecular Subtypes; or the more recent CRIS-subtypes of colorectal cancer, and what this means for potential stratified medicine. 4. Many novel studies or trials are ongoing in precision medicine, for example an aspirin trial that stratifies on the basis of PIK3CA mutation is underway in the UK, and these have not been highlighted. 5. Summary tables of evidence may aid presentation of information for the reader - the current format is very text-heavy in long paragraphs. 6. In the conclusions, IGF1-R is introduced as a target for new therapies, but this has not been discussed before this point. IGFBP3 is mentioned earlier in the review, but further discussion would be needed to explain this conclusion.

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Name of journal: World Journal of Clinical Cases

Manuscript NO: 41852

Title: Biomarkers in colorectal cancer: current clinical utility and future perspectives

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Reviewer's country: China

Science editor: Jin-Lei Wang

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SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
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			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

I hope the paper will be published to guide more researchers.

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Pleasanton, CA 94588, USA
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