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## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 25860

**Title:** Evaluation of prognostic and predictive biomarkers of response to anti-EGFR therapy in metastatic colorectal cancer patients: a systematic review

**Reviewer's code:** 00505467

**Reviewer's country:** Greece

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2016-03-25 16:12

**Date reviewed:** 2016-04-13 01:37

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

### COMMENTS TO AUTHORS

This review should provide explanations about the methodology applied in order the authors to perform the review. The authors should provide in the discussion section a perspective of where the research should be heading or what seems to be the pitfalls of research up until now according to their review. References must be updated i.e. reference 1 there is an updated ref from 2016 from almost the same authors.



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**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 25860

**Title:** Evaluation of prognostic and predictive biomarkers of response to anti-EGFR therapy in metastatic colorectal cancer patients: a systematic review

**Reviewer's code:** 03326259

**Reviewer's country:** Taiwan

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2016-03-25 16:12

**Date reviewed:** 2016-04-20 18:31

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input checked="" type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

### COMMENTS TO AUTHORS

Manuscript entitled "Evaluation of prognostic and predictive biomarkers of response to anti-EGFR therapy in metastatic colorectal cancer patients: a systematic review" by Lo Nigro C et al. This manuscript is well-written and is interesting. I suggest that this manuscript is acceptable pending minor revision. Comments: Polymorphism of certain genes has also been linked to the response of anti-EGFR therapy. The authors should also include that into this review.



**ESPS PEER-REVIEW REPORT**

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 25860

**Title:** Evaluation of prognostic and predictive biomarkers of response to anti-EGFR therapy in metastatic colorectal cancer patients: a systematic review

**Reviewer’s code:** 03551372

**Reviewer’s country:** China

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2016-03-25 16:12

**Date reviewed:** 2016-04-29 16:33

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

**COMMENTS TO AUTHORS**

Manuscript entitled “Evaluation of prognostic and predictive biomarkers of response to anti-EGFR therapy in metastatic colorectal cancer patients: a systematic review” focused on progress in the personalized treatment of metastatic colorectal cancer and discussed the potential of new prognostic and predictive biomarkers in selecting patients treated with anti-EGFR therapy. Overall, this is an interesting paper. However improvements and corrections are required: 1) The order of the biomarkers need to be adjusted. For example, it starts with KRAS mutation followed by NRAS mutation etc, and KRAS mutant clones were described before EGFR mutation. It will be better if the description of the same molecule can be grouped together. 2) This review discussed two prognostic biomarkers: BRAF mutations and ADCC activity. Why just these two? 3) In the discussion, it stated that there are ongoing studies assessing the predictive value of the number of copies of the EGFR gene, mutations in the NRAS, PI3KCA, TP53 and PTEN genes. However, there is no description on TP53 in any other sections. This needs to be added.

## ESPS PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 25860

**Title:** Evaluation of prognostic and predictive biomarkers of response to anti-EGFR therapy in metastatic colorectal cancer patients: a systematic review

**Reviewer's code:** 02980806

**Reviewer's country:** China

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2016-03-25 16:12

**Date reviewed:** 2016-05-03 17:51

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input checked="" type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
		BPG Search:	<input checked="" type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

### COMMENTS TO AUTHORS

This review summarized the biomarkers of anti-EGFR therapy in mCRC, proposing KRAS mutation, BRAF mutation, NRAS mutation, PIK3CA mutation, PTEN alteration might be beneficial to the selection of anti-EGFR therapy. These biomarkers were familiar to us. Therefore, the innovation of this review was not enough. Some improvements and corrections are required: (1) AS RAS mutational status was the recognized biomarker, the authors need to focus more content on RAS wild-type. There are various reviews published about the resistance mechanisms of anti-EGFR therapy, but this review didn't include the latest one, for example, HER-2 amplification, EGFR ligands amphiregulin and epiregulin, and some acquired resistance mechanisms. (2) The order to describe the biomarkers needs to be adjusted. The order in abstract, core tip, text, discussion and conclusion was inconsistent. In addition, the authors mentioned "TP53" in discussion, but not in any section of the review. (3) The content of abstract was too simple to summarize the review. More information was needed to provide about the significance of the review. (4) The discussion was needed to provide the clinical practice value of these biomarkers.



**ESPS PEER-REVIEW REPORT**

**Name of journal:** World Journal of Gastroenterology

**ESPS manuscript NO:** 25860

**Title:** Evaluation of prognostic and predictive biomarkers of response to anti-EGFR therapy in metastatic colorectal cancer patients: a systematic review

**Reviewer's code:** 02570566

**Reviewer's country:** South Korea

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2016-03-25 16:12

**Date reviewed:** 2016-05-03 09:31

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
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<input type="checkbox"/> Grade E: Poor		<input checked="" type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

**COMMENTS TO AUTHORS**

This manuscript by Nigro et al. entitled "Evaluation of prognostic and predictive biomarkers of response to anti-EGFR therapy in metastatic colorectal cancer patients: systematic review" focuses on progress in the personalized treatment of mCRC and discusses the potential of new prognostic and predictive biomarkers in selecting patients treated with anti-EGFR therapy. The authors evaluated not only the KRAS mutational status but also BRAF, NRAS, PIK3CA and PTEN alterations which might be beneficial to the selection of patients who are likely to respond to anti-EGFR therapies. However discussion section with KRAS, BRAF NRAS, PTEN is fairly explanation. The authors should extend the information in the discussion section. I provide following recommendations to improve the manuscript further. Particular Suggestions regarding the manuscript (Minor comments): 1. Perspective role and future direction in using prognostic and predictive biomarkers in response to anti-EGFR in metastatic CRC patients. 2. Actively discuss in KRAS, BRAF NRAS, PTEN mutation with anti-EGFR therapy in discuss section.