BAISHIDENG PUBLISHING GROUP INC
8226 Regency Drive, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242 Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com http://www.wjgnet.com

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Oncology
ESPS manuscript NO: 26101
Title: Molecular predictive markers in tumors of the gastrointestinal tract
Reviewer's code: 02526196
Reviewer's country: Denmark
Science editor: Jing Yu
Date sent for review: 2016-04-01 11:45
Date reviewed: 2016-04-09 21:50

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[Y] Grade A: Priority publishing	Google Search:	[Y] Accept
[Y] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[ ] Minor revision
[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

Peer review for World Journal of Gastroenterology Ms: ESPS Manuscript NO: 26101 Authors: Eirini Papadopoulou, Vasiliki Metaxa-Mariatou, Georgios Tsaousis, Nikolaos Tsoulos,Angeliki Tsirigoti, Chrisoula Efstathiadou, Angela Apessos, Konstantinos Agiannitopoulos, Georgia Pepe, Eugenia Bourkoula, George Nasioulas Title: Molecular predictive markers in tumors of the gastrointestinal tract. GENERAL COMMENTS: This review mainly describe the advance of molecular biomarkers in tumors of the gastrointestinal tract. For example, among top 30 mutated genes of esophageal and gastric cancers, TP53 is the highest. The biomarkers can be divided into predictive and prognostic, the former provides information on the potential benefit of the administrated treatment and the later provides information on the possible outcome of cancer in a particular patient regardless of treatment. Therefore, knowing the biomarkers of gastrointestinal tumors is very important for the therapeutical approach as the drugs target specific molecules involved in carcinogenesis. Furthermore, the review briefly introduce the concept of Liquid Biopsy in use for tumor characterization. The review also introduce the Next Generation Sequencing (NGS) in

use for the detection of mutations and the determination of the patient's tumor molecular profile. The manuscript is good for the readership of WJG, especially for the gastroenterologist and patients with gastrointestinal cancer, even relevant for the normal population. SPECIFIC COMMENTS: (1) The overall structure of the manuscript is complete. (2) The Introduction section of the manuscript is well structured. It clearly presented the purpose of this review. (3) The authors provided comprehensive discussion on the basis of the cited literatures. (4) The conclusion is clear and well. (5) The manuscript cited all important and relevant references. (6) The manuscript described the advances of molecular biomarkers for the most gastrointestinal malignant tumors, such as esophageal cancer, gastric cancer and colorectal cancer. Furthermore the Liquid Biopsy and Next Generation Sequencing are briefly and clearly introduced as well. (7) The title of the manuscript contains key words, and the title is interesting enough to attract readers' attention. (8) The topic of the manuscript is suitable for World Journal of Gastroenterology. (9) The language of the manuscript is good. Minor comments. Page 14, line 7: "asuitable" should be corrected as "suitable", therefore the following sentence " ...is sometimes of very bad quality and not asuitable for molecular analysis[88]." should be read as " ...is sometimes of very bad quality and not suitable for molecular analysis[88]." Conclusions The manuscript is concise, clear, comprehensive, and convincing. The content of this review has value for publication.

BAISHIDENG PUBLISHING GROUP INC
8226 Regency Drive, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242 Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com http://www.wjgnet.com

ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Oncology
ESPS manuscript NO: 26101
Title: Molecular predictive markers in tumors of the gastrointestinal tract
Reviewer's code: 03633805
Reviewer's country: Croatia
Science editor: Jing Yu
Date sent for review: 2016-04-01 11:45
Date reviewed: 2016-04-29 08:19

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[Y] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[ ] Minor revision
[ ] Grade E: Poor		[Y] No	[Y] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

Data presented through tables and figures could have potential clinical relevance. The language is satisfactory with simple, short and easily comprehensive construction of sentences. However, the manuscript lacks a necessary scientific depth and innovation in explaining the presented data. In some sections, the text is inconsistent with an uneven approach to all four analyzed gastrointestinal cancers included in the manuscript. In this regard, I will try to list some of the major and minor shortcomings that should be addressed: Major remarks: 1. In analysis of frequency of mutations in the background of the particular GI cancer (figures 1.-6.) it would be useful to suggest and explain which of these alterations have the potential role of predicting resistance to targeted therapy already clinically approved for each analyzed cancer (e.g. trastuzumab in gastric cancer and imatinib in GIST) corroborated with eventually present (pre)clinical results. Namely, in this manuscript , an approach of including the markers whose role is to predict resistance to particular therapy is only implemented in colorectal cancer and not in others (you've mentioned Ras, BRAF, PI3KCA and PTEN biomarkers of resistance to EGFR inhibitors in CRC). In this case, introduction section should shortly explain and discriminate between so called positive and negative predictive

markers where positive predictive markers play a role of positive selection of patients suitable for particular therapy and negative predictive biomarkers have a role of resistance prediction to therapy. 2. In analysis of data from figure 1.-6, there is a lack of Your own scientific suggestion which of alterations could represent positive predictive markers for some other targeted therapies that are already FDA approved in treatment of other non-GI cancer types.These should also be mentioned in the conclusion section. 3. In analysis of biomarkers in CRC You have decided to include markers whose primary function is prognostic (MSI), while for the rest of cancer types the text is more-less strictly based on predictive markers, as the manuscript title implies. For that reason I recommend either expanding a topic on prognostic markers in all GI cancer types included or extracting the prognostic part form the CRC section 4. Some manuscript parts exhibit data with a superficial and incomplete approach while some other parts are unnecessary. Here are some examples: -what are concrete, detailed results of preclinical and clinical testing of EGFR and HER2 inhibitors in esophageal cancer and what type of molecular stratification is recommended in the application of these therapy? -are there any detailed (pre)clinical results regarding the application of anti-HER2 therapy other than trastuzumab in gastric cancer? -testing for Ras mutation as a predictor of resistance to EGFR inhibitors in CRC should be explained in a more detail (for example, it is proposed an extension of Ras testing beyond previously recommended exon 2 region and this should be properly updated in the text) -it would be useful to mention why targeting BRAF mutation in CRC , although relatively frequently present in CRC, does not show positive results in clinics and what can be learned from that fact about potential biomarkers - data describing frequency of Ras mutation in other non-GI cancers are not relevant for this topic 5. Conclusion section should provide some scientific vision and recommendation for future directions Minor remarks: 1. Different structure of the manuscript subtitles is preferred with merging the paragraph of GEP in CRC with Liquid biopsy and NGS under one mutual subtitle (suggestion: Emerging methods in utilization and detection of biomarkers) 2. Abstract should be conceived with more skills with extraction of irrelevant and implementation of more relevant information while keeping it concise (for example I suggest deleting second and third se