

## ESPS PEER-REVIEW REPORT

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

**ESPS manuscript NO:** 27523

**Title:** CpG island methylator phenotype in adenocarcinomas from the digestive tract: Methods, conclusions, and controversies

**Reviewer's code:** 03408355

**Reviewer's country:** United States

**Science editor:** Xue-Mei Gong

**Date sent for review:** 2016-06-06 10:46

**Date reviewed:** 2016-07-31 11:00

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"/> Duplicate publication	
<input 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 checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Minor revision
	<input type="checkbox"/> Grade D: Rejected	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

The paper entitled "The CpG island methylator phenotype in adenocarcinomas from the digestive tract: methods, conclusions, and controversies" focused on the role of a specific phenotype in the development of multiple pancreatic and gastrointestinal adenocarcinomas. The study was well conducted and presented. The following were some minor concerns: 1. The subtitles could be numerated, which could help the readers understand better. 2. Pancreatic cancer and gastrointestinal cancer could be described, respectively. 3. This paper could be revised following the text style of a review, and the methods could be removed or shortened.

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**Title:** CpG island methylator phenotype in adenocarcinomas from the digestive tract: Methods, conclusions, and controversies

**Reviewer's code:** 00181208

**Reviewer's country:** Greece

**Science editor:** Xue-Mei Gong

**Date sent for review:** 2016-06-06 10:46

**Date reviewed:** 2016-08-03 01:14

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 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 type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		<input type="checkbox"/> No	<input type="checkbox"/> Major revision
		BPG Search:	
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		<input type="checkbox"/> Plagiarism	
		<input type="checkbox"/> No	

## COMMENTS TO AUTHORS

This is a valuable commentary on CIMP in GI cancers summarizing part of the literature and authors' own studies. Some specific comments for the authors to consider: 1. In page 3, 2nd paragraph, it is mentioned that hypermethylation results in the formation of repressive chromatin. In the 2nd paragraph of p.4 is noted, though, that repressive modifications are already present when DNA methylation is effectuated. These seem to be contradictory. Authors should provide an overall model possibly accompanied with a figure of the processes and key players such as DNMTs and polycomb repressors. This model may discuss also how disparate upstream molecular lesions in different cancers may result to similar down-stream methylation events (or vice versa) and could be integrated with the BRAF discussion in p. 11. 2. In page 5, the panels used for the evaluation of methylation could be of interest for the reader, possibly in a table form. 3. Related to point 1, in p. 15 and table 5, one would like to make some categorization and pathway integration of the differentially mutated genes to fit into the model. 4. In p.16 in the discussion on confounding factors, authors should discuss how significant they believe that the limited number of samples and tumor heterogeneity is for the



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validity of their results. A further discussion of alternatives to computation modeling for future sampling (e.g. tumor microdissection) could be appropriate at this point.

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**Title:** CpG island methylator phenotype in adenocarcinomas from the digestive tract: Methods, conclusions, and controversies

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**Reviewer's country:** United States

**Science editor:** Xue-Mei Gong

**Date sent for review:** 2016-06-06 10:46

**Date reviewed:** 2016-08-01 05:20

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input checked="" type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input 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 type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		BPG Search:	<input type="checkbox"/> Major revision
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		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
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## COMMENTS TO AUTHORS

A well written and thorough review by an experienced group. Congratulations for this excellent work.

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**Title:** CpG island methylator phenotype in adenocarcinomas from the digestive tract: Methods, conclusions, and controversies

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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 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
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## COMMENTS TO AUTHORS

In this commentary, Sanchez-Vega et al. presented an overview of previous studies on the molecular profiles of GI tumors based on CIMP status, and their own research using TCGA data. This manuscript is well written and described in detail. However, it is not easy to follow the flow. Overall, this manuscript seems to be diffused. The authors tried to cover too many subjects. A table containing information for previous studies will be extremely helpful for audience. The conclusion of this manuscript is not clearly described.