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PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 87526

Title: Early results of the integrative epigenomic-transcriptomic landscape of colorectal adenoma and cancer

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 00503405
Position: Editorial Board
Academic degree: MD, PhD
Professional title: Senior Lecturer, Senior Scientist
Reviewer's Country/Territory: Hungary
Author's Country/Territory: China

Manuscript submission date: 2023-08-17
Reviewer chosen by: Yu-Lu Chen
Reviewer accepted review: 2023-09-17 12:31
Reviewer performed review: 2023-09-18 15:53
Review time: 1 Day and 3 Hours

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [Y] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [Y] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [Y] Grade C: Fair [ ] Grade D: No creativity or innovation

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Scientific significance of the conclusion in this manuscript	[ ] Grade A: Excellent [ ] Grade B: Good [ ] Grade C: Fair [Y] Grade D: No scientific significance
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [ ] Major revision [Y] Rejection
Re-review	[ ] Yes [Y] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The authors of this article performed methylation analysis of colon adenoma and CRC samples using SeqCap targeted bisulfite sequencing and RNA-seq analysis. When 22 CRC samples and 25 ADE samples were compared, the global methylation was higher in the CRC samples. However, the methylation patterns for differentially methylated position genes, chromatin signatures, and repeated elements were the same for both groups. With the help of RNA-Seq gene expression data, they found 14 meDEGs, but only the methylation of AGTR1 and NECAB1 could predict the prognosis. Although their objectives, techniques, and complex in silico studies used are state-of-the-art, I have fundamental problems with the design of the research. For the adenoma group, the samples should at least have been divided into low- and high-grade adenomas, not to mention their histological type (tubular, tubulo-villous, or villous). Also, for CRC samples, samples should have been subdivided into at least early and advanced grades. It has been previously shown that promoter mutational abnormalities in CRC driver genes can be detected in early adenomas. It would have been good to compare the results with this article (PLoS One. 2015 Aug 20;10(8):e0133836. doi:

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10.1371/journal.pone.0133836.) Another shortcoming of the article is its descriptive nature. In at least one colon cancer cell line, it would have been worthwhile to investigate the consequences of restoring methylation status in a subset of genes (e.g., by 5-aza-2' deoxycytidine treatment). Given these shortcomings, I do not consider the article suitable for publication.

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Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 02944288
Position: Editorial Board
Academic degree: MD
Professional title: Assistant Professor, Lecturer, Surgeon
Reviewer's Country/Territory: Russia
Author's Country/Territory: China

Manuscript submission date: 2023-08-17

Reviewer chosen by: Yu-Lu Chen

Reviewer accepted review: 2023-10-03 08:13

Reviewer performed review: 2023-10-09 08:43

Review time: 6 Days

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
Creativity or innovation of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No creativity or innovation

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Scientific significance of the conclusion in this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No scientific significance
Language quality	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection
Re-review	[Y] Yes [ ] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Dear authors. Weaknesses or deficiencies in the manuscript are: 1) Too small amount of samples. Especially taking into account results of some other authors. I would recommend to add more samples to the study and rename it as "Early Results..." 2) If authors wanted to identify exacts drivers from adenoma to carcinoma progression? They have to compare exactly late stage adenomas and early stage carcinomas. But they did not divide adenomas and carcinomas into early and late stage subgroups. I also recommend to withdraw from the manuscript the words about identification drivers from adenoma to carcinoma and divide both mentioned groups into early and late stage. 3) Authors posted their conclusions in the end of discussion section – it's better to post it in the separate conclusion section. This could be easily corrected

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Reviewer's code: 05524138
Position: Peer Reviewer
Academic degree: MD, PhD
Professional title: Chief Doctor, Consultant Physician-Scientist
Reviewer's Country/Territory: Kazakhstan
Author's Country/Territory: China

Manuscript submission date: 2023-08-17
Reviewer chosen by: Yu-Lu Chen
Reviewer accepted review: 2023-11-04 12:08
Reviewer performed review: 2023-11-04 12:19
Review time: 1 Hour

Scientific quality	[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Novelty of this manuscript	[ ] Grade A: Excellent [Y] Grade B: Good [ ] Grade C: Fair [ ] Grade D: No novelty
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Re-review	[ ] Yes [Y] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous
	Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

Dear authors, in the article you did not specify how you received 5-centimeter sections of normal tissue? By what method were they obtained, surgical resection of the intestine or ESD? And why are they not indicated from which part of the large intestine samples of normal tissue, adenomas and tumor material were obtained?