

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 72475

Title: Differential DNA methylation analysis of SUMF2, ADAMT , and PXDN provides novel insights into colorectal cancer prognosis prediction in Taiwan

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 01489938

Position: Editorial Board

Academic degree: AGAF, FACC, MD

Professional title: Director, Full Professor

Reviewer's Country/Territory: Hungary

Author's Country/Territory: Taiwan

Manuscript submission date: 2021-10-17

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-10-19 16:08

Reviewer performed review: 2021-10-19 16:41

Review time: 1 Hour

Scientific quality	☐ Grade A: Excellent ☐ Grade B: Very good ☒ Grade C: Good ☐ Grade D: Fair ☐ Grade E: Do not publish
Language quality	☒ Grade A: Priority publishing ☐ 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 ☐ Rejection
Re-review	☐ Yes ☒ No

Peer-reviewer statements	Peer-Review: ☒ Anonymous ☐ Onymous Conflicts-of-Interest: ☐ Yes ☒ No
-------------------------------------	---

SPECIFIC COMMENTS TO AUTHORS

In this original article the authors focused on the association between CRC prognosis and the status and level of differential DNA methylation of selected genes. The methylation status of SUMF2, ADAMTS5, and PXDN in tumor tissue and tumor-free adjacent areas were evaluated via MS-PCR, and the methylation degrees of SUMF2 and ADAMTS5 were assessed using EpiTYPER DNA methylation analysis. The relationships of gene methylation with RFS, PFS, and OS were evaluated. They found that CpG_3+CpG_7 hypermethylation of SUMF2 from tumor tissue is associated with significantly shorter PFS and OS compared with CpG_3+CpG_7 hypomethylation. Contrary, CpG_2 and CpG_13 hypermethylation of ADAMTS5 from normal tissue is associated with a significantly longer RFS compared with CpG_2 and CpG_13 hypomethylation. The study is well designed, the used methodology is adequate, the results are clear, and the discussion is moderate, critical, and logical. One aspects needs more explanation: - the selection of the 3 candidate genes is understandable, but it must be visualized what other genes were amongst the (at least) TOP10 candidates.

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 72475

Title: Differential DNA methylation analysis of SUMF2, ADAMT , and PXDN provides novel insights into colorectal cancer prognosis prediction in Taiwan

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 04135204

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Associate Professor

Reviewer's Country/Territory: China

Author's Country/Territory: Taiwan

Manuscript submission date: 2021-10-17

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-10-20 02:40

Reviewer performed review: 2021-10-22 06:52

Review time: 2 Days and 4 Hours

Scientific quality	☐ Grade A: Excellent ☒ Grade B: Very good ☐ Grade C: Good ☐ Grade D: Fair ☐ Grade E: Do not publish
Language quality	☐ Grade A: Priority publishing ☒ 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 ☐ Rejection
Re-review	☐ Yes ☒ No



**Baishideng
Publishing
Group**

7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

Peer-reviewer statements	Peer-Review: [☒] Anonymous [☐] Onymous Conflicts-of-Interest: [☐] Yes [☒] No
-------------------------------------	---

SPECIFIC COMMENTS TO AUTHORS

1 Title. Does the title reflect the main subject/hypothesis of the manuscript? Yes. 2 Abstract. Does the abstract summarize and reflect the work described in the manuscript? Yes. 3 Key words. Do the key words reflect the focus of the manuscript? Yes. 4 Background. Does the manuscript adequately describe the background, present status and significance of the study? Yes. 5 Methods. Does the manuscript describe methods (e.g., experiments, data analysis, surveys, and clinical trials, etc.) in adequate detail? Yes. 6 Results. Are the research objectives achieved by the experiments used in this study? What are the contributions that the study has made for research progress in this field? Yes. 7 Discussion. Does the manuscript interpret the findings adequately and appropriately, highlighting the key points concisely, clearly and logically? Are the findings and their applicability/relevance to the literature stated in a clear and definite manner? Is the discussion accurate and does it discuss the paper's scientific significance and/or relevance to clinical practice sufficiently? Yes. 8 Illustrations and tables. Are the figures, diagrams and tables sufficient, good quality and appropriately illustrative of the paper contents? Do figures require labeling with arrows, asterisks etc., better legends? Yes. 9 Biostatistics. Does the manuscript meet the requirements of biostatistics? Yes. Please analyze the chi-square statistics in Table1 and provide the p value for each column. 10 Units. Does the manuscript meet the requirements of use of SI units? Yes. 11 References. Does the manuscript cite appropriately the latest, important and authoritative references in the introduction and discussion sections? Does the author self-cite, omit, incorrectly cite and/or over-cite references? Yes. 12 Quality of manuscript organization and presentation. Is the manuscript well, concisely and coherently



**Baishideng
Publishing
Group**

7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
<https://www.wjgnet.com>

organized and presented? Is the style, language and grammar accurate and appropriate? Yes. 13 Research methods and reporting. Authors should have prepared their manuscripts according to manuscript type and the appropriate categories, as follows: (1) CARE Checklist (2013) - Case report; (2) CONSORT 2010 Statement - Clinical Trials study, Prospective study, Randomized Controlled trial, Randomized Clinical trial; (3) PRISMA 2009 Checklist - Evidence-Based Medicine, Systematic review, Meta-Analysis; (4) STROBE Statement - Case Control study, Observational study, Retrospective Cohort study; and (5) The ARRIVE Guidelines - Basic study. Did the author prepare the manuscript according to the appropriate research methods and reporting? Yes. 14 Ethics statements. For all manuscripts involving human studies and/or animal experiments, author(s) must submit the related formal ethics documents that were reviewed and approved by their local ethical review committee. Did the manuscript meet the requirements of ethics? Yes.

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 72475

Title: Differential DNA methylation analysis of SUMF2, ADAMT , and PXDN provides novel insights into colorectal cancer prognosis prediction in Taiwan

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03478911

Position: Associate Editor

Academic degree: PhD

Professional title: Chief Technician, Executive Vice President, Research Assistant Professor

Reviewer's Country/Territory: South Korea

Author's Country/Territory: Taiwan

Manuscript submission date: 2021-10-17

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-10-17 20:57

Reviewer performed review: 2021-10-25 05:18

Review time: 7 Days and 8 Hours

Scientific quality	☐ Grade A: Excellent ☐ Grade B: Very good ☒ Grade C: Good ☐ Grade D: Fair ☐ Grade E: Do not publish
Language quality	☐ Grade A: Priority publishing ☒ 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 ☐ Rejection

Re-review	[☒] Yes [☐] No
Peer-reviewer statements	Peer-Review: [☒] Anonymous [☐] Onymous Conflicts-of-Interest: [☐] Yes [☒] No

SPECIFIC COMMENTS TO AUTHORS

This study investigated the association of changes in DNA methylation of candidate genes in tumor tissue and adjacent normal tissues to evaluate colorectal cancer (CRC) prognosis. The methylation on CpG sites in certain genes has been shown to be significantly associated with CRC recurrence, progression, and survival. This is an interesting study and has clinically significant implications for researchers targeting epigenetics, but supplementation of the following points will be required.

[Introduction] The theoretical background of how the three selected genes (SUMF2, ADAMTS5, and PXDN) are related to the progression of colorectal cancer is missing.

[Methods] 1. A specific description of how to gather specimens in patients including adjacent normal regions to analyze gene methylation is missing. 2. The description of most steps for extracting DNA from a biopsy sample was omitted (Any processes before using the extraction kit).

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 72475

Title: Differential DNA methylation analysis of SUMF2, ADAMT , and PXDN provides novel insights into colorectal cancer prognosis prediction in Taiwan

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06079635

Position: Peer Reviewer

Academic degree: BSc, MSc, PhD

Professional title: Assistant Professor

Reviewer's Country/Territory: Pakistan

Author's Country/Territory: Taiwan

Manuscript submission date: 2021-10-17

Reviewer chosen by: AI Technique

Reviewer accepted review: 2021-10-21 06:30

Reviewer performed review: 2021-10-27 07:49

Review time: 6 Days and 1 Hour

Scientific quality	☐ Grade A: Excellent ☐ Grade B: Very good ☐ Grade C: Good ☒ Grade D: Fair ☐ Grade E: Do not publish
Language quality	☐ Grade A: Priority publishing ☒ 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 ☐ Rejection
Re-review	☒ Yes ☐ No

Peer-reviewer statements	Peer-Review: [☒] Anonymous [☐] Onymous Conflicts-of-Interest: [☐] Yes [☒] No
-------------------------------------	---

SPECIFIC COMMENTS TO AUTHORS

The manuscript titled, 'Differential DNA methylation analysis provides novel insights into colorectal cancer prognosis prediction in Taiwan', by Jing-Quan et al., has investigated the DNA methylation of three genes in a local cohort of CRC patients from Taiwan. This is an interesting study and of late, role of epigenetic factors including DNA methylation in causation and progression of cancers has become an active and expanding area of research. The few comments regarding the present manuscript are: a) Title of the research is rather vague given that only three genes have been investigated for DNA methylation. It will be good to modify the title according to the work undertaken. b) Background section in the abstract is too general, should be re-written to focus more on the research work conducted. c) Conclusion sub-section of the abstract states 'fundamental observations.....', which again is too broad a conclusion and should be re-written to describe the findings. d) Primers sequences and PCR reaction parameters can be summarized in a Table. This will improve the flow of the experimental procedures described in the methods section. At present, these lengthy details make it hard to follow the procedural details. e) The method by which DNA methylation was quantified at the sites of interest should be clearly detailed. At present, it is not clear how authors have quantified the DNA methylation at the selected regions of the target genes. f) Results sections should show the results of the PCRs i.e. the amplified product and gel-pictures with relevant controls g) There is no mention of controls for the PCRs undertaken, they should be included too in the methods section.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

Name of journal: *World Journal of Gastroenterology*

Manuscript NO: 72475

Title: Differential DNA methylation analysis of SUMF2, ADAMT , and PXDN provides novel insights into colorectal cancer prognosis prediction in Taiwan

Provenance and peer review: Invited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 06079635

Position: Peer Reviewer

Academic degree: BSc, MSc, PhD

Professional title: Assistant Professor

Reviewer's Country/Territory: Pakistan

Author's Country/Territory: Taiwan

Manuscript submission date: 2021-10-17

Reviewer chosen by: Ya-Juan Ma

Reviewer accepted review: 2022-01-06 10:14

Reviewer performed review: 2022-01-07 12:00

Review time: 1 Day and 1 Hour

Scientific quality	☐ Grade A: Excellent ☐ Grade B: Very good ☒ Grade C: Good ☐ Grade D: Fair ☐ Grade E: Do not publish
Language quality	☐ Grade A: Priority publishing ☒ 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 ☐ Rejection
Peer-reviewer	Peer-Review: ☒ Anonymous ☐ Onymous



**Baishideng
Publishing
Group**

7041 Koll Center Parkway, Suite
160, Pleasanton, CA 94566, USA
Telephone: +1-925-399-1568
E-mail: bpgoffice@wjgnet.com
https://www.wjgnet.com

statements

Conflicts-of-Interest: [] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The authors have revised the manuscript substantially based on the comments. Few grammar and syntax errors are still to be corrected e.g. 'mo' in methods section has not been elaborated as 'months' in the manuscript. In Figure 2, it is not clearly mentioned that what is the difference between 'negative control' and 'sterile water' as both are referred to as 'negative control' in the methods and materials section.