

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 87150

Title: Association between heat shock factor protein 4 methylation and colorectal cancer risk and potential molecular mechanisms: A bioinformatics study

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 05480683

Position: Peer Reviewer

Academic degree: PhD

Professional title: Academic Fellow, Academic Research, Adjunct Professor

Reviewer's Country/Territory: Italy

Author's Country/Territory: China

Manuscript submission date: 2023-07-28

Reviewer chosen by: AI Technique

Reviewer accepted review: 2023-07-29 12:36

Reviewer performed review: 2023-07-29 13:19

Review time: 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input checked="" type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation

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

SPECIFIC COMMENTS TO AUTHORS

Manuscript title: Association and potential molecular mechanisms between HSF4 methylation and colorectal cancer risk: a bioinformatics study Article type: Original Research Authors: Wenjing Zhang, Kelin Yue, Jingzhai Wang, Yu Zhang Journal: World Journal of Gastrointestinal Oncology Comments and Suggestions for Authors Please see several comments and my observations for improving the manuscript which I consider potentially suitable for World Journal of Gastrointestinal Oncology. In my opinion, the publication of this interesting work is recommended. However, improvements are necessary. a) The work, which is a complex computational study, is detailed, well conducted, and well organized. The experimental design is strong, given the numerous methodologies/bioinformatic analyses applied. An undoubted limitation is the lack of experimental validation of the data being obtained in silico on HSF4. Methods and results are well written and described. Figures are highly explicative and clear. The discussion supports the main study findings. b) Abstract (but also discussion), “hub gene” should be plural c) More recently published supporting references should be included on CRC and methylation defects, as example: 1.

<https://clinicalepigeneticsjournal.biomedcentral.com/articles/10.1186/s13148-023-0151>

8-5 2. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6266092/> 3.

<https://clinicalepigeneticsjournal.biomedcentral.com/articles/10.1186/s13148-023-0151>

6-7 4. <https://pubmed.ncbi.nlm.nih.gov/33762255/> 5.

<https://pubmed.ncbi.nlm.nih.gov/37400791/> 6.

<https://www.nature.com/articles/s41598-023-35631-5> d) Acronyms such as , FDA

etc..WHO should be explained for non-expert readers. Please check the work for the presence of additional, unexplained, abbreviations. e) Introduction. "DNA methylation

is a process of information and is widely applied in cancer prediction and diagnosis [8,9]." I recommend including these two additional references on DNA

methylation and cancer as a support

(<https://jamanetwork.com/journals/jamadermatology/article-abstract/2524840> and

<https://www.frontiersin.org/articles/10.3389/fgene.2019.01150/full>) f) Limitations

and conclusions should be reorganized in order to improve the reading/quality of the

discussion. Limitations should be moved from the conclusive paragraph and placed

before conclusions. Conclusions should instead improved by giving a succinct

description of the main study findings and future applications. Moreover, authors are

also encouraged to include more details on the validation experiment that can be

conducted. g) Methods, section2.3 Please include this additional, recently published,

reference for the PPI network and the use of Cytoscape PMID: 37436928 h) GO

enrichment, have the GO analyses for cellular components and biological function been

performed?

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Title: Association between heat shock factor protein 4 methylation and colorectal cancer risk and potential molecular mechanisms: A bioinformatics study

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03031516

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Associate Professor, Doctor

Reviewer's Country/Territory: Japan

Author's Country/Territory: China

Manuscript submission date: 2023-07-28

Reviewer chosen by: Geng-Long Liu (Quit 2023)

Reviewer accepted review: 2023-08-23 23:15

Reviewer performed review: 2023-08-30 13:43

Review time: 6 Days and 14 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input checked="" type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
Creativity or innovation of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No creativity or innovation

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

SPECIFIC COMMENTS TO AUTHORS

From this study, methylation status of HSF4 did not correlate to the prognosis of CRC. However, a previous study showed the methylation correlated with the prognosis, according to the authors' description. I recommend them to study the subtype of CRC that is correlated with the prognosis. Also, the methodology may have problem. Alteration of the method will save the data of this vigorous study. Line 29, page 2 It's not appropriate to stress China data, if the journal is international

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Title: Association between heat shock factor protein 4 methylation and colorectal cancer risk and potential molecular mechanisms: A bioinformatics study

Provenance and peer review: Unsolicited manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 03031311

Position: Peer Reviewer

Academic degree: MD, PhD

Professional title: Assistant Professor, Staff Physician

Reviewer's Country/Territory: United States

Author's Country/Territory: China

Manuscript submission date: 2023-07-28

Reviewer chosen by: Yu-Lu Chen

Reviewer accepted review: 2023-09-20 18:56

Reviewer performed review: 2023-09-20 19:21

Review time: 1 Hour

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Very good <input type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
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Scientific significance of the conclusion in this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No scientific significance
Language quality	<input type="checkbox"/> Grade A: Priority publishing <input checked="" type="checkbox"/> Grade B: Minor language polishing <input type="checkbox"/> Grade C: A great deal of language polishing <input type="checkbox"/> Grade D: Rejection
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Peer-reviewer statements	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous
	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

Congratulations on the manuscript. Well written, and conclusions are consistent with findings. Please add limitations in the manuscript.

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Peer-review model: Single blind

Reviewer's code: 03522829

Position: Peer Reviewer

Academic degree: PhD

Professional title: Assistant Professor

Reviewer's Country/Territory: Egypt

Author's Country/Territory: China

Manuscript submission date: 2023-07-28

Reviewer chosen by: Yu-Lu Chen

Reviewer accepted review: 2023-09-15 08:18

Reviewer performed review: 2023-09-24 04:47

Review time: 8 Days and 20 Hours

Scientific quality	<input type="checkbox"/> Grade A: Excellent <input type="checkbox"/> Grade B: Very good <input checked="" type="checkbox"/> Grade C: Good <input type="checkbox"/> Grade D: Fair <input type="checkbox"/> Grade E: Do not publish
Novelty of this manuscript	<input type="checkbox"/> Grade A: Excellent <input checked="" type="checkbox"/> Grade B: Good <input type="checkbox"/> Grade C: Fair <input type="checkbox"/> Grade D: No novelty
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	Conflicts-of-Interest: <input type="checkbox"/> Yes <input checked="" type="checkbox"/> No

SPECIFIC COMMENTS TO AUTHORS

The present study was proposed to investigate the correlation between HSF4 methylation and CRC risk, and to uncover the underlying molecular mechanisms. Actually, the current proposal is interesting and well-written. Therefore, I recommend that the current study be published after minor revisions as follows: 1- Please add a diagrammatic figure to propose the possible mechanistic pathway for these findings 2- Please discuss whether TCGA data is important to study the complex interaction within the tumor microenvironment of cancer as well as cancer cells. reference: SnapShot: TP53 status and macrophages infiltration in TCGA-analyzed tumors. Int Immunopharmacol. 2020 Sep;86:106758. doi: 10.1016/j.intimp.2020.106758.