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PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Oncology

Manuscript NO: 47852

Title: Protein expression trends of DNMT1 in gastrointestinal diseases: from benign to precancerous lesions to cancer

Reviewer's code: 03806663

Reviewer's country: Egypt

Science editor: Ying Dou

Reviewer accepted review: 2019-07-19 19:22

Reviewer performed review: 2019-07-21 10:52

Review time: 1 Day and 15 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	[ ] Accept (High priority)	Peer-Review:
[ ] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] Accept (General priority)	[Y] Anonymous
[ ] Grade C: Good	[Y] Grade C: A great deal of language polishing	[Y] Minor revision	[ ] Onymous
[Y] Grade D: Fair	[ ] Grade D: Rejection	[ ] Major revision	Peer-reviewer's expertise on the topic of the manuscript:
[ ] Grade E: Do not publish		[ ] Rejection	[Y] Advanced
			[ ] General
			[ ] No expertise
			Conflicts-of-Interest:
			[ ] Yes
			[Y] No

SPECIFIC COMMENTS TO AUTHORS

1- DNMT1 is a tissue biomarker and it is a disadvantage as it needs invasive manuever)

Answer: In this research, we reported the expression features of DNMT1 protein by IHC in human tissue，which provided some research clues that DNMT1 is a gene

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with significant differential expression in gastrointestinal diseases and we hope to detect DNMT1 using serological tests in the next study to make DNMT1 better for clinical noninvasive diagnosis.

2- the sensitivity and specificity of this biomarker is not high, i mean the fallacies are also high

Answer: Although the sensitivity and specificity of this biomarker is not high, but DNMT1 has a certain ability to distinguish the severity of the disease. The overexpression of DNMT1 can be seen in high grade intraepithelial neoplasia or tumor samples, which means DNMT1 is a warning biomarker for some patients and could remind them to accept further examination.

3- you need to formulate figures to be more informative

Answer: In accordance with your suggestion, we have further supplemented the chart description to make it more informative.

4- some comments are included in the uploaded file

Answer: This was modified in the article.

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PEER-REVIEW REPORT

Name of journal: World Journal of Gastrointestinal Oncology

Manuscript NO: 47852

Title: Protein expression trends of DNMT1 in gastrointestinal diseases: from benign to precancerous lesions to cancer

Reviewer's code: 03270609

Reviewer's country: Russia

Science editor: Ying Dou

Reviewer accepted review: 2019-07-20 05:35

Reviewer performed review: 2019-07-24 18:56

Review time: 4 Days and 13 Hours

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
[ ] Grade A: Excellent [ ] Grade B: Very good [Y] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish	[ ] Grade A: Priority publishing [Y] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection	[ ] Accept (High priority) [ ] Accept (General priority) [Y] Minor revision [ ] Major revision [ ] Rejection	Peer-Review: [ ] Anonymous [Y] Onymous Peer-reviewer's expertise on the topic of the manuscript: [ ] Advanced [Y] General [ ] No expertise Conflicts-of-Interest: [ ] Yes [Y] No

SPECIFIC COMMENTS TO AUTHORS

The authors presented an interesting manuscript substantiating the expression trend of DNMT1 from benign to precancerous to cancer, which allows the use this marker both for early diagnosis and for the timely treatment of precancerous diseases, thereby

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preventing the development of a malignant tumor. At the same time, the authors should discuss a number of comments presented below.

1. Abstract. Remarks. - The full text of the "HIN" abbreviation is missing. Perhaps the authors mean "GHIN".

   本段需明确回答： "HIN" 缩写 是否 missing？是否等同"GHIN" 即可

   Answer: - "HIN" means high-grade intraepithelial neoplasia, and "GHIN" means gastric high-grade intraepithelial neoplasia. You can find the full meaning of "HIN" in the sentence of "Intraepithelial neoplasia (IN), especially high-grade intraepithelial neoplasia (HIN)….."

   - It is not clear what the authors mean by "normal intestinal mucosa".

   Answer: "normal intestinal mucosa" means the glandular structure of intestinal tissue is normal, with no or only mild inflammation.

2. Keywords. Remarks. I think "expression trend" has a dubious relationship to keywords. At the same time, the authors did not reflect in keywords such phrase as "intraepithelial neoplasia".

   Answer: This was modified in the article. "expression trend" was deleted, and "intraepithelial neoplasia" was added.

3. Methods. Remarks. - It is not clear what the authors mean by "normal intestinal mucosa".

   Answer: - The use of some parenthetic words seems unsuccessful. For example, "Meanwhile, there were 297 cases of colorectal disease..."

   Answer: The article was retouched again and changed the inappropriate parenthetic words. - Perhaps, when describing the IHC method, there is no sense in giving the numbering of solutions in parentheses (reagent A, B, etc.)

   Answer: These were deleted in the article. - This sentence is inaccurate: "The scores were judged by semi-quantitative integration method,...." Answer: This sentence was

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corrected to "Semiquantitative scoring criterion was used to evaluate the expression of DNMT1 in nucleus,…."

-It is necessary to give a more accurate gradation of the number of stained cells, specifying the boundaries of inclusion. It is not clear in the text how the authors assessed the extreme indicators. For example, 1/3 refers to 1 or 2 points, etc. - Perhaps, this sentence is also inaccurate: «6~9 scores were divided into strong positive expression as "+++", 2~4 score was moderate positive expression as "++", and 0~1 score was negative or weak positive expression as "+".

Answer: This sentence was revised in the article. (marked yellow in the text)

- It is not clear why the authors used rank sum test for statistical analysis. If they compared the frequency of signs, they should have used the Chi-square test.

-Answer: Statistical analysis of immunohistochemical scores can be performed using chi-square test (grouped by negative or positive levels, like - , +, ++, +++) or rank sum analysis (grouped by scores, like 0-9), and in our project, we use the latter method for statistical analysis.

4. Results. The research objectives were achieved in this study. The authors proposed a rather original method for assessing the expression of DNMT1 in tissue. They showed the possibility of using the determination of the level of expression of this marker for screening early cancer of the stomach and colon, as well as diseases of the stomach and intestines associated with a high risk of malignancy. The data obtained can be used both for the diagnosis of early cancer of the stomach and colon, and to reduce the incidence of this pathology through timely prescribed treatment. Remarks. - It is unclear what "The expression of DNMT1 was practically in the nucleus..." means, this should be clarified.

Answer: This was modified to "Representative photomicrographs of

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immunohistochemical staining of DNMT1 can be seen in Figure 1. The positive staining is brownish yellow particles. "

- It is inaccurate term: "gastric small pit epithelium" - Incorrect phrases are also present, for example: "…the positive expression in CSG group was very low (0/90)" - 0 of 90 is a negative indicator. Other inaccurate phrases are probably the following: " The negative or weak positive expression rates in AG/GIM and GLIN groups were separately 55.56% (40/72) and 38.89% (21/54), and the moderate positive expression rates were not very high, which were 44.44% (32/72) and 57.41% (31/54), respectively"; "The negative or weak positive expression rate was unobvious, with 4.88% (4/82), and the remaining part was 34.15% (28/82)".

Answer: This whole part was modified in the article. (marked yellow in the text)

5. The discussion requires some stylistic and grammatical correction.

   Answer: We polished the article again.

6. The figures, diagrams and tables are good quality and appropriately illustrative of the paper contents. Remarks. - In the captions for the figures and tables it is necessary to decipher the abbreviations in the notes (for example, CSG, AG/GIM, GLIN and e.g.).

   -Answer: This was modified in this article. (marked yellow in the text)

   - Figure 2. No axis "y" designation.

   -Answer: In Figures, axis "y" means cases, and it was modified in this article.

   - Figure 2 and table 1 as well as the figure 4 and table 2 duplicate data.

   -Answer: Figure 2 and table 1 as well as the figure 4 and table 2 are duplicate data. The tables are to show the exact data, and the figures are to show the comparison between each group more intuitively.

7. There are no serious remarks on other points.