Answering reviewers

Reviewer #1:

Scientific Quality: Grade C (Good)

Language Quality: Grade C (A great deal of language polishing)

Conclusion: Minor revision

Specific Comments to Authors:

The title could reflect the main subject the manuscript; The abstract could summarize and reflect the work described in the manuscript; The key words could reflect the focus of the manuscript; The manuscript adequately describes the background; The manuscript appropriately cites the latest, important and authoritative references in the Introduction and Discussion sections. In this review, the authors summarized mutations of TP53 and CDH1 in gastric cancer (GC) from various perspectives. Including TP53 as an important tumor suppressor gene, TP53 encoded p53 protein is an essential regulatory factor in normal cellular physiology, TP53 mutation in tumor and GC, and TP53 mutation in GC's progression. The authors also described CDH1 encoding for epithelial cadherin (E-cadherin), CDH1 mutation and epithelial mesenchymal transition (EMT), the relationship and diffuse gastric cancer, and the authors also summarized CDH1 mutations are associated with a poor prognosis, as well as CDH1 hypermethylation in GC. In the end, the authors indicated clinical indications for TP53 and CDH1 mutations in GC. But the manuscript still has some limitation: 1. Please indicate the proportion of TP53 and CDH1 mutations in GC in Chinese and other countries; 2. Please edit English language.

Response: Thank you for your comment.

Zhang et al. reported the mutated TP53 in 58.14% gastric cancer patients using the data from a single center of Chinese population (Zhang L, Wang Y, Li Z, Lin D,

Liu Y, Zhou L, Wang D, Wu A, Li Z. Clinicopathological features of tumor mutation burden, Epstein-Barr virus infection, microsatellite instability and PD-L1 status in Chinese patients with gastric cancer. Diagn Pathol. 2021 May 1;16(1):38. doi: 10.1186/s13000-021-01099-y. PMID: 33933102; PMCID: PMC8088709.). After searching the pubmed, we have not found exact proportion of TP53 mutation in GC in Chinese and other countries, which remains to be studied.

DGC is predisposed to persons who have sporadic or inherited CDH1 gene mutations. CDH1 mutations occur at a rate of about 25% in sporadic DGC and can approach 50% in hereditary DGC (Blair VR, McLeod M, Carneiro F, et al (2020) Hereditary diffuse gastric cancer: updated clinical practice guidelines. The Lancet Oncology 21:e386-e397). Liu et al. found the mutation rates of 32 genes, including TP53, SPEN, FAT1, and CDH1 exceeded 10%. Besides, CDH1 mutations were significantly associated with diffuse gastric cancer. (Liu HL, Peng H, Huang CH, Zhou HY, Ge J. Mutational separation and clinical outcomes of TP53 and CDH1 in gastric cancer. World J Gastrointest Surg 2023; In press) After searching the pubmed, we have not found exact proportion of CDH1 mutation in GC in Chinese and other countries, which remains to be studied.

The English language has been polished by a professional English language editing company, and the certificate has been uploaded.

EDITORIAL OFFICE'S COMMENTS

(1) Science editor:

The manuscript has been peer-reviewed, and it is ready for the first decision.

Language Quality: Grade C (A great deal of language polishing)

Scientific Quality: Grade C (Good)

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, and full text of the manuscript, all of which have met the basic publishing requirements of the World Journal of Gastrointestinal Surgery, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.

The quality of the English language of the manuscript does not meet the requirements of the journal. Before final acceptance, it is recommended that the authors provide the English Language Certificate issued by a professional English language editing company. Please visit the following website for the professional English language editing companies we recommend: https://www.wjgnet.com/bpg/gerinfo/240.

Response: Thank you for your comment.

The English language has been polished by a professional English language editing company, and the certificate has been uploaded.

Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.

Response: Thank you for your comment.

The table has been revised.

Table 1 The gene methylation in gastric cancer

Cell process	Gene

Cell cycle regulation	Cyclin E, CDC25B, p27, p53, RB, CHFR, hsMAD2,PRDM5
Cell adherence	CDH1
DNA repair	MLH1, MSH2,PMS2
Invasion and migration	HOXA10,PRL-3
Apoptosis	BNIP3

Please upload the approved grant application form(s) or funding agency copy of any approval document(s).

Response: Thank you for your comment.

The approved grant application form has been uploaded.

Please describe the article you comment in the main text, and add it to the reference list: Liu HL, Peng H, Huang CH, Zhou HY, Ge J. Mutational separation and clinical outcomes of TP53 and CDH1 in gastric cancer. World J Gastrointest Surg 2023; In press

Response: Thank you for your comment.

The article we comment has been described in the main text, and added to the reference list.

"Liu et al. found the mutation rates of 32 genes, including TP53, SPEN, FAT1, and CDH1 exceeded 10%. Besides, CDH1 mutations were significantly associated with diffuse gastric cancer[48]"

The abstract is too long, please short it. The abstract should be no more than 200 words.

Response: Thank you for your comment.

The abstract has been revised into 186 words.

"In this editorial we comment on the article by He-Li Liu published in the recent

issue of the World Journal of Gastroenterology. A common gene mutation in gastric cancer is the TP53 mutation. As a tumor suppressor gene, TP53 is implicated in more than half of all tumor occurrences. TP53 gene mutations in gastric cancer tissue may be related with clinical pathological aspects. The TP53 mutation arose late in the progression of gastric cancer and aided in the final switch to malignancy. CDH1 encodes E-cadherin, which is involved in cell-to-cell adhesion, epithelial structure maintenance, cell polarity, differentiation, and intracellular signaling pathway modulation. CDH1 mutations and functional loss can result in DGC, and CDH1 mutations can serve as independent prognostic indicators for poor prognosis. Gastric cancer patients can benefit from genetic counseling and testing for CDH1 mutations. Demethylation therapy may assist to postpone the onset and progression of gastric cancer. The investigation of TP53 and CDH1 gene mutations in gastric cancer allows for the investigation of the relationship between these two gene mutations, as well as providing some basis for evaluating the prognosis of gastric cancer patients. ”