

PEER-REVIEW REPORT

Name of journal: *World Journal of Gastrointestinal Oncology*

Manuscript NO: 87941

Title: Immune-related lncRNA ZNF710-A -201 promotes the metastasis and invasion of gastric cancer cells

Provenance and peer review: Unsolicited Manuscript; Externally peer reviewed

Peer-review model: Single blind

Reviewer's code: 01551432

Position: Editorial Board

Academic degree: MD, PhD

Professional title: Doctor

Reviewer's Country/Territory: Japan

Author's Country/Territory: China

Manuscript submission date: 2023-09-04

Reviewer chosen by: Yu-Lu Chen

Reviewer accepted review: 2023-10-24 10:11

Reviewer performed review: 2023-10-26 07:44

Review time: 1 Day and 21 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 Grade E: Do not publish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
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 checked="" 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

Dear Authors, Thank you for submitting your manuscript entitled, "Immune-related lncRNA ZNF710-AS1-201 promotes metastasis and invasion in gastric cancer cells" in WJG. The manuscript is well written and compactly summarized. The topic is interesting and timely. However, some major criticisms should be addressed as the followings. Major 1) Clinically, highly differentiated gastric cancer has more multi-organ and lymph node metastasis than undifferentiated gastric cancer, but less gastric wall invasion and peritoneal invasion. 2) Although there is a significant difference between the low and high expression groups for differentiation level and lymph node metastasis in Table 2. p-value is close to 0.05. It is stated that these two groups are divided by a median expression threshold, is this correct and general? Because depending on the threshold setting, there would not be a significant difference between the two groups for the previous feature. 3) Considering this, instead of comparing between two groups of low and high expression, it would be easier to understand if ZNF710 expression levels were quantitatively compared between three or four groups of gastric cancer histopathological types, i.e., highly differentiated, (moderately) differentiated, poorly



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differentiated, and ring cell carcinoma, but what do you think? Thanks. Takuya Watanabe

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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
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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

SPECIFIC COMMENTS TO AUTHORS This work studies the relationship between the advancement of the gastric cancer and ZNF710-AS1-201, an immune-related long non-coding RNA that is upregulated in gastric cancer cells. Authors found that the amount of ZNF710-AS1-201 in the tissue is related with the type of immune cells that are infiltrated in the tissue and with the sensitivity to antitumor drugs. Furthermore, they observed that, in gastric cancer cells, ZNF710-AS1-201 promotes cell viability, proliferation as well as cell metastasis and invasion while it inhibits cell apoptosis. This study provides valuable data to increase knowledge on the development of metastasis and on the treatment with anticancer therapy in cases of gastric cancer. This is a well written paper. However, I consider that it should be improved at several points shown below. Abstract I think it is useful for the reader to include in the top of the abstract that ZNF710 is a transcription factor and that ZNF710-AS1-201 is an immune-related long non-coding RNA that is upregulated in gastric cancer cells. Introduction: Some abbreviations should be included in full the first time that they appear in the text: vascular endothelial growth factor (VEGF). The same can be applied for overall survival

(OS) and disease-free survival (DFS) in the Results section. Results: Results from functional enrichment analysis (FEA) based on ZNF710-AS1-201 are not clearly explained. Authors state that a significant enrichments is found in several expressed genes. However, there are not information about the differences observed between tissues with high- and low- ZNF710-AS1-201 levels. The fourth paragraph of the Results section on page 1s ("ZNF710-AS1-201 was closely related to GC") should be the first one because it shows the level of ZNF710-AS1-201 in the gastric cancer samples. I think these results are used by the authors to separate the samples in two groups: high- and low-level groups. If so, please specify the range of ZNF710-AS1-201 levels for both groups. "GES-1" is referred in the text of Results as "normal gastric mucosa cells" whereas in Fig 4 legend is a "normal human gastric cancer cell line" Results from the transfection of HGC-27 and MKN-45 cells with ZNF710-AS1-201 plasmids should be given in the text of the Results section because only a brief statement is given: "The findings demonstrated favorable transfection effectiveness ($P < 0.05$, Figure 4E-F)". In the text of Results, authors describe the results of cell proliferation in HGC-27 and MKN-45 cells after the treatment of 24, 48, and 72 hours. However, in the figure 5B, only one histogram is given for each type of cells. So, what is the time of incubation for the results showed in Fig 5B? The same can be applied for the cell invasion in the figure 7C. Authors stated "low expression of ZNF710-AS1-201 significantly enhanced MKN-45 cell apoptosis at 24h, 48h, and 72h", however, this is not true for 24h, as can be seen in Fig 6D. Authors state "The findings indicated that the alterations in IDH2, SEMA4B, ARHGAP10, RGMB, hsa-miR-93-5p, and ZNF710-AS1-202 did not exhibit consistency or statistical significance following the overexpression or underexpression of ZNF710-AS1-201". However, Fig 8 show that all of them showed statistically significant changes, either in HGC-27 or in MKN-45 cells. Thus, I suggest rewriting this sentence. In addition, the second paragraph on page 15 discusses these results. In general, I suggest



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not including the p value in the text of the Results section because it can be seen in each figure. In fact, authors always include “ $P < 0.05$ ” in the text while several p values ($P < 0.05$, $P < 0.01$ or $P < 0.001$) can be seen in the figures. The term “NGC-27” throughout the text in Results and Discussion should be replaced by “HGC-27”. In the second paragraph of the Results section, I suggest to add “antitumor” before “drugs” Discussion: I think that in the second paragraph of page 14, by “... G protein-coupled peptide receptor activity and ion channel activity et al.”, authors mean “... ion channel activity, and others” Figures: In general, the font size of the figures is too small, especially in Fig 8.

RE-REVIEW REPORT OF REVISED MANUSCRIPT

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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 checked="" type="checkbox"/> Accept (General priority) <input type="checkbox"/> Minor revision <input type="checkbox"/> Major revision <input type="checkbox"/> Rejection
Peer-reviewer	Peer-Review: <input checked="" type="checkbox"/> Anonymous <input type="checkbox"/> Onymous



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statements

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

SPECIFIC COMMENTS TO AUTHORS

The manuscript has been properly revised and I am O.K. as it stands.