Peer Review File

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Comment 1: What progress has been made with the treatment and biomarkers for gastric cancer? The relevant content should be included in the introduction.

Reply 1: We have generally reviewed the progress in the treatment and biomarkers for gastric cancer in the introduction.

Changes in the text: Page 4, line 79-82; 85-87.

Comment 2: In the paper, a total of 971 differentially expressed lncRNAs (DElncRNAs), 144 differentially expressed miRNAs (DEmiRNAs), and 2,789 differentially expressed mRNAs (DEmRNAs) were identified. Please list these differentially expressed lncRNAs, miRNAs, and mRNAs in a supplementary table.

Reply 2: We have listed all the differentially expressed lncRNAs, miRNAs, and mRNAs in supplementary table1-6.

Changes in the text: None.

Comment 3: Please choose a representative differentially expressed lncRNA, miRNA, and mRNA and test their expression. The paper is missing experimental data.

Reply 3: We apologize for this. We are aware that a follow-up experiment like RT-PCR is important for the validation of differentially expressed lncRNAs, miRNAs, and mRNAs. However, because of the outbreak of COVID19, it is difficult to get the reagents. According to some similar studies, such as (Wang J et al. Cancer Cell International. 2019, PMID:31827401), (Hu J et al. Translational Cancer Research.

2019, PMID:31737498), we validated the expression of 3 representative lncRNAs that constructed the risk-scoring system in GEPIA database (Fig.6).

Many similar studies also missed experimental data, such as (Zhao D, Journal of Cancer. 2020, PMID:31892978), (Li S et al. Journal of Cancer Research Clinical Oncology. 2020, PMID:32124023), (Yao Y et al. Bioscience Reports. 2020, PMID:31950990). Compared to these studies, we not only constructed a ceRNA network and identified a novel lncRNA based prognostic biomarker, but also validated that this lncRNA-based risk-scoring system is independent of other clinical features via using univariate and multivariate Cox independence analyses. Additionally, this risk-scoring system was positively associated with tumor grade, suggesting a potential of utilizing the system in GC diagnosis (Fig. 7). A nomogram based on these 3 lncRNAs (ADAMTS9-AS1, C15orf54, and AL391152.1) combined with other clinical information was generated to further predict the prognosis of GC patients, which can convenient for clinical use.

Changes in the text: Page 9, line 181-192; Page 12, line 258-268. Additional Figures 6&7.

Comment 4: What is the purpose of setting a risk score system? Was the system tested based on available cases?

Replay: We aimed to screen out novel lncRNAs for prognosis of patients with GC and to provide new insights into the potential features of lncRNAs as therapeutic

targets. the expression of 3 representative lncRNAs that constructed the risk-scoring system were validated in GEPIA database (Fig. 6).

Changes in text: Page5, line 104-109; Page 9, line 180-182; Page 12, line 258-263. Added Fig. 6.

Comments 5: Please increase the possible mechanism analysis. This will better support the conclusions of the study.

Replay: We performed Gene Set Enrichment Analyses to identify enriched KEGG pathways to disclose the potential biological mechanisms of the risk-scoring system.

Changes in text: Page 9, line 189-192; Page 13, line 283-292. Added Fig. 8.

Comments 6: There have been many similar papers published before, such as (J Cell Biochem. 2019 Oct;120(10):17898-17911), (Cancer Cell Int. 2019 Jul 16;19:183. doi: 10.1186/s12935-019-0905-z) and (Cancer Med. 2020 Jan 10. doi: 10.1002/cam4.2760). What is the novel idea in this paper? Please provide detail in the introduction.

Replay: Zhang X et al. (J Cell Biochem. 2019 Oct;120(10):17898-17911) identified 3 hub-lncRNAs and revealed their function. We constructed a risk-scoring system based on ceRNA network and validated its robustness via independence evaluation. A predictive nomogram was generated to predict the prognosis of GC patients.

Guan YJ et al. (Cancer Cell Int. 2019 Jul 16;19:183. doi: 10.1186/s12935-019-0905-z) constructed a ceRNA network based on circRNA-miRNA-mRNA, not based on lncRNA.

Qi M et al. (Cancer Med. 2020 Jan 10. doi: 10.1002/cam4.2760) also constructed a risk system based on ceRNA analysis. Compared to this paper, we validated our

system via independence evaluation, and established a predictive nomogram to predict the prognosis of GC patients.

Other similar studies also constructed a risk system, but all of them were not validated via independence assessment. Compared to those studies, we constructed a nomogram to further predict the prognosis of GC patients, which can convenient for clinical use. And we also validated that this lncRNA-based risk-scoring system is independent of other clinical features via using univariate and multivariate Cox independence analyses. Additionally, this risk-scoring system was positively related to tumor grade, suggesting a potential of utilizing the system in GC diagnosis. We discussed these differences in Page 16-17, line 356-364.

Changes in text: Page 16-17, line 349-357.