Peer Review File

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Reviewer A

The paper titled “Construction of a prognostic signature for mucinous colonic adenocarcinoma based on N7-methylguanosine-related long noncoding RNAs” is interesting. The m7G-related lncRNA prognostic signature has potential value for the prognosis and diagnosis of mucinous colonic adenocarcinoma. However, there are several minor issues that if addressed would significantly improve the manuscript.

1) It is recommended to increase the research of the potential value of the m7G-related lncRNA risk model in predicting immunotherapy response and drug sensitivity in mucinous colonic adenocarcinoma patients.

Reply 1: Thanks for your advice! We have added the study on immunophenotypic score (IPS), but due to unexpected experimental conditions, we have not added the study on drug sensitivity prediction for the time being, and we intend to complete it as soon as possible.

Changes in the text: We have modified our text as advised (see Page 8-9, line 234-239; Page 13,line 369-377).

2) The identifications in the figure are inconsistent with those in the figure legends, for example, A and B are used in manuscript and figure legends, but are not used in the Figure 3. Uniform identification is recommended.

Reply 2: We are sorry for this error and have corrected it!

Changes in the text: We have modified our Figure as advised (See revised Figure 3).

3) How does m7G-related lncRNAs interact with other signal networks in the progression of mucinous colonic adenocarcinoma? What dual role does it play in increasing/inhibiting tumor progression? It is recommended to add relevant contents.

Reply 3: Thank you very much for your advice! Studies on the interaction of m7G-associated lncRNAs with other signaling networks in mucinous colonic adenocarcinoma are lacking. Your suggestion provides a direction for our next research. We may work on this in a follow-up study.

4) What is the patterns and prognostic roles of TMB and immune infiltration in colon cancer? It is recommended to add relevant content.

Reply 4: Thanks for your suggestions, we've added them to the discussion section.

Changes in the text: We added the prediction results in the text (see Page 15-16, line 446-449; Page 16, line 457-464).

5) It is suggested to increase in vivo and in vitro experimental verification, which may be more meaningful.

Reply 5: Thank you very much for pointing out this important issue. We agree with you. Unfortunately, due to limited conditions, we do not have additional experimental verification. However, through the following two points, our research content will become more complete.

①In theory, direct RNA sequencing can detect any given modification in a natural RNA molecule in real time and simultaneously. Therefore, we chose to use the m7GFinder tool in m7GHub to predict the five m7G-related lncRNAs selected by us (The transcriptome sequence file of AC254629.1 gene could not be found.), and the results showed that m7G modification may occur on LINC01133 and SMIM2-AS1.
②In Figure 3A, there were significant differences in the expression of these six genes in tumor samples and adjacent tissue samples.
Changes in the text: We added the prediction results in the text (see Page 9, line 241-245;Page 13, line 379-385).

6) The introduction part of this paper is not comprehensive enough, and the similar papers have not been cited, such as "Constructing and validating of m7G-related genes prognostic signature for hepatocellular carcinoma and immune infiltration: potential biomarkers for predicting the overall survival, J Gastrointest Oncol, PMID: 366360517". It is recommended to quote this article.
Reply 6: We made some changes to the introduction and added a quote from the article.
Changes in the text: We have modified our text as advised (see Page 4, line 111,117-120; Page 5, line 127-147).

7) The biological characteristics of m7G-related lncRNAs and its research progress in tumors should be added to the discussion.
Reply 7: Thanks for your suggestions, we've added them to the discussion section.
Changes in the text: We have modified our text as advised (see Page 14, line 404-408).

8) It may be more meaningful to suggest to increase the functional research of related key lncRNAs.
Reply 8: Thanks for your suggestions, we've added them to the discussion section.
Changes in the text: We have modified our text as advised (see Page 14-15, line 414-423).

Reviewer B

First, the title needs to indicate the development and validation of the prognosis prediction model.
Reply 1: Thanks for your suggestion, we have changed the title.
Changes in the text: We have modified our text as advised (see Page 1, line 2).

Second, the abstract needs some revisions. The background did not describe the potential clinical significance of this research focus. The methods need to describe the clinical sample and prognosis outcome in the dataset and how the training and validation samples were obtained and how the predictive accuracy was assessed. The results need to briefly describe the clinical characteristics of the study sample and the prognosis outcome in the whole sample, as well as the AUC values in the training and validation samples. The conclusion needs to delete the comments on the diagnosis since the authors only developed a prognosis prediction model.

Reply 2: Thanks for your suggestion, we have revised the summary content. We add the potential clinical implications of this study in the background. In method, We added information on how to obtain training and test sets and how to evaluate prediction accuracy. In the results, we also briefly describe the outcome of the whole sample, as well as the AUC values of the training set and the test set. And we have removed the comment on the diagnosis in the conclusion.
Changes in the text: We have modified our text as advised (see Page 2-3, line 43-81).

Third, the introduction of the main text needs to have an extensive review on what has been known on the prognostic biomarkers and prognosis prediction models in MC patients, as well as comments on the limitations of prior studies and the potential clinical significance of this research focus. It is inadequate that the authors only described the knowledge gap as the rationale of this study.
Reply 3: At present, no studies have been found on prognostic biomarkers and prognostic prediction models for patients with MC, and our study is the first study on prognostic biomarkers for patients with MC. We review several studies of Colon-related biomarkers and prognostic prediction models in the introduction.
Changes in the text: We have modified our text as advised (see Page 5, line 135-141).

Fourth, in the methodology, please describe the clinical sample, prognosis outcome, and the generation of training and validation samples. In statistics, please ensure $P<0.05$ is two-sided and the threshold AUC value for a good prediction model.
Reply 4: Thanks for your suggestion, we have added the relevant content.
Changes in the text: We have modified our text as advised (see Page 7, line 192; Page 10-11, line 294-305).

Finally, please cite several related papers: 1. Lian L, Xu XF, Shen XM, Huang TA, Li XM, Han SG, Zhou C, Xia YY. Pattern of distant metastases and predictive nomograms in colorectal mucinous adenocarcinoma: a SEER analysis. J Gastrointest Oncol 2021;12(6):2906-2918. doi: 10.21037/jgo-21-824. 2. Guarini C, Todisco A, Tucci M, Porta C, Mannavola F. Massive hyper-progression during anti-PD-1 immunotherapy in a young patient with metastatic mucinous adenocarcinoma of the right colon: a case report and literature review. Precis Cancer Med 2021;4:30. 3. Xu X, Shen W, Wang D, Li N, Huang Z, Sheng J, Rucker AJ, Mao W, Xu H, Cheng G. Clinical features and prognosis of resectable pulmonary primary invasive mucinous adenocarcinoma. Transl Lung Cancer Res 2022;11(3):420-431. doi: 10.21037/tlcr-22-190.
Reply 5: Thanks for your suggestion, we have added the relevant content.
Changes in the text: We have modified our text as advised (see Page 14, line 394).

Reviewer C

The work noncoding should be written as non-coding, please change the text accordingly
Reply 1: Thank you for your advice, I'm sorry for our mistake. we have mofified the relevant content.

Changes in the text: We have modified our text as advised (see Page 1, line 3; Page 2, line 40; Page 3, line 87; Page 4, line 106; Page 17, line 502; Page 23, line 676; Page 24, line 684,699,708; Page 25, line 718,727; Page 27, line 752; Page 33, line 765).

The authors used the Pearson correlation analysis to evaluate the correlation between m7G and long non-coding RNAs. Was it checked if both variables are normally distributed? If one of the variables does not have a normal distribution the Spearman analysis should be used instead
Reply 2: Thank you for reminding us, the data is normally distributed.

On page 3, line 87 the word nonmucinous should be written as non-mucinous
Reply 3: Thanks for your suggestion, we have modified the relevant content.
Changes in the text: We have modified our text as advised (see Page 4, line 96).

On page 11, lines 197 to 200, the information is already present in the method section so it should be removed
Reply 4: Thank you for your reminder! We have deleted it.

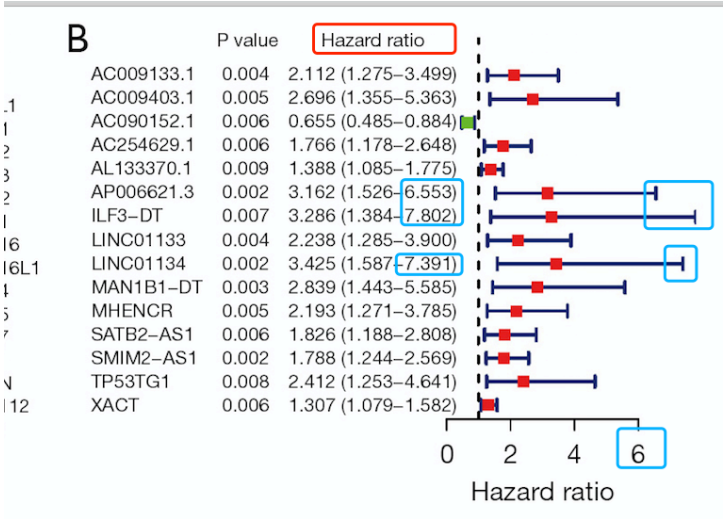
On page 11, line 307 the software CIBERSORT was misspelled as CIBERSOFT, please check the text for any other instances
Reply 5: Thanks for your suggestion, we have modified the relevant content.
Changes in the text: We have modified our text as advised (see Page 2, line 55; Page 8, line 218,220).

The text could benefit from a general revision the identify instances of double spaces (e. g lines 310 and 365)

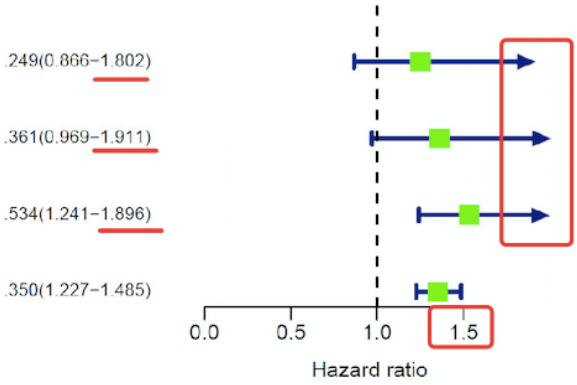
Reviewer D

1. **Figure 2**

a. Please add (95%CI) after HR.
b. To standardize the results, the part that exceeds the horizontal coordinates should be indicated by arrows, or please extend the X-axis.



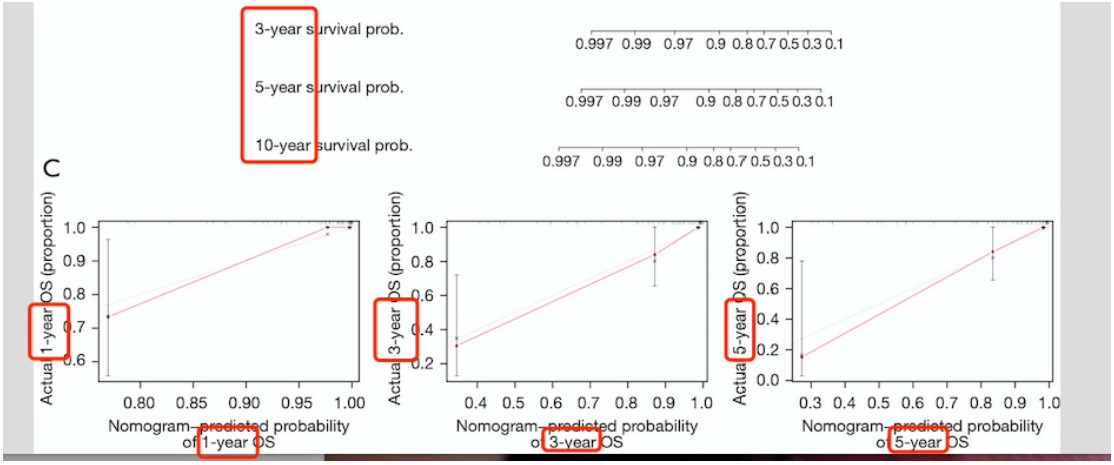
Here is an example:



Reply5: We have made the changes and attached pictures of the changes.

2. Figure 5

Please confirm if the year is correct.



Reply6: Thanks for the heads up that the year in the chart is correct.

3. Table 1

Please double-check the accuracy of data.

7 **Table 1** Clinical characteristics of mucinous adenocarcinoma patients

Variables	Value (n=114)
Age (years), n (%)	=72
≤65	26 (36.1)
>65	38 (52.8)
Unknown	8 (11.1)
Gender, n (%)	=60
Female	32 (44.4)
Male	8 (11.1)

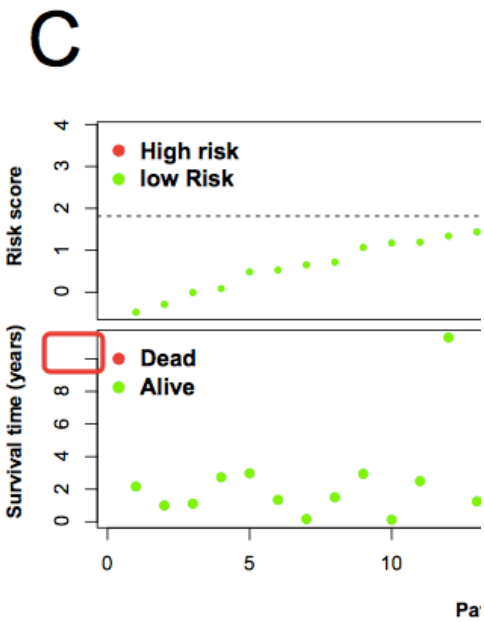
Reply7: Apologies for our mistake, changes have been made.

4. Please provide the figure legends of Supplementary Figures 2, 3, 4.

Reply8: We have made some typographical changes to the original three supplementary figures 2, 3, and 4, which have become supplementary figures 2, 3, and have added figure legends in the text.

5. Figure S2

Please supplement the number in Y-axis.



Reply9: Thanks for the heads up, we've added it.

6. Reference/citation

a. The author's name does not match the citation. Please check and revise.

Claire Rougeulle et al. demonstrated a unique role for XACT in controlling the initiation of inactivation of the human X-chromosome (错误!未找到引用源。).

50. allot C, Huret C, Lesecque Y, et al. XACT, a long noncoding transcript coating the active X chromosome in human pluripotent cells. Nat Genet. 2013 Mar;45(3):239-41.

b. The authors mentioned "studies...", while only one reference was cited. Change "Studies" to "A study" or add more citations. Please revise. Please number references consecutively in the order in which they are first mentioned in the text.

In recent years, many studies have found that lncRNA can act as cis- or trans-factors at the transcriptional, posttranscriptional, or translational levels, which may contribute to the occurrence and development of cancer (8).

Other studies have reported that the expression of lncRNA TP53 TG1 is downregulated in gastric cancer, functioning as a tumor suppressor (11).

Several studies have found that MHENCR predicts poor outcomes in patients with CRC and modulates tumorigenesis by blocking miR-532-p (49).
Reply10: Thanks for the heads up, we've made the changes.