Peer Review File

Article information: https://dx.doi.org/10.21037/jgo-24-52

Reviewer A

The paper titled "LINC01977 promotes colorectal cancer growth and metastasis by enhancing aerobic glycolysis via the ERK/c-Myc axis" is interesting. This study is the first to report that LINC01977 facilitates CRC proliferation, metastasis, and aerobic glycolysis through c-Myc, suggesting its potential as a therapeutic target for CRC treatment. However, there are several minor issues that if addressed would significantly improve the manuscript.

1) The abstract is not sufficient and needs further modification. The research background did not indicate the clinical needs of the research focus.

Reply:We think this is an excellent suggestion. We have indicated the clinical needs of the research focus in the background.

Changes in the text: We have modified our text as advised (see Page 1, line 32-33).

2) What are the correlations between LINC01977 and colorectal cancer staging, degree of differentiation, neural invasion, lymphatic metastasis and survival prognosis? It is recommended to add relevant content.

Reply: Based on our study, we found significant correlations between LINC01977 expression and several clinicopathological characteristics of colorectal cancer (CRC), such as colorectal cancer staging (in figure 2D), lymphatic metastasis (in figure 2E) and survival prognosis (in figure 2G-I). However, no significant correlations were observed with degree of differentiation or neural invasion.

Changes in the text: We have modified our text as advised (see Page 9, line 297-298).

3) There are many lncRNA that promote colorectal cancer growth and metastasis. Why did the author choose LINC01977 for research? Please describe the reason.

Reply: Your suggestion really means a lot to us. Previous studies have suggested a potential role of LINC01977 in CRC, and preliminary evidence could have shown that LINC01977 is frequently up-regulated in CRC tissues, such differential expression patterns make it an interesting candidate for further investigation. Initial functional studies might have hinted at the involvement of LINC01977 in promoting CRC growth and metastasis. By considering these factors, we likely reasoned that studying LINC01977 in CRC could provide valuable insights into its specific contribution to tumor development, metastasis, and potential therapeutic targeting.

Changes in the text: None

4) What is the impact of this study on the further treatment and prognosis of colorectal cancer? It is recommended to include relevant content in the discussion.

Reply:We have indicated the impact of this study on the further treatment and prognosis of colorectal cancer.

Changes in the text: We have modified our text as advised (see Page 14, line 450-454).

5) The introduction part of this paper is not comprehensive enough, and the similar papers have not been cited, such as "Comprehensive analysis of immune related lncRNAs in the tumor microenvironment of stage II-III colorectal cancer, PMID: 34790388". It is recommended to quote the article.

Reply:We have quoted the article "Comprehensive analysis of immune related lncRNAs in the tumor microenvironment of stage II-III colorectal cancer, PMID: 34790388".

Changes in the text: We have modified our text as advised (see Page 16, line 523-525).

6) Can LINC01977 be used as a potential biomarker for patient risk stratification and local regional metastasis in colorectal cancer? It is recommended to add relevant content.

Reply:We sincerely appreciate the valuable comments. Given the significant associations observed between LINC01977 expression and clinicopathological characteristics in colorectal cancer, there is a possibility that LINC01977 could serve as a potential biomarker for patient risk stratification and local regional metastasis assessment. However, it should be noted that additional studies are needed to confirm the prognostic value of LINC01977 as a standalone biomarker or in combination with other established markers. Prospective investigations involving diverse patient populations and rigorous validation are essential before considering its implementation in routine clinical practice. Further research is warranted to establish its clinical utility and validate its predictive power.

Changes in the text:Changes in the text: We have modified our text as advised (see Page 14, line 454-458).

7) It is suggested that the research progress of lncRNA in colorectal cancer should be added to the discussion.

Reply:Thank you for pointing this out. We have added the research progress of lncRNA in colorectal cancer to the discussion

Changes in the text: We have modified our text as advised (see Page 12-13, line 406-407).

Reviewer B

1. Figure 1

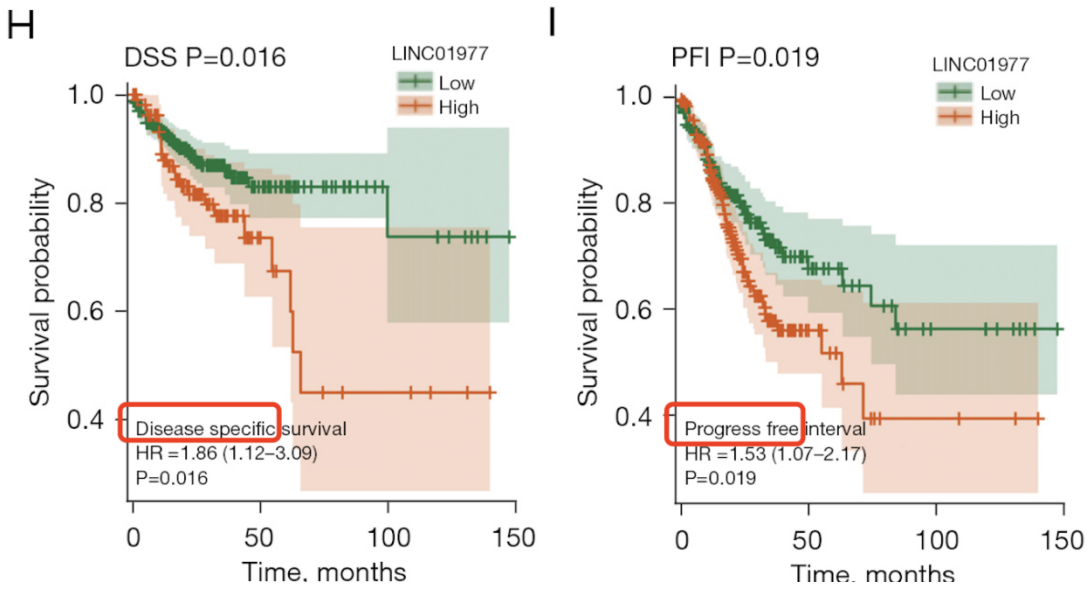
There seems to be no "*" in Figure 1, while it was explained in the legend. Please check and revise.

Reply: We have deleted "*" in our text as advised.

2. Figure 2H and 2I

2.1 "Disease specific" should be changed to "Disease-specific";

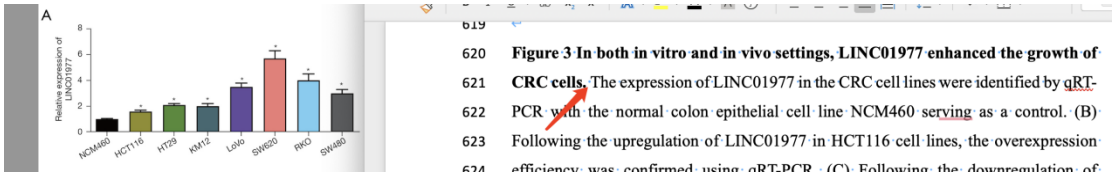
2.2 "Progress free" should be changed to "Progression-free".



Reply: We have modified Figure 2H and 2I as advised

3. Figure 3

Is "(A)" missing here? Please check and revise.



Reply :We have added "(A)" as advised.

4. Figure 4C-4H, Figure 6E & 6G

Please state observation method or staining method in the legend

Reply: We have modified in our text as advised.

5. Figure 6

Is "(A)" missing here? Please check and revise.

663 **Figure 6 LINC01977 regulated aerobic glycolysis, proliferation, and metastasis of**
664 **CRC cells through the regulation of c-Myc.** The protein levels of p-ERK, ERK, pS62-
665 c-Myc, and c-Myc were assessed when LINC01977 was overexpressed or
666 downregulated. (B) CCK-8 assays revealed that LINC01977 knockdown caused

Reply: We have modified in our text as advised.

6. Figure S1

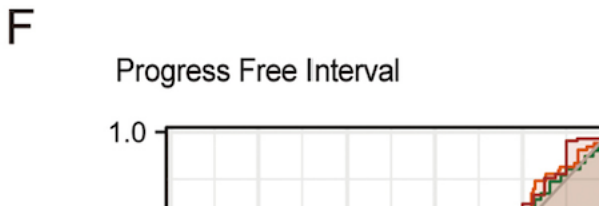
Should “(I)” be “(F)”. Please check and revise.

676 **Figure S1 In the TCGA cohort, clinicopathologic characteristics and subgroup**
677 **analysis of the survival curves of CRC patients were compared based on the high**
678 **and low levels of LINC01977. (A)** Association of LINC01977 expression with primary
679 therapy outcome. (B,C) Survival curves of stage N0-1 and stage N2 subgroups in
680 patients with CRC were compared based on LINC01977-high and LINC01977-low
681 levels of PFI. (D,E) Survival curves of pathologic stage I and stage II–IV subgroups in
682 patients with CRC were compared based on LINC01977-high and LINC01977-low
683 levels of PFI. (I) The time-dependent ROC provided the area under the curve (AUC)

Reply: We have modified in our text as advised.

7. Figure S1F

“progress free” should be changed to “progression-free”.



Reply :We have modified Figure S1F as advised