Reviewer A

Comment 1: This study is based on the analysis of the bioinformatic study. The functional research on GNL3L should be increased, which may be more meaningful.

Reply 1: Our research, through comprehensive bioinformatics analysis and IHC validation, indicates notable overexpression of GNL3L in ESCC. Furthermore, we identified a potential association of this phenomena with the STAT3 signaling pathway. However, it is crucial to acknowledge certain limitations in our study, such as a lack of analysis clarifying the precise mechanisms through which GNL3L induces STAT3 phosphorylation to promote the malignant progression of ESCC. These aspects necessitate further exploration in future research through cellular functional experiments, animal models, or organoid systems.

Changes in the text: No change.

Comment 2: There have been many studies on ESCC. What is the difference between this study and previous studies? What is the innovation? These need to be described in the introduction.

Reply 2: We have already provided explanations in the introduction section (see Page 4, line 90-99).

Changes in the text: No change.

Comment 3: Can GNL3L be used as a potential biomarker for patient risk stratification and local regional metastasis in ESCC? It is recommended to add relevant content.

Reply 3: Thank you for your valuable feedback. It is worth exploring whether GNL3L can serve as a biomarker for risk stratification and local metastasis and recurrence. However, this is not the focus of our research in this article. Currently, we have analyzed the prognosis and further exploration is needed in the future.

Changes in the text: No change.

Comment 4: What is the impact of this study on the further treatment and prognosis of ESCC? It is recommended to include relevant content in the discussion.

Reply 4: We have already provided explanations in the discussion section (see Page 9, line 260-272).

Changes in the text: No change.

Comment 5: The abstract is not sufficient and needs further modification. The research background did not indicate the clinical needs of the research focus.

Reply 5: We have already provided explanations in the abstract section (see Page 2, line 45-46).

Changes in the text: No change.

Comment 6: The introduction part of this paper is not comprehensive enough, and the similar papers have not been cited, such as "Microarray analysis of miRNA based on the regional lymph node metastasis status of esophageal squamous cell carcinoma, Transl Cancer Res, PMID: 35116259". It is recommended to quote the article.

Reply 6: Thank you to the reviewer for providing valuable suggestions. There may be some literature worth citing, but the focus of this study is on prognostic markers for esophageal cancer, not regional lymph node metastasis, so this article "Microarray analysis of miRNA based on the regional lymph node metastasis status of esophageal squamous cell carcinoma, Transl Cancer Res, PMID: 35116259" was not cited.

Changes in the text: No change.

Comment 7: Therapeutic advances in potential targets of the ESCC microenvironment and the research progress of GNL3L are suggested to be added to the discussion.

Reply 7: The research progress of GNL3L have been added to the discussion(see Page 9, line 260-272). However, "Therapeutic advances in potential targets of the ESCC microenvironment" is not the focus of this study.

Changes in the text: No change.

Comment 1: Please check all abbreviations in the abstract, highlight box, and the main text. Abbreviated terms should be full when they first appear.

For example,

TNM in abstract

GTP in Introduction

Reply: Thank you for your suggestion. I have made the necessary revisions in the manuscript.

Changes in the text: see Page 3, line 60/Page 4, line 89/Page 5, line 131.

Comment 2: 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.

Studies have indicated that increased STAT3 signaling orchestrates the expression of the master regulator TWIST, leading to epithelial-mesenchymal transition (EMT) and metastasis (22).

Reply: Thank you for your suggestion. I have made the necessary revisions in the manuscript.

Changes in the text: see Page 9, line 276.

Comment 3: Table 2

Should "T/2" be "T1/T2"? Please check and confirm.

T stage (T3/4 vs. T/2)

.

Reply: Thank you for your suggestion. I have made the necessary revisions in the manuscript.

Changes in the text: see Page 19.

Comment 4: ALL abbreviations used in each table/figure or table/figure description should be defined in a footnote below the corresponding table/figure. Please check all figures/tables and provide correspondingly.
For example, HR, CI, TNM in Table 2
Reply: Thank you for your suggestion. I have made the necessary revisions in the manuscript.

Changes in the text: see Page 16, line 446-448/see Page 17, line 454-455/see Page 17-18, line 461-462/see Page 19, line 467-469/see Page 19, line 472-475.

Comment 5: Figure 1E
The correct format for the y-axis should be one of the following, please revise.
a) If the description is "Percent survival", the numbers should be 0-100.
b) If the description is "Survival", the numbers should be 0-1.0.
Reply: Thank you for your suggestion. I have made the necessary revisions in the manuscript.

Changes in the text: see Page 14, Figure 1.

Comment 6: Figure 1
, *, ****: please explain their meaning in the legend.
Reply: Thank you for your suggestion. We have a note We have a note in the footnote of each table/figure (*, significant difference with P<0.05)

Comment 7: Figure 1A: Should it be "COAD"? Please check.

Reply: Thank you for your suggestion. I have made the necessary revisions in the manuscript.

Changes in the text: see Page 14, Figure 1.

Comment 8: Figure 3
Please add "(A)" in the legend accordingly.

450 Figure 3 Patients with a high expression of GNL3L and pSTAT3 had poor prognosis.

451 High expression of GNL3L was associated with poor prognosis (P=0.012); (B) high

452 expression of pSTAT3 was associated with poor prognosis (P<0.001). Low, low

453 expression; High, high expression.

Reply: Thank you for your suggestion. I have made the necessary revisions in the manuscript.

Changes in the text: see Page 17,line 452.