

Peer Review File

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Reviewer A

In this study, the authors analyzed KLRB1 expression levels in publicly available databases and investigated its association with clinical and pathological variables. Enrichment analysis revealed potential signaling pathways and biological functions linked to KLRB1. Statistical methods, including Spearman correlation and multigene prediction models, were employed to assess the relationship between KLRB1 expression and immune cell infiltration. Diagnostic and prognostic evaluations were conducted using Kaplan-Meier survival curves, ROC curves, histogram models, and Cox regression analysis. Functional assays, such as protein blot analysis, RT-qPCR, and cell proliferation assays, were utilized to elucidate the impact of KLRB1 on cell behavior. Their findings indicate that KLRB1 expression is decreased in lung cancer compared to healthy tissue and influences the MAPK/ERK signaling pathway, thereby modulating LUAD growth and proliferation. Specifically, I have some suggestions to improve this manuscript.

1) The overall writing has some formatting issues, like wording, spacing, and some redundancy. I suggest the authors check the grammar and avoid any typos. More importantly, the writing needs improvement for readers to understand more easily.

Reply: Thank you very much for your review and feedback. I have thoroughly checked and touched up the paper to ensure language quality and readability.

(2) There are a lot of similar bioinformatics work revealing biomarkers. I would recommend the authors discuss such work (e.g., PMID: 35173534) that uses survival analysis to help reveal potential biomarkers.

Reply: As per your request, I have added to the article some studies using bioinformatics methods to reveal biomarkers associated with tumor prognosis(see Page 23-25, line 487-531).

(3) I recommend the authors to include some discussions on related studies using different omics data (PMID: 33461059; PMID: 35284940), which helps expand the scope of the study.

Reply: As you requested, I have added to the discussion some discourse on related studies using different omics data.

Reviewer B

1. Figure 1

Since the figure 1G was obtained from the HPA dataset, please follow the policy from the HPA database (<https://www.proteinatlas.org/about/licence>).

Reply: We've removed Figure 1G.

2. Figure 2

a) As there are no symbols “* , **” in the figure, please delete the explanations in the legend.

b) Please check if figure 2D’s legend match with the figure 2D.

Reply:(a) We have deleted the symbols “* , **” in the legend (see Page33, line 720). (b) Figure 2D’s legend match with the figure 2D. Figure 2D contains the different components of the GO enrichment analysis, including the biological function (BP), cellular component (CC) and molecular function (MF) categories.

3. Figure 4

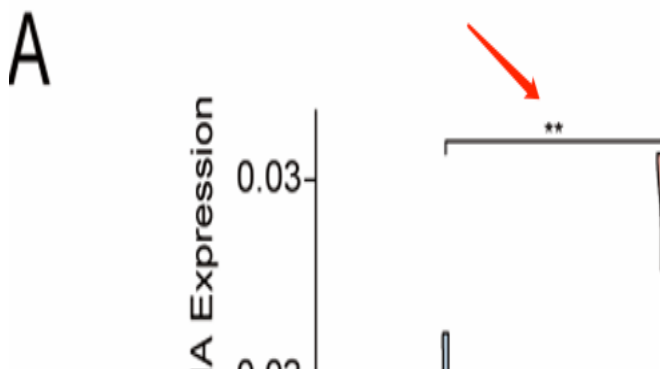
Please specified what type of the figure is of figure 4B in the legend. Western blotting?

Reply: We have modified our text as advised (see Page 34, line 734-735).

4. Figure 7

a) Figure 7A and 7B were not cited in the main text, please add the citation. They should be cited between figure 6D and 7C.

b) Please provide the meaning of the symbol “***” in the legend.



Reply: (a) We have added the citation (see Page 19, line 400). (b) We have provided the meaning of the symbol “*” in the legend (see Page 35, line 762).**

5. Figure 8

a) Please provide the staining method of Figure 8C and 8D in the legend.

- b) Please provide the scale bar in the figure or magnification in the legend for 8C.
c) a) As there are no symbols “* , **” in the figure, please delete the explanations in the legend.

Reply: (a) We add the staining method of Figure 8C and 8D in the legend (see Page 35-36, line 768-773). (b) We provide the scale bar in magnification in the legend for 8C (see Page 36, line 771). (c) We delete the explanations in the legend (see Page 36 line 774).

6. Supplementary Figure S2

Please provide the meaning of the symbol “***” in the legend.

Reply: We have modified our text as advised (see Supplementary Figure S2 legend).

7. Supplementary Table S5

- a) Supplementary Table S5 was not cited in the main text, please revise.
b) Please define the meanings of all abbreviations in the table footnote.

Reply: (a) The Supplementary Table S5 was cited in the main text (see Page 18, line 383). (b) We define the meanings of all abbreviations under the table.

8. References/Citations

Please check if the author’s name matches with the citation.

512 influence the body's immune system. Pierre T et al revealed that metabolism influences
513 the immune microenvironment of melanoma and predicts the response of tumor patients
514 to anti-PD-1 immune checkpoint blockade therapy by combining the metabolism of
515 different metabolic components, such as glucose metabolism, lipid metabolism, and
516 amino acid metabolism (25). The novel multiomics integration strategy used, including

Reply: We have modified our text (see Page 21, line 449-452)