

Peer Review File

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Reviewer A

The authors introduced cuproptosis-related genes, dihydrolipoyl transacetylase (DLAT) as novel biomarker for liver cancer by TCGA data analysis and cell line study. This kind of study was hot issue for cancer bioinformatics recently. Some part should be revised.

Comment 1: Abstract: Method part was lengthy!

Reply 1: We have rewritten the method part.

Changes in the text: Line 46-53.

Comment 2: Introduction: The goal of this study should be emphasized.

Reply 2: The goal of this study has been emphasized in the introduction part.

Changes in the text: Line 138-143.

Comment 3: Discussion: Compared to massive result data, interesting or novel information was weak. Clinical value of these data should be presented more.

Reply 3: We have highlighted the novel points of the study and added a discussion on the clinical value and this model.

Changes in the text: Line 560-568.

Comment 4: Reference style should be checked.

Reply 4: The reference style has been corrected accordingly.

Changes in the text: Line 723-834.

Reviewer B

The paper titled “Identification of DLAT as a potential therapeutic target via a novel cuproptosis-related gene signature for the prediction of liver cancer prognosis” is interesting. Cuproptosis-related genes contribute to tumor development and can aid the prediction of LC patient prognosis. DLAT is a potential LC prognostic and therapeutic target. However, there are several minor issues that if addressed would significantly improve the manuscript.

Comment 1: How does cuproptosis poisoning affect the diversity and complexity of the immune microenvironment, mutation landscape, and biological behavior of liver cancer? What role does DLAT play in this process? Suggest adding relevant content.

Reply 1: We have discussed the relationship between cuproptosis and the microenvironment in the discussion part.

Changes in the text: Line 597-632.

Comment 2: The letters labeled A, B, and D in Figure 3 are missing C. However, Figure 3D did not appear in the result description and figure legend, only A, B, and C. Please carefully check and make corrections.

Reply 2: We found the mistake, and the figure legend has been corrected in Figure 3.

Comment 3: The description of some methods is too simplistic. Suggest providing a detailed description.

Reply 3: We have provided a detailed description of the methods.

Changes in the text: Line 259-269, 272-289, 291-307, 309-323.

Comment 4: Figures 1-4, 6, 8, 10-11 are not clear enough, please upload again.

Reply 4: The figures have been updated with clearer versions.

Comment 5: The introduction part of this paper is not comprehensive enough, and similar papers have not been cited, such as “Cuproptosis-related molecular classification and gene signature of hepatocellular carcinoma and experimental verification, PMID: 38617510”. It is recommended to quote the articles.

Reply 5: The reference has been added.

Changes in the text: Line 134-137.

Comment 6: Is high-level DLAT an independent prognostic factor for shorter overall survival? What biological functions are DLAT and its related genes mainly involved in? Suggest adding relevant content.

Reply 6: This has been added in the discussion part.

Changes in the text: Line 597-632.