

Peer Review File

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Reviewer A

Nicely written article analyzing the significance of LYPD3 expression in lung cancer. Please find my minor comments:

1. Line 72: Suggest to re-phrase: Exocarta is an exosome database that was used...

Response 1: We revised “Exocarta (<http://www.exocarta.org/>) is an exosome database that we use to screen for exosome molecules in lung cancer.” to “Exocarta(<http://www.exocarta.org/>) was used to screen for exosome molecules in lung cancer.” in **Line 72**.

2. Line 170/171: Figure 3 legend: what do you mean by correction?

Response 2: Thanks. We revised the legend (B, C) to “B. Univariate cox analysis between LYPD3 and clinical pathological factors. C. Multivariate cox analysis between LYPD3 and clinical pathological factors.” in **line 170-172**.

3. Line 177: Instead of categorizing LYPD3 mRNA expression into high and low expression groups (median threshold), did you consider analyzing the expression as a continuous variable?

Response 3: Thank you for your kind comments, we agree with your opinion. Indeed, we analyzed the expression as a continuous variable, but this was not explicitly stated in the manuscript. To make it clear, we have revised “We further used the median value of LYPD3 mRNA expression as the threshold to divide samples from the TCGA database into high and low LYPD3 expression groups, screening out 531 positively correlated genes and 1094 negatively correlated genes” to “We further screened out 531 positively correlated genes as high LYPD3 expression group, and 1094 negatively correlated genes as low LYPD3 expression group, based on the median value of LYPD3 mRNA expression.” in **Line 176-178**.

Reviewer B

1. Please check if any reference should be cited in the following sentence:

- **Studies** have shown that exosomes can affect tumor growth and metastasis, paraneoplastic syndrome, and treatment resistance.
- **Studies** have shown that patients with high TMB may have a stronger immune response and be more sensitive to immune checkpoint inhibitors.

Response 1: Thanks. We have cited the reference (31, 32) and (36, 37) in the above sentence.

2. Figures

Figure 1

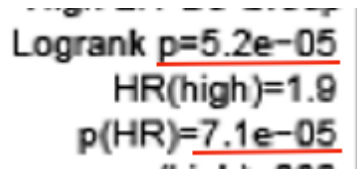
- 1) Please provide a **label** to indicate the meaning of different color dots in Figure 1C.

Response 1): Thanks. We have added the label according to the recommended format.

- 2) Please remove “Percent” in the Y-axis description as the rate is 0-1 in Figure 1D.

Response 2): Thanks. We have deleted the Percent.

- 3) Please unify the data format in the text and Figures. For example, “7.1e-5” in the text and “7.1e⁻⁵” in Figure 1D. Same for Figure 1E, 5D-5F, 6C-6G. Please check through and revise.



Logrank p=5.2e-05
HR(high)=1.9
p(HR)=7.1e-05

Response 3): Thank you for your suggestion. We have modified the picture according to your suggestion.

Figure 3

- 4) Please add a unit to “Age” in Figure 3A.

Response 4): Thank you for your suggestion. We have modified the picture according to your suggestion.

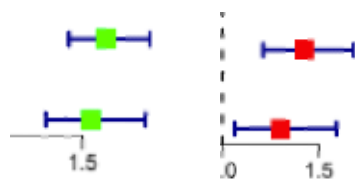
- 5) It is suggested to revise “Hazard ratio” to “Hazard ratio (95% CI)” in Figures 3B-3C.

Hazard ratio

1.223(1.132-1.321)

Response 5): Thank you for your suggestion. We have modified the picture according to your suggestion.

- 6) It is suggested to extend the scale bar to 2.0 in Figures 3B-3C.



Response 6): Thank you for your suggestion. We have modified the picture according to your suggestion.

- 7) There is no asterisk in Figure 3, please remove the explanation from the legend of Figure 3.

$*p < 0.05$, $**p < 0.01$, $***p < 0.001$. ↵

Response 7): Thanks. We have removed it in line 436.