

Reviewer A

The authors used data from The Cancer Genome Atlas (TCGA) to identify cuproptosis-related genes (CPRGs) and categorized bladder cancer (BLCA) patients into three molecular clusters based on these genes. They analyzed the tumor microenvironment (TME) using ssGSEA and CIBERSORT, finding that one cluster, associated with poor prognosis, had significant CD4+ and CD8+ T cell infiltration. Their risk score model, based on CPRGs, predicted patient survival and suggested a potential for CPRGs in guiding immunotherapy decisions.

In general, I only have stylistic and minor comments.

Abstract:

At line 34, provide statistical findings to strengthen the results, such as hazard ratios (HR), confidence intervals (CI), and p-values to indicate significance.

Re: Thank you for your suggestion. I have modified line 53 of the revised version. The P value is annotated according to Figure 3B.

Introduction:

I suggest to shift the introduction to focus more on the specific research topic, emphasizing the significance of CPRGs and tumor microenvironment (TME) in bladder cancer (BLCA) rather than presenting a broad epidemiological overview:

- Line 53–58: In my humble opinion, the authors should condense or remove any general epidemiological data to sharpen focus on the research problem.

Re: Thank you for your suggestion. Based on your suggestion, I deleted the third and fourth sentences, which are reflected in lines 74-76 of the revised version.

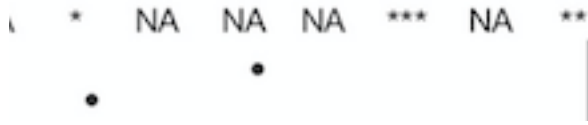
- Lines 59–68: As aforementioned, the authors should dive into the relevance of CPRGs, their role in immune infiltration, and how they could be leveraged as biomarkers or therapeutic targets in BLCA.

Re: Thank you for your suggestion. We will add the corresponding content in the corresponding position of the second paragraph, corresponding to lines 98-99.

Reviewer B

1. Figure 1

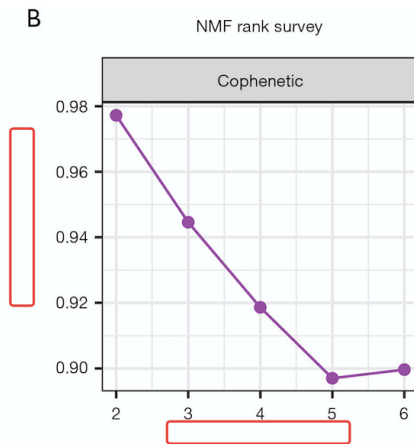
Please explain “*”, **, ***” in figure legend.



Re: Changed as requested

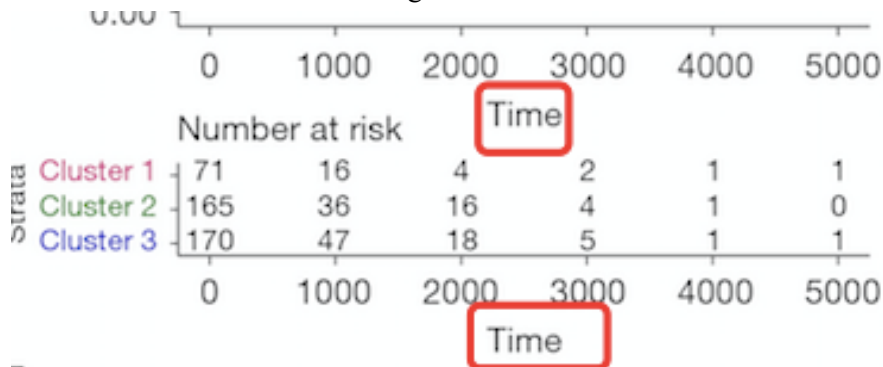
2. Figure 2

a. Please add description for the Y- axis X-axis in figure 2B.



Re: Changed as requested

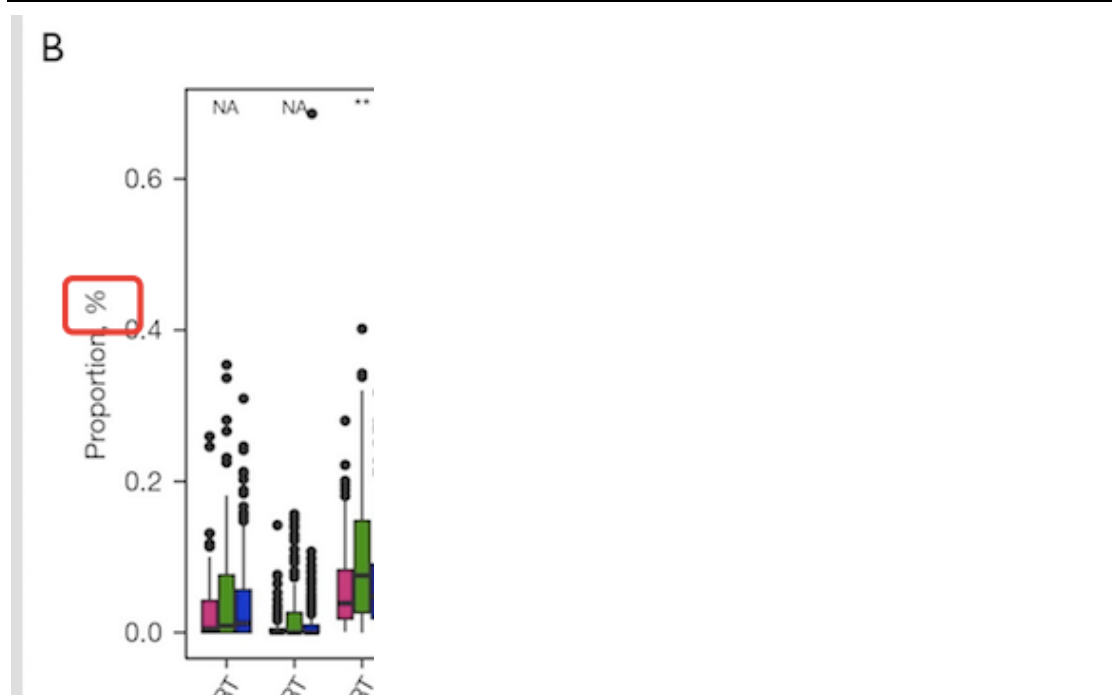
b. Please add the unit of time in figure 2C.



Re: Changed as requested

3. Figure 3

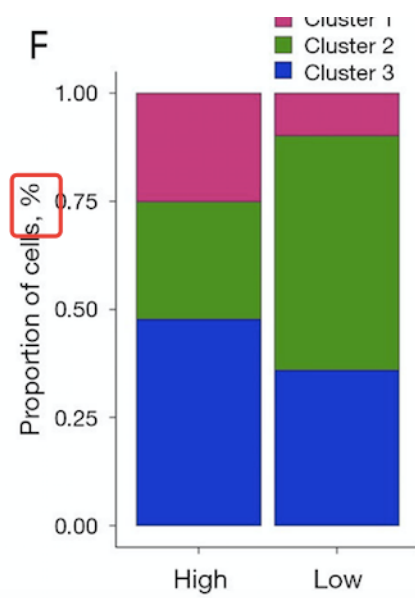
Please delete (%), as the number is from 0.0-0.6.



Re: Changed as requested

4. Figure 4

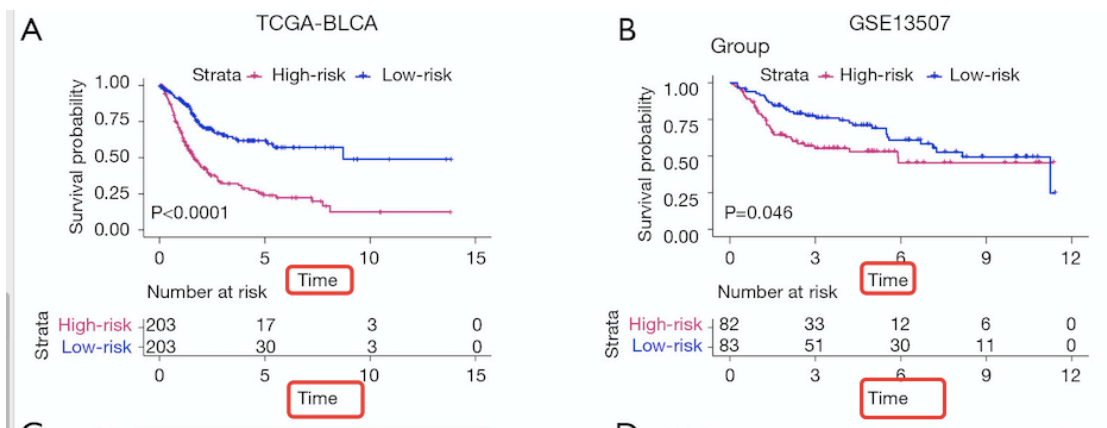
Please delete (%), as the number is from 0.0-1.0.



Re: Changed as requested

5. Figure 5

Please indicate the unit of time.



Re: Changed as requested

6. Figure 7

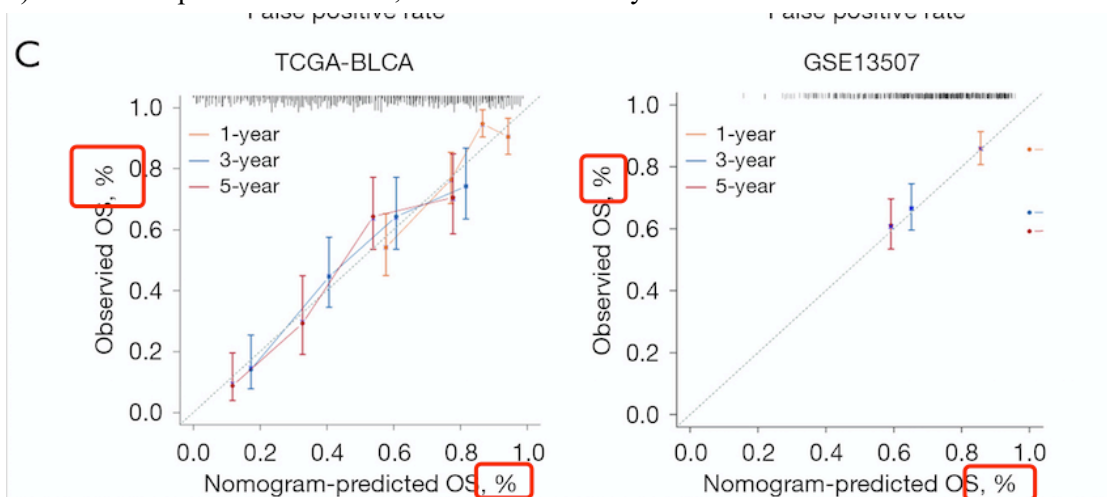
a. Please explain “***” in figure legend.



Re: Changed as requested

b. The correct format for the x-axis and y-axis should be one of the following, please revise.

- a) If the description is with %, the numbers usually should be 0-100.
- b) If the description is without %, the numbers usually should be 0-1.0.



Re: Changed as requested b) without %

7. Figure S1

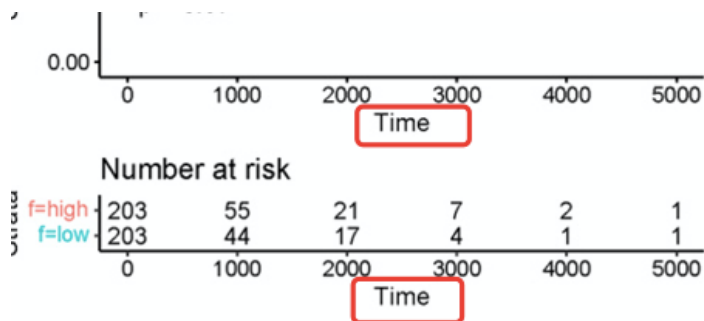
a. Please revise “Hazard ratio” to “Hazard ratio (95% CI)”.

Hazard ratio
0.952(0.773–1.173)

0.899(0.643–1.257)

Re: Changed as requested

b. Please indicate the unit of time.



Re: Changed as requested

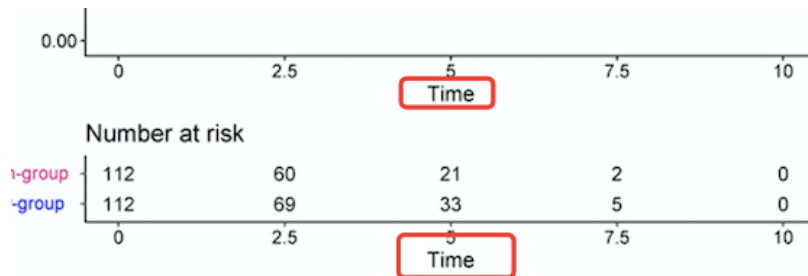
8. Figure S2

Please explain “***” in figure legend.

Re: Changed as requested

9. Figure S4

a. Please indicate the unit of time.



Re: Changed as requested

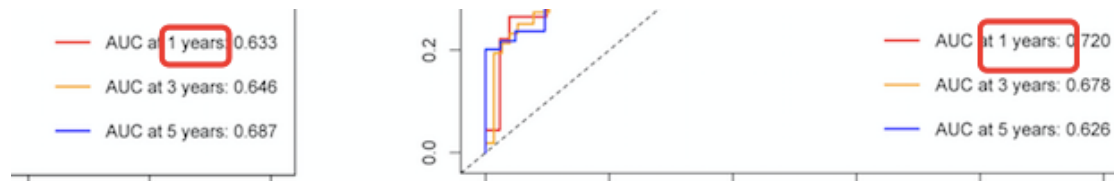
b. Please revise “1 years” to “1 year”.

— AUC at 1 years: 0.740
 — AUC at 2 years: 0.805

Re: Changed as requested

10. Figure S5

Please revise “1 years” to “1 year”.



Re: Changed as requested

11. Table S2

- a. Please provide a table head.
- b. Please indicate the unit of “OS.time”.

	A	B	C	D	E	F	G
1		cluster	neoplasm_tumor_stag	OS		X_PATIENT	OS.time
2	TCGA.E7.A	cluster2	High Grade	Stagell	0	TCGA-E7-	13
3	TCGA.GC.A	cluster3	High Grade	Stagelll	0	TCGA-GC-	15
4	TCGA.E7.A	cluster3	High Grade	Stagell	0	TCGA-E7-	17

Re: Changed as requested

12. Table S3

Please provide a table head.

	A	B
1		lasso_coef
2	GOLT1A	-0.00577
3	STXBP2	-0.02566
4	DCXR	0.135932
5	ILVRI	0.091837

Re: Changed as requested