

Response to Reviewer 1's Comments

- The introduction has been revised to provide sufficient background and include relevant references.
- We checked the references, added missing ones, and re-confirmed that we cited literature related to the study.
- We checked and corrected whether the method was properly explained.
- We checked that the results were presented clearly and corrected any unclear parts.
- The conclusion was rewritten with key points supported by research results.

Areas for Improvement:

- **Discussion on Contradictory Findings:** There is little discussion about why certain genes identified in previous studies did not show survival specificity in this study. Addressing these discrepancies would enrich the discussion.

Response: Discussion of our findings is somewhat limited because many of the key genes we discovered have not previously been reported for survival specificity in PRCC. Most of the cases where relevant data were available were based on ccRCC rather than PRCC, so there were limitations in discussing direct correlation with our PRCC results. However, as you pointed out, additions or modifications were made in the Discussion so that the shortcomings could be fully discussed based on the available data.

- **Article Readability:** It's crucial to make the text clearer and more direct. Currently, there are many complex sentences and an excessive use of technical jargon that can make reading difficult. Try simplifying the language where possible and breaking up longer sentences into smaller segments to enhance overall comprehension.

Response: We have revised the Introduction and Discussion sections to address your concerns and highlighted the revised parts. We simplified the language where possible and broke up longer sentences into smaller segments to enhance overall comprehension. We believe these revisions have improved the clarity and directness of the text.

- **Organization of Graphic Materials:** Graphic materials, such as figures and tables, are essential for illustrating data and supporting your arguments. However, their current arrangement might be somewhat confusing. Ensure that each graphic element is clearly linked to the text that references it, and that legends are concise and informative. Consider reorganizing or redesigning some graphics for better integration into the document's flow.

Response: We have addressed the readability and size of graphic materials, such as tables and figures. Specifically, we have adjusted the positioning and size of Figure 2 and Figure 3 to enhance visibility. Due to time constraints, Figures 2 and 3 have been changed to make them more visible. However, if the resolution of the figures needs to be higher, additional drawing work may need to be done again.

Additionally, we have ensured that each graphic element is clearly linked to the corresponding text and that legends are both concise and informative.

- **Enhancing the Discussion:** The discussion section is crucial for emphasizing the importance and implications of your findings. It could currently benefit from a more engaging and

critical approach. Discuss in more depth how your results compare with existing publications and what new value they add to the field. You might also expand on how these findings could influence future research or clinical practice, making the discussion not just more informative but also more stimulating and compelling for the reader.

Response: We have enhanced the discussion section to better emphasize the importance and implications of our findings.

- Recent studies, including those documented in the article with PMID: 37685983, have highlighted the importance of cancer stem cell signaling pathways such as Notch, Wnt, and Hedgehog in clear cell renal cell carcinoma, suggesting that these pathways may also be crucial in other renal carcinoma subtypes such as papillary renal cell carcinoma. This knowledge could expand our understanding of tumorigenicity and genetic variation in renal tumors, complementing our current efforts to identify survival-specific biomarkers in PRCC using next-generation sequencing panels. Please cite and discuss this.

Response: We have addressed the reviewer's comment by adding the following sentence and reference to line 450-452: "Lasorsa et al. highlighted the importance of cancer stem cell signaling pathways such as Notch, Wnt and Hedgehog in ccRCC, and proposed a treatment strategy targeting cancer stem cells, which are presumed to cause cancer recurrence and metastasis²⁵."

- In addition, recent research has underscored the importance of MUC1, a mucin frequently overexpressed in various epithelial malignancies including renal carcinoma types (PMID: 38540735). This work reviews the role of MUC1 in cancer cell proliferation, metabolic reprogramming, chemoresistance, and angiogenesis. Considering our discovery of genetic markers in papillary renal cell carcinoma, exploring the overexpression of MUC1 in our context could provide deeper insights into the interactions between genetic pathways and pathological processes in RCC, potentially guiding the development of targeted therapies. Please cite and discuss it in your paper.

Response: To address the reviewer's feedback, we have incorporated the following content into our manuscript in lines 662-672: "Mucin 17, cell surface associated (MUC17) was recently reported in RCC as one of a diverse set of mucin gene variants, many variants of MUC17 were reported to exist⁶⁷. It is associated with shorter overall survival and a trend of shorter progression-free survival in RCC patients, implying a potential role for mucin gene variants in influencing prognosis and treatment response. Among the 7 died patients out of 12 with metastases in the TCGA cohort, three patients (25.0%) had MUC17 mutations in our study. Alterations in mucin family genes are common in ccRCC, and it is noteworthy that recent studies have highlighted the importance of mucin, which is frequently overexpressed in various epithelial malignancies, including RCC⁶⁸. Mucins such as MUC17 and MUC1 have been reported in relevant studies in renal cell carcinoma⁶⁸, although MUC1 was not identified as a survival-specific gene in our study."

- check typos

Response: We have addressed the reviewer's feedback regarding typos by carefully reviewing and correcting any errors found in the manuscript.