Peer Review File

Article information: https://dx.doi.org/10.21037/tcr-24-449

Reviewer A

Comment 1: The title should be revised to reflect the study's flow, mentioning prognosis first, followed by immune infiltration.
Reply: Thanks for your suggestion. We have revised the Title of the manuscript accordingly.
Changes in the text: p1, line 1-2

Comment 2: The abstract should be more concise, particularly in the Background subsection. Key results should be highlighted.
Reply: Thanks for your suggestion. We have revised the Abstract according to your suggestion. The revision has been marked in yellow in the revised draft.
Changes in the text: p2, line 16-43

Comment 3: Data processing and selection criteria should be detailed in the Methods section.
Reply: Thanks for your suggestion. We have revised it accordingly. The revision is marked in yellow in the revised draft.
Changes in the text: p5-6, line 84-93

Comment 4: The datasets used for each analysis should be clearly described in both the Methods section and the figure legends.
Reply: Thanks for your suggestion. We have added the datasets used for each analysis into the Methods and Figure Legends. The revisions are marked in yellow in the revised manuscript.
Changes in the text: p5-6, line 84-93; p20-22, line 474-507

Comment 5: The number of tissue samples used for the qRT-PCR experiment should be mentioned in the Methods section.
Reply: Thanks for your suggestion. We have added the number of tissue samples used for the qRT-PCR in the revised manuscript. The revision is marked in yellow.
Changes in the text: p7, line 122-123

Comment 6: Differential expression of FUT10 in KIRC at the protein level should be explored. The UALCAN (CPTAC dataset) and/or Human Protein Atlas (HPA) databases can be used for this purpose.
Reply: Thanks for your suggestion. The expression level analysis of FUT10 protein cannot be achieved via UALCAN (CPTAC dataset) website. But we acquired the mRNA expression data of FUT10 from UALCAN website and the protein expression data of FUT10 from HPA website. We have added these results into the revised Figure 1. The revisions have been marked in yellow in the revised manuscript and Figure 1.
Changes in the text: p6, line 94-96; p8, line 136-140; p21, line 478-481

Comment 7: Figure 1A represents data from unpaired tissues, whereas Figure 1D represents data from paired tissues. This information should be clearly described in the figure legend.
Reply: Thanks for your suggestion. We have revised it in the Figure legends and highlighted the revisions in the revised draft.
Changes in the text: p21, line 474-481

Comment 8: The KM analysis of overall survival (OS) in Figure 3C should be moved to Figure 3B, followed by KM analysis of progression-free survival (PFS) and disease-specific survival (DSS) to maintain consistency with other results.
Reply: Thanks for your suggestion. We have revised it accordingly. The revision can be found in revised Figure 3.
Changes in the text: p9, line157-159; p21, line 487-489

Comment 9: In Figure 6, it is unclear why the positive associations with ARL8B, STAM2, APPL1, ERLIN2, ANKFY1, and BAG4 were highlighted among several genes correlated with FUT10. The rationale behind this should be mentioned.
Reply: Thanks for your comment. We have revised it accordingly. The revisions are highlighted in the revised manuscript.
Changes in the text: p10, line 175-178; p13, line243-245

Comment 10: In Figure 7, the term “Tcm cells” needs clarification. The possible underlying mechanisms and biological significance of the relationship between FUT10 and Tcm cells and other immune cells should be discussed.
Reply:
Changes in the text: p10, line 186; p22, line 502

Comment 11: The statement “As of April 4, 2023, there were only 606 study reports of PID in tumors” on page 12, lines 218-219 should be revised. Over 600 reports are not “only.” A revised statement could be, “To our knowledge, numerous previous reports…”
Reply: Thanks for your comment. We have corrected it accordingly, and marked the revision in yellow.
Changes in the text: p13, line 236-237

Comment 12: Since human tissues were used in this study, ethical approval is required. The authors should include an ethical statement and provide the reference number of ethics approval in the manuscript.
Reply: Thanks for your comment. The organization used in this study was purchased from Shanghai Outdo Biotech Company, China, so no ethics approval is required.
Changes in the text: p7, line122-123

Comment 13: The study’s limitations and the necessity for further experimental and clinical validations should be discussed.
Reply: Thanks for your suggestion. The limitations of this study have been added in the revised manuscript. And the revisions are highlighted in yellow.

Changes in the text: p15, line 273-278

Comment 14: The language could be further simplified for better readability, and the flow of the article could be improved by connecting sections more cohesively. English-language editing is highly recommended.
Reply: Thanks for your suggestion. We have asked someone specializing in medical English to help polish our manuscript.

Reviewer B

Comment 1: RCC is essentially a metabolic disease characterized by a reprogramming of energetic metabolism (PMID: 36960789; PMID: 30983433, PMID: 36430837, PMID: 36310399). In particular the metabolic flux through glycolysis is partitioned (PMID: 29371925, PMID: 28933387, PMID: 25945836), and mitochondrial bioenergetics and OxPhox are impaired, as well as lipid metabolism (PMID: 30538212; PMID: 32861643, PMID: 29371925, PMID: 36430448, PMID: 38540735). In this scenario, it has been shown that fucosyltransferases are important regulators of metabolic activity of mucins (such as MUC1) in ccRCC (PMID: 38540735; PMID: 36902242; PMID: 36430448). These findings should be referenced and discussed.
Reply: Thanks for your suggestion. We have added these in the Discussion section. The revision is marked in yellow in the revised manuscript.
Changes in the text: p11-12, line 208-212

Comment 2: In addition, renal cell carcinoma is one of the most immune-infiltrated tumors (PMID: 31527133, PMID: 30738745; PMID: 27063186). Emerging evidence suggests that the activation of specific metabolic pathway have a role in regulating angiogenesis and inflammatory signatures (PMID: 32345771, PMID: 28359744). Features of the tumor microenvironment heavily affect disease biology and may affect responses to systemic therapy (PMID: 38003705; PMID: 37189689; PMID: 33265926; PMID: 36902242; PMID: 37373581). FUT10 can modulate immune cell infiltration and regulate immunoflogosis. These processes should be explored and discussed.
Reply: Thanks for your suggestion. We have added these in the Discussion section. The revision is marked in yellow in the revised manuscript.
Changes in the text: p14, line 255-259

Comment 3: The entire study was based on data mining (only PCR experiments were performed), the lack of independent validation with additional functional wet lab experiments using cell lines or clinical specimens weakens this study. The author should specify this limitation in the discussion.
Reply: Thanks for your suggestion. The limitations of this study have been added in the revised manuscript. And the revisions are highlighted in yellow.
Changes in the text: p15, line 273-278