

For research article

Response to Reviewer 2 Comments

1. Summary

Thank you very much for taking the time to review this manuscript. Please find the detailed responses below and the corresponding revisions/corrections red highlighted/in track changes in the re-submitted files.

2. Questions for General Evaluation	Reviewer's Evaluation	Response and Revisions
Does the introduction provide sufficient background and include all relevant references?	Can be improved	
Are all the cited references relevant to the research?	Can be improved	
Is the research design appropriate?	Yes	
Are the methods adequately described?	Can be improved	
Are the results clearly presented?	Can be improved	
Are the conclusions supported by the results?	Yes	

3. Point-by-point response to Comments and Suggestions for Authors

1. Comments 1: Title

The current title, "YAP/TAZ promote GLUT1 expression, and these factors correlate with prognosis in uterine endometrial cancer," reads like a full sentence. Please revise it to follow standard scientific titling conventions and more concisely reflect the core focus of the manuscript.

Response 1:

Thank you for pointing this out to us. In response to your suggestion, we have revised the manuscript title to follow standard scientific conventions and present the core findings more concisely. The revised title is YAP/TAZ Promote GLUT1 Expression and Are Associated with Prognosis in Endometrial Cancer

2. Comments 2: Introduction

Please include a brief overview of the Hippo signaling pathway, outlining its main

components, and how its dysregulation contributes to cancer progression, particularly in endometrial cancer.

Response 2:

Thank you for your valuable suggestion. We have added a brief overview of the Hippo signaling pathway in the Introduction section, describing its key components, biological functions, and how its dysregulation, particularly YAP/TAZ overexpression, contributes to cancer progression, including endometrial cancer (page 2, lines 61–70).

3. Comments 3: Methods

In the “Cell Culture” section, specify the complete maintenance conditions for both cell lines used (e.g., temperature, CO₂ concentration) to ensure reproducibility.

Response 3:

Thank you for your helpful comment. In response, we added the complete maintenance conditions for cell culture, including temperature, CO₂ concentration, and passage frequency, to ensure reproducibility. Specifically, we have now stated that cells were cultured at 37 °C in a humidified atmosphere with 5% CO₂ and passaged twice weekly (page 2, lines 90–91).

4. Comments 4: Results

1) In Section 3.1, the data from Figures 2 and 3 should be described more thoroughly in the text to help readers interpret the findings more easily.

Response 4:

Thank you for your valuable comment. In response, we expanded the description of Figures 2 and 3 in Section 3.1. Specifically, we clarified the rationale and methods used to evaluate the role of YAP/TAZ in regulating GLUT1 expression, including the use of a constitutively active YAP mutant (YAP-5SA)₁ and combined experiments with TAZ knockdown. These additions provided a greater context for interpreting the findings (page 5, lines 186–187, 190–196).

5. Comments 5: Results

2) In Table 1, bold the category labels to enhance readability and visual clarity.

Response 5:

Thank you for your helpful suggestion. In response, we bolded the category labels in Table 1 to improve readability and enhance visual clarity as requested.

6. Comments 6: Results

3) Please revise Table 2 to improve clarity.

Response 6:

Thank you for your helpful suggestion. Response: We have revised Table 2 to improve readability by bolding the category labels. Additionally, because the original table contained a large amount of data, we split it into two separate tables (now presented as Table 2 and 3) to enhance clarity and allow for easier interpretation of the results.

7. Comments 7: Results

4) In Section 3.4, expand the descriptions of Figures 5 and 6. When discussing AUC values, clarify what thresholds are considered indicative of good vs. poor predictive performance.

Response 7:

Thank you for your helpful suggestion. In response, we have expanded the description of Figures 5 and 6 in Section 3.4 to provide detailed information on the cutoff values, AUCs, sensitivities, and specificities of the IRSs for each protein in predicting both progression-free survival (PFS) and overall survival (OS) (page 11, lines 285–300). We have also added information regarding statistical significance (p-values) in figures and the figure legends (Figure 5 and 6). Additionally, we have corrected the error in the reported value for TAZ nuclear (Figure 6). These revisions have been made to enhance the clarity and interpretability of the data related to prognostic performance.

1. Comments 8: Discussion

Include a section discussing future research directions, including potential experimental strategies to validate YAP/TAZ as predictive biomarkers or therapeutic targets in endometrial cancer. Consider also addressing the translational potential of targeting the Hippo pathway or GLUT1 in therapeutic development.

Response 8:

Thank you for your insightful comment. In response, we have added a paragraph in the Discussion section outlining potential future research directions. This includes experimental strategies to further validate YAP/TAZ as a predictive biomarker or therapeutic target in endometrial cancer. Specifically, we discuss the interplay between KRAS mutations and Hippo signaling, as well as the overexpression of GLUT1. We also introduced the potential therapeutic relevance of the combined inhibition of KRAS and TEAD based on recent evidence. These additions addressed both the mechanistic and translational aspects of our findings (page 18, lines 435–441).

4. Response to Comments on the Quality of English Language

Point 1:

Response 1: (in red)

5. Additional clarifications