

Peer Review File

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Review comments

Comment 1: The abstract should be divided into 4 parts “background, methods, results and conclusion”. Please revise.

Reply 1: Thank you for the detailed review. We have carefully and thoroughly proofread the abstract to follow the pattern of four parts.

Changes in the text: we have modified our text as advised (see lines 26-55).

Comment 2: There were many similar reports (J Cancer. 2020 Mar 4;11(10):3027-3040) and (Int J Mol Sci. 2021 Feb 2;22(3):1474) about the prognostic prediction of m6A related genes in tumors in PubMed. What is the novel idea in the paper? Please elaborate clearly in the introduction.

Reply 2: Thanks for suggesting elaborating our novel idea in the introduction. Although there are many similar reports about the prognostic prediction of m6A related genes in tumors, but m6A modification together with its regulators may play the exact opposite role in different tumor types. We mainly study the prognostic prediction and tumor immune microenvironment with the m6A-related genes in the CESC.

Changes in the text: we have modified our text as advised (see lines 100-107).

Comment 3: In the study, different subtypes significantly correlate with survival prognosis, immune microenvironment, and PD-L1 expression. What were the functions of m6A in immune microenvironment and PD-L1 expression in CESC? Please state in the introduction.

Reply 3: Thanks for your great suggestion explaining the functions of m6A in the immune microenvironment and PD-L1 expression in CESC. Many reports have found the function of m6A in the immune microenvironment and PD-L1 expression, but the roles of m6A in CESC remain uncertain. And we have added some reports about the functions of m6A in the introduction.

Changes in the text: we have modified our text as advised (see lines 97-99).

Comment 4: The m6A related gene was the crucial topic in the study. How about the research progress of m6A in CESC? Please supplement in the introduction.

Reply 4: We would like to take this opportunity to thank you for reminding us to dig the research progress of m6A in CESC. We search again for the research about the m6A in CESC, but the study still is barren. Although we have listed the research in the manuscript, we gather them again in the introduction to share with the readers.

Changes in the text: we have modified our text as advised (see lines 104, references 20-

22).

Comment 5: It was advised to further validate the expressions of five-genes (IGF2BP1, IGF2BP2, HNRNPA2B1, YTHDF1, RBM15) by real world data.

Reply 5: Thanks for your great suggestion on further validating the expressions of five genes (IGF2BP1, IGF2BP2, HNRNPA2B1, YTHDF1, RBM15) by real-world data. We are in the process of collecting clinical tissues, but the process is pretty slow. We analyze the expression of the genes in GSE7803 to validate the expressions of five genes. But the expressions of IGF2BP1 aren't detected. We display the four genes' expression in Supplemental Figure 1.

Changes in the text: we have modified our text as advised (see lines 130, 263-265, Supplemental Figure 1).

Comment 6: What were the advantages of the established prognostic prediction of m6A related genes? Please state in the discussion.

Reply 6: Thank you very much for your constructive comments and suggestions, which would help us improve the paper's quality. Establishing the prognostic prediction of m6A-related genes may help us to understand the epigenetic regulatory role and identify the influence on the immune microenvironment and immunotherapy in CESC. And it would offer the appropriate treatment plan for the CESC.

Changes in the text: we have modified our text as advised (see lines 310-313).

Comment 7: In the figure legends, please state clearly the subtype 1 and subtype 2.

Reply 7: Thank you for the detailed review. We used the Consensus Cluster analysis to divide the database into two subtypes, but the criteria for the classification are challenging to define. To clear the division of the different groups of the CESC, we further develop a prediction model. And we clearly described the subtypes 1 and 2 in the figure legends.

Changes in the text: we have modified our text as advised (see lines 525-526).

Comment 8: What were the associations and progress between m6A and immune cell infiltration? Please supplement in the discussion

Reply 8: Thanks for your great suggestion on improving the accessibility of our manuscript. The m6A plays a vital role in cancer progression and significantly affects responsiveness to immunotherapy. And alteration of the m6A modification in tumor cells influences the infiltration, activation, and effector functions of infiltrated immune cells. We have added the associations and progress between m6A and immune cell infiltration in our manuscript with references.

Changes in the text: we have modified our text as advised (see lines 331-336).