

Thank you for the time and effort of editors and reviewers put into our manuscript. We revised the manuscript based on comments of reviewer and made a point-by-point response. The changes in the manuscript are highlighted in yellow. We are pleased to additional comments and suggestions.

Reviewer #1.

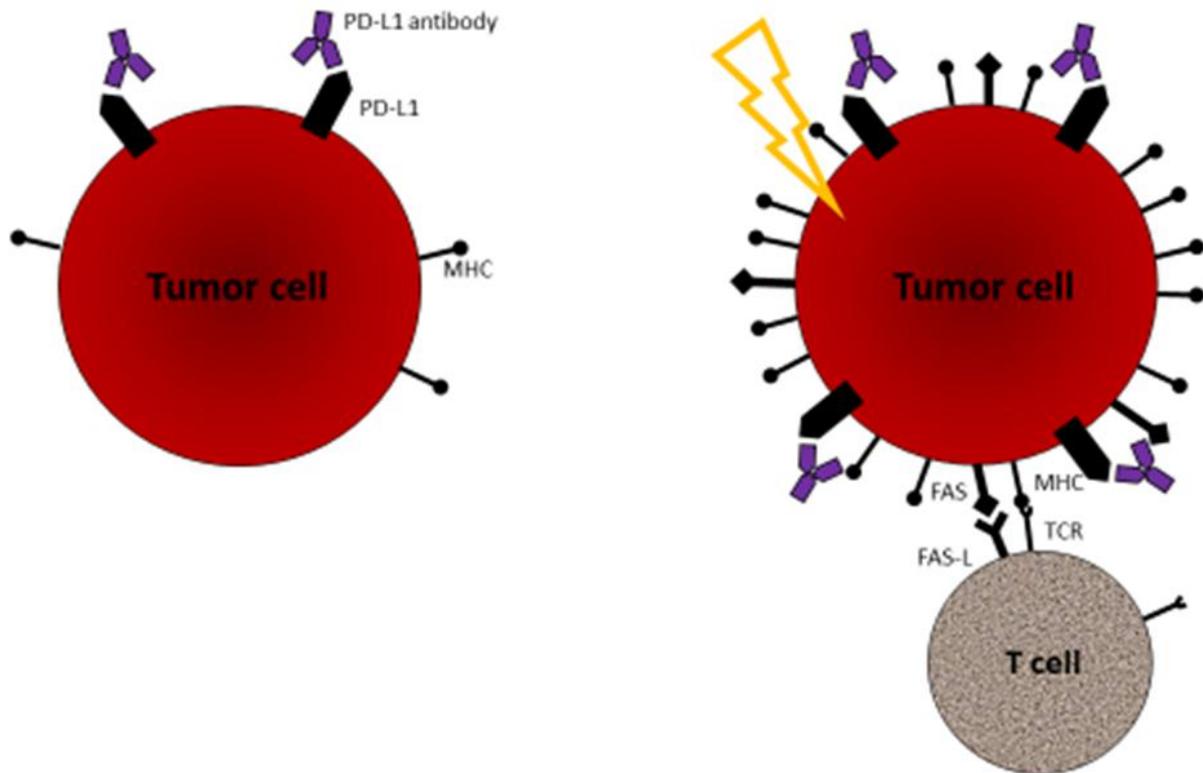
Thanks for your interesting article, however I have some comments. The reinvigoration of T-cells should be clarified by short paragraph or graph. I recommend to add explanatory graphs demonstrating immune check point inhibitor (ICI) mechanism alone and the combination of ICI and radiotherapy. There are some spelling mistakes.

Response> Thank you for your valuable comments. As you comment, we added the paragraph that explaining the importance of reinvigoration of T cell in page 4, line 5-10. The explanatory graphs demonstrating the mechanisms when combining the ICI and radiotherapy is created and summarized in figure 1. I am extremely sorry for several spelling mistakes. I revised the spelling mistakes.

Revised paragraph>

The infiltrating dysfunctional T cells by immunosuppressive mechanisms in TME is one of the reason for failed ICI [13,14]. The exhausted T cells can explain the lack of response in ICI. To elevate the efficacy of ICI response, converting the dysfunctional T cell into functional T cell is important. The reinvigorating exhausted T cell is expected to improve the outcome of ICI. The successful reinvigoration of T cell function would recover the antitumor activity [15].

Revised figure 1>



Reviewer #2

A highly valuable review of exciting new approaches to hepatocellular carcinoma that incorporate radiotherapy and immune checkpoint inhibitors. Useful to all professionals dealing with HCC.

Response> We appreciate your comments and much encouraged. Thank you for your valuable comments.

Reviewer #3

Recent evidence suggests radiotherapy may modulate a patient's immune system, particularly when delivered in high doses over few fractions with conformal techniques; moreover, stimulation of the immune system by irradiation can convert "nonresponder" to "responder". In clinical practice, the synergistic effect of radiotherapy-immunotherapy has been demonstrated in some cancers such as head and neck cancer. In the review, the authors summarized immune modulation caused by radiation and the current trials of RT-ICI combination treatment as well as future perspectives. This is a good review, which providing an issue to be discussed for novel therapeutic strategies of HCC. If possible, some precise molecular mechanisms of RT activating

g specific immune cells in HCC should be supplemented; meanwhile, some grammar errors should be corrected, for example, "The different types of radiation-induced immune modulation by different fractionation scheme of radiation is summarized in figure 1." The "is" should be changed to "are".

Response> Thank you for your comments. The data regarding the precise molecular mechanisms of RT activating specific immune cells in HCC is not well defined in current status. To demonstrate molecular mechanisms of RT activating specific immune cells in HCC, further preclinical and clinical data are needed. Also, I am extremely sorry about some of grammar errors. I revised the errors. Thank you again for your critical comments.