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1st Revision

Reviewer's code: 01573970

COMMENTS TO AUTHORS

The manuscript entitled 'Tumor heterogeneity of gastric cancer: from the perspective of tumor-initiating cell' by Gao et al. provides an extensive review of the field of gastric cancer stem cells. They summarize the field from the identification and validation of gastric tumor initiating cells, origins of GTICs, plasticity and regulatory mechanisms of GTICs, and finally clinical implications of targeting GTICs. Overall, the manuscript is well written and extensive in its scope. However, for reader's benefits, the authors may improve the manuscript in a few ways. 1. Providing illustrative figures would be helpful for readers to understand and catch the main concepts of the manuscript. For example, the authors may provide figures for the 'origin of GTICs' and 'plasticity of GTICs and its regulatory mechanisms', respectively. 2. Too many sentences in a paragraph is disturbing to read. I found some sentences longer than 20 lines. They are better to be split into smaller units. 3. Give references for Table 2 (GTIC-targeted therapeutic strategies/agents). Also, make the table fit into a page margin. 4. Some grammatical errors are found throughout the manuscript (i.e. the advance of in new techniques in...; multiples studies....; TICs install the intratumor.....).

REPLIES from the author

Thank you very much for your kindly revision and comments which I find both helpful and critical. I hereby have made modifications accordingly and the following statements are the point-to-point replies to four comments you have made.

1. **Two figures have been added to illustrate 1) the origination of GATIC and 2) the plasticity of GATIC, respectively.**
2. **Some long sentences have been modified into shorter ones to facilitate reading. The modifications are highlighted in red with underlines for easy-tracking.**
3. **References for Table 2 have been added. The table has also been modified to properly fit into the page.**
4. **Grammatical errors have been corrected. The modifications are highlighted in red with underlines for easy-tracking.**



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2nd Revision

Reviewer's code: 02537457

COMMENTS TO AUTHORS

1. Please define whether the "GTICs" is well-accepted for GASTRIC tumor-initiating cells. "GTICs" is used as glioma tumor-initiating cells in 2016 by Sancho-Martinez et al. in their paper "Establishment of human iPSC-based models for the study and targeting of glioma initiating cells" (Nature Communications).

REPLIES from the author

Thank you very much for your kindly revision. I find your comments very critical as the term "GTIC" has been used in the context of glioma. Therefore, I have re-termed the tumor-initiating cell of gastric cancer as "GATIC" representing **g**astric **t**umor-**i**nitiating **c**ell.