

Dear editor

We thank the reviewers for their valuable time spent reviewing our manuscript and for the constructive suggestions they provided. We carefully considered these comments and made changes accordingly to improve our review thanks to the valuable advice of the reviewers. Now we are convinced that our paper has much more significance and we can solve the concerns of reviewers. We wish to get the chance that the reviewers can re-review our revised paper. Thank you so much.

Please find point-by-point responses to the comments below.

#Reviewer: 1

Specific Comments to Authors:

Authors reviewed hot and cold CRCs, and the available immunotherapy options. The article is well written, easy to follow. I recommend the following additions: - In most cases, authors present the mechanisms only, that can be potentially used, followed by "their preclinical and clinical development has only recently begun". If possible, please give more detail what mechanism of action are they trying to exploit, etc.? - Authors should also present possible methods that are in development / clinical trials, that can be used to make the tumor "hotter". E.g., a good candidate is modulated electro-hyperthermia. Please check abbreviations, e.g., ACT was not resolved. There are a few typos or small grammar issues here and there. Please carefully check those during the revision process.

Reply: Thank you for your positive comments. We give more detail of mechanism of preclinical and clinical development in the "2.1 Increasing tumor inflammation" section. In terms of ways to make the tumor "hotter", We added "2.4 Other possible methods that can be used to make the tumor "hotter"" section to enrich our article. Finally, we fixed the "abbreviations",

"typos" and "grammar" errors.

#Reviewer: 2

Specific Comments to Authors: 1- I would like to suggest adding a figure to the review, describing the difference between cold and hot CRC. 2- A table showing the ICIs that could be in CRC, their mechanisms of action, and their utilization level is a must.

Reply: Thank you for your positive comments. We added a figure and a table as suggested.