

Format for ANSWERING REVIEWERS

August 23, 2015

Dear Editor,



Please find enclosed the edited manuscript in Word format (file name: 20671-Review.doc).

Title: Targeting cancer testis antigens for biomarkers and immunotherapy in colorectal cancer: Current status and challenges

Author: Anil Suri, Nirmala Jagadish, Shikha Saini, Namita Gupta

Name of Journal: *World Journal of Gastrointestinal Oncology*

ESPS Manuscript NO: 20671

To reviewers

Reviewer 1

1) In the introduction, 4th line, you mention "gastrointestinal carcinoid tumors. I would suggest replacing this by "neuroendocrine neoplasms", to include whole spectrum from carcinoid to neuroendocrine carcinoma.

Author's response: As suggested changed accordingly on page number 3 and highlighted in yellow color.

2) In the section "Discovery of CT antigens", you mention Her2 as an example of tumor shared antigens. You after mention that tumor shared antigens cannot serve as targeted therapy. This doesn't apply to the given example, as Herceptin is used to treat specifically cancers overexpressing Her2.

Author's response: The example has been changed from Her2 to MUC1 on page number 4 and highlighted in yellow color.

3) In the section "CT antigens in colorectal cancer. 7th line, there's an ";" in the middle of a sentence, after "that's why".

Author's response: ";" has been deleted

4) In the section "SPAG9", you use the abbreviation EOC without defining it earlier in the text.

Author's response: As suggested the abbreviation has been defined on page number 10 and highlighted in yellow color.

Reviewer 2

The manuscript "Targeting Cancer testis antigens for biomarkers and immunotherapy in

colorectal cancer: current status and challenges” by Suri A et al, reviews the role of cancer testis antigen in CRC and their possible employment as biomarkers and target for immunotherapy. The authors have summarized many previous findings in a well-organized description of the function of this class of molecules in both physiological and pathological conditions. My comments are the following: Minor revisions:

1) There is no mention to a wide gene expression analysis for these molecules that would help to clarify whether and how these antigens are expressed in other somatic tissues in physiological conditions. In the text is reported that two independent groups found a weak expression of CAGE in a portion of normal matched tissue specimens. Moreover, the expression of POTE gene was confirmed by in situ RNA hybridization in several other normal tissues (page 8 “current challenge” paragraph). The authors propose that matched adjacent non-cancerous tissues may not be considered as ‘normal’ because these tissues might have underlying, undiagnosed disease and cite Chen et al. who reported variations in the expression of CTA genes in sets of disease free normal tissues, suggesting that CT antigens might be expressed before clinical manifestation or histopathopathological changes in the tissues. In this regard, a note should be added on a classification of these molecules based on their expression profile in normal tissues as reported by Hofmann et al in PNAS 2008.

Author’s response: As suggested the CT gene classification has been added from the reference of Hofmann et al, 2008 in PNAS on page number 8

2) Few typing mistakes need to be addressed:

a) “Cancer testis antigen” appears capitalized thought the text. However, in the abstract (8th row) and at the end of the introduction (page 3, second to last row) is not capitalized.

Author’s response: As mentioned corrections have been done and highlighted in yellow color.

b) The first sentence of “function of CT antigens”: “Although a lot of clinical research and trials has been conducted to explore the clinical potential of cancer testis antigens but their role in carcinogenesis is still poorly-understood”. The author should use either “Although..., their role is still poorly understood”.” or “A lot of..., but their role is still poorly understood”.

Author’s response: As mentioned correction has been done and highlighted in yellow color.

c) At the end of the manuscript please correct the sentence: “The combination of CT antigens that can be employed for this purpose needs to explore” with “The combination of CT antigens that can be employed for this purpose needs to be explored”

Author’s response: As mentioned correction has been done and highlighted in yellow color.

d) Correct punctuation in line 1 of the introduction (an extra “,” after third common cancer in both...) and line 7 of the “CANCER TESTIS (CT) ANTIGENS IN COLORECTAL CANCER” paragraph (there's an “;” after "that's why").

Author’s response: As mentioned correction has been done and highlighted in yellow color.

To Editor

Thanks for giving us an opportunity to revise our review [Revised: Review ID (01177411)] on this important topic which needs immediate attention of investigators all over the world. Colorectal cancer (CRC) is one of the most commonly diagnosed cancers in both men and women, posing a serious demographic and economic burden worldwide.

I must thank both the reviewers whose input has immensely improved our manuscript. Accordingly we have addressed all the minor revisions mentioned by the reviewers and have modified in our revised review which is highlighted in yellow color.

We hope that this review is now accepted in your esteemed journal and will be beneficial having wide coverage to all researchers and clinicians around the globe.

All co-authors have read and approved the manuscript for submission and have no conflict of interest. This manuscript, as full length review article and has not been previously submitted for publication elsewhere.

Please find below the information which I want to bring to your kind attention:

1. 20671-Revised manuscript: Yes we have revised our manuscript
2. 20671-Answering reviewers: Yes all the comments are addressed
3. 20671-Copyright assignment: We have signed but we have not done CrossCheck program.
4. 20671-Audio core tip: **cannot be provided since we do not have the facility to make audio recordings**
5. 20671- Conflict-of-interest statement: **Yes I am providing this**
6. 20671- Google Scholar **Screen shot taken and is provided**
7. 20671- CrossCheck: **We are Government organization and hence due to lack of funding we cannot perform CrossCheck at our Institute.**

This review is submitted for publication.

With best of my regards,

Truly yours

Anil Suri

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