

April 14, 2020

To

Na Ma, Vice-Editor-in-Chief

World Journal of Clinical Oncology

Baishideng Publishing Group Inc

Dear Dr. Na Ma

We thank you for the opportunity to revise our manuscript in response to the Reviewers' comments. We have carefully considered the comments and have responded to them below. In addition, we have made several changes in the manuscript that have addressed the concerns of the Reviewers.

Reviewer #1:

“This is an interesting and well conceived review paper authored by the experienced authors, who are well published and contributed to the field. Conclusion: Minor revision”

1. The paper would greatly benefit from the revisions making it better understandable by the readers. The authors should more clearly explain what MUTYH is, provide simple diagrams illustrating how it works in a normal, non-mutated conditions and how this is changed in mutated condition. A very clear, step-by -step explanation and diagrammatic illustrations will greatly enhance this paper, and will be appreciated by the readers.

According to Reviewer's suggestion we provided more details about MUTYH in an additional figure (Figure 2) illustrating how MUTYH works in normal and in mutated conditions. Furthermore, in this additional figure, we illustrated all cancers associated to MUTYH alterations, discussed in the text.

2. I suggest changing the title to: “MUTYH, a base excision repair enzyme mutation plays a crucial role in various cancers beyond polyposis” or similar.

We would prefer not to change the title because, although MUTYH is more involved in tumor diseases (as highlighted in figure 2) in this review we would like to emphasize its role, albeit perhaps secondary but still present, also in other non-tumor conditions. We have proposed a more explanatory running title that underlines what is covered in the review.

3. The authors can focused this paper on cancers and just mention in 1 or 2 paragraphs other conditions.

According to Reviewer's suggestion we revised in the manuscript the paragraphs relating to the role of MUTYH in cancer diseases focusing on the role of MUTYH germline mutations as well as its role in sporadic cancers.

4. The authors may cite the below paper published in the World J Gastrointest Oncol. 2019. Lorca V, Garre P. Current status of the genetic susceptibility in attenuated adenomatous polyposis. World J Gastrointest Oncol. 2019 Dec 15;11(12):1101-1114. doi: 10.4251/wjgo.v11.i12.1101. Review. PMID: 31908716

Following the Reviewer's suggestion we added the reference by Lorca V, Garre P. World J Gastrointest Oncol. 2019, 11(12):1101-1114.

Reviewer #2

“Well designed with a fluent style. I recommend it to be published in this journal”

We thank the reviewer for the comment.

We think that we have addressed the Reviewer's comments and hope that the manuscript is now acceptable for publication in *World Journal of Clinical Oncology*.

We look forward to hearing from you soon.

Sincerely,

Maria Cristina Curia