

Dear Jia-Ping Yan,

We are grateful to you and to the reviewers for considering this manuscript for publication and for finding it of “significant interest” for the scientific community, as stated by both reviewers. Indeed, the original comments and remarks made by you and the reviewers helped us to significantly improve the manuscript. A point-by-point response is appended to this letter and as you suggest all the sentences highlighted in the crosscheck report were rephrased.

We very much appreciate your willingness to review the manuscript in light of the further information now provided and to ascertain if our manuscript is suitable for publication in the *World Journal of Clinical Oncology*.

Sincerely,

Dr. Maria I Vaccaro



Response to reviewers

Reviewer 1

In the paper, the authors summarized the progress in glycoconjugation field, particularly for gastrointestinal tumors, and discussed the effect of targeting properties of glycosylated antitumoral agents on gastrointestinal tumors. This is very interesting review with potential application. However, there are several suggestions for the improvement of the review.

1. Please supplement an overview of recent progress in glycoconjugate vaccines targeting tumor.

This is a very good point, and we addressed your comment adding a new item on the new version of the manuscript describing new carbohydrate-based vaccines in page 8, lines 268-308.

2. Please provide a table with summarized characteristics of antitumoral drug glycoconjugates including chemical structure, pharmacodynamics, efficacy and possible ongoing trials.

We added the information suggested on table 1.

3. References in recent two years should be updated.

We updated references in the new version of the manuscript (ref. number: 20;50;70-78). Certainly these references were helpful for reinforced the conclusions of the manuscript.

Reviewer 2

The manuscript by Molejon et al. is a review of the use of conjugation of sugars (glycoconjugation) to existing chemotherapeutic agents. Anti-tumor activity is largely considered in the context of gastrointestinal tumors. While rather narrow in scope, the compilation of information about this group of therapeutics could be of use to some. Value could be enhanced by inclusion of additional information in Table 1.

Despite what it says on Lines 141- 142, no cytotoxic or other comparison between the glycoconjugate and the respective parent compound is provided in the Table. This would enhance overall utility, enhancing comparisons, which are otherwise scattered in the text.

We added the following information on table 1: chemical structures of each glycoconjugates, efficacy and the comparison with the aglycone. We also specified the cell lines used for the evaluation of the glycoconjugates as well as the aglycones.

Similarly, the Figure is fairly uninformative. It could be improved for the nonspecialist by inclusion of the actual sugar structures (instead of simple shapes), and this would complement the structures shown in the Table.

The figure was modified according the reviewer suggestion. We complemented it with the sugars structures.

Multiple errors also need correction. One of the agents is incorrect in the table (Glufosamide). There are symbols missing on lines 215-216. Mice is the plural of mouse (line 264). Line 173: derived, not derivate. Lines 303 and 307: synthesized, not synthetized.

The mistakes pointed out were addressed and modified. The whole manuscript was rechecked.

Dear Dr. Jin-Lei Wang,

Attached to this letter you will find our revised and language-edited manuscript entitled “Glycoconjugation: An approach to cancer therapeutics”, which we will be grateful to you for considering for publication in the *World Journal of Clinical Oncology*.

The original manuscript has been reviewed and thoroughly edited by a retired academic career investigator and native English speaker, as requested by the editor-in-chief. You will also find attached his certificate guaranteeing the quality of the English in the manuscript along with a statement of his qualifications. We are convinced that the revisions made will facilitate the interpretation of our work to your readership.

I and the other authors thank you for your consideration and look forward to learning your final decision.

Yours faithfully,

Dr. Maria I Vaccaro

CERTIFICATION OF ENGLISH-LANGUAGE QUALITY

Donald F, Haggerty, Ph. D.

In my capacity as a privately employed translator and editor registered with the Argentine national entity Administración Federal de Ingresos Públicos (AFIP), I hereby certify that the English-language in the enclosed manuscript by Molejon *et al.* is in appropriate style of formal writing for publication in any stringently reviewed organ, scientific or otherwise.

As a retired academic career investigator with a B. S. degree in biochemistry from Yale University and a Ph. D. in biological chemistry from the University of California at Los Angeles, my publications are listed in the *Internet* along with the articles that have cited them at <https://www.researchgate.net/scientific.../39731466_Donald_F_Haggerty> or can be found by a search in *Google* with *Donald F. Haggerty* plus *phenylalanine hydroxylase* as the key terms.