

Format for ANSWERING REVIEWERS



April 7, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: 8313-review.doc).

Title: Immune therapy for HPV-related cancers

Author: Ricardo Rosales, Carlos Rosales

Name of Journal: *World Journal of Clinical Oncology*

ESPS Manuscript NO: 8313

The manuscript has been improved according to the suggestions of reviewers:

1 Format has been updated

2 Revision has been made according to the suggestions of the reviewer

a) The reviewer indicated that the description of the virus life cell cycle and expression of early and late genes was not necessary in the introduction, and he/she suggested removing it. We agree with the reviewer that this information was redundant and we have eliminated it.

b) The reviewer pointed out that the immune response against HPV described in the manuscript did not refer only to this virus, but it described instead an immune response against any virus. The reviewer suggested presenting only the immune response known to HPV and cervical cancer. We agree with the reviewer in that we originally presented a general view of the immune response against viruses. We have corrected the manuscript so that it now refers only to immune responses specific to HPV.

c) The reviewer also suggested including in the section "evasion mechanisms of the immune response", the role of Th2/Th3 cytokines in cervical cancer development. We are grateful to the reviewer for his/her suggestion. We had mentioned very briefly the role of the different cytokines in the development of HPV persistent infection and progression to cancer. We have now included a complete description of the shift in cytokine production that correlated with tumor progression. The revised manuscript shows the new text highlighted in yellow at page 9, line 7, and also at page 10, line 22.

d) The reviewer pointed out that there is a lot of information in the literature regarding the cellular immune response in patients with HPV infection, cervical lesions and with cervical cancer. The reviewer suggested including this information to better understand the respond of patients' immune system to the immune therapy. We thank the reviewer for his/her suggestion. Although we had mentioned the various types of immune cell

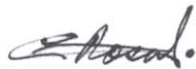
responses in our original manuscript, these responses were not clear because they were presented in different sections. We have now included a new paragraph in the revised manuscript describing in a single place the cellular immune responses described in patients. This text is highlighted in yellow at page 11, line 10.

e) Finally, the reviewer suggested making an additional effort to reduce the size of the manuscript and the numbers of citations. We have eliminated many redundant references by leaving only the more recent ones or the more representative of a particular point. The revised manuscript is shorter than the original one and has about 25 fewer citations.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the *World Journal of Clinical Oncology*.

Sincerely yours,

A handwritten signature in black ink, appearing to read 'C. Rosales'.

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