Author's response to reviews

Title: Molecular characterization of EGFR, PDGFRA and VEGFR-2 in cervical adenosquamous carcinoma

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Ms. No. 1399523955244370

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BMC Cancer

Dear Dr. Jessie Ann Le Good,

Many thanks for your email on the above manuscript.

We are grateful for the kind comments on our manuscript made by the reviewers. We have made the amendments to the manuscript to accommodate the reviewers’ comments. Please find below a detailed ‘point-by-point’ response to the reviewers’ comments.

Reviewer: Gabor Kari

1. We agree with the reviewer and described the statistics used under the heading “Statistical analysis” in the Material and Methods (page 10).

2. As described in the material and methods, all antibodies used were previously published by our group in other malignancies, being the detailed protocol of immunohistochemistry already described. In order to make the text clear, we have added a detailed version of the used protocol with information on the corresponding positive and negative controls used in the present study (pages 8 and 9). Concerning the inclusion of pictures of the negative controls in figure 1,
we think that it will not improve the quality of the picture and it fact it could lead to misinterpretation of figure 1. Nevertheless, we are sending you the negative controls in an extra figure, for reviewer’s evaluation. We intend not to include this extra figure in the manuscript, but if the reviewer finds it fundamental to the final version of the manuscript, we can include it in figure 1.

3. We thank the reviewer’s pertinent question and, following his suggestion, we elaborate the potential impact of the silent mutation in the discussion section (page 13)

4. The manuscript and figure legend were reviewed and corrected for grammatical mistakes.

5. We agree with the reviewer and added a new table (Table1), including the available clinico-pathological data.

Reviewer: Timothy Showalter

The grammatical error was corrected.

Reviewer: Deborah Citrin

Minor revisions

2. We have added the retrospective nature of the cases and mentioned this fact in the material and methods section (page 8).

3. All the clinical data is now available in the new table 1 and the summary of clinical features is described in the material and methods section (page 8).

4. In fact, it was due to tissue limitation that PDGFRA immunohistochemistry was not performed in all cases. In the legend of the new table 2 we explain this fact.

5. In the revised version, table 3 is not included (please see explanation below)

Importantly, during the review process, we realized that the data related to EGFR immunohistochemistry was previously reported by our group (Baltazar F, Filho AL, Pinheiro C, Moreira MA, Queiroz GS, Oton GJ et al.: Cyclooxygenase-2 and epidermal growth factor receptor expressions in different histological subtypes of cervical carcinomas. Int J Gynecol Pathol 2007, 26: 235-241) and was not mentioned in the submitted manuscript, leading to the assumption that the data was original.

As we are currently working with a few series of cervical cancer cases from distinct Institutions, we believed that these data was different from the previously reported (Baltazar F, Filho AL, Pinheiro C, Moreira MA, Queiroz GS, Oton GJ et al.: Cyclooxygenase-2 and epidermal growth factor receptor expressions in different histological subtypes of cervical carcinomas. Int J Gynecol Pathol 2007, 26: 235-241). We truly regret this fact and we would like to put this to your and
the reviewers’ consideration.

Accordingly, in the revised version of the manuscript, we mentioned our previous work and, in order to clarify this issue, made the necessary changes in the text, including the deletion of former Table 3, since the EGFR immunohistochemistry data has already been correlated with the clinical features.

We hope to have clarified satisfactorily the points raised by the reviewers and that the new alterations now proposed will not change the reviewers and your decision concerning the relevance and interest of our study.

If we can be of any further assistance, please do not hesitate to contact us.

We look forward to hearing from you in due course.

Rui Manuel Reis,
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