OPEN PEER REVIEW

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Archives of Neuroscience
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Peer Review Report for "Expression of Pro-Apoptotic P53 Tumor Suppressor Gene in Pituitary Adenomas: Comparison with Anti-Apoptotic Bcl-2 Oncoprotein "

Author(s): Francisco Tortosa

Review Timeline:

Submit Date: 22 Mar 2018
Revised Date: 23 Jul 2018
Accepted Date: 24 Oct 2018

Revision (0)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision** (0)

26 Jun 2018

Dear AE,
The manuscript entitle"Expression of Pro-apoptotic P53 Tumor Suppressor Gene in Pituitary Adenomas: Comparison with Anti-apoptotic Bcl-2 Oncoprotein " was reviewed. Briefly, it doesn't provide any new information. The problems going with this manuscript are as follows:
- It needs vigorous English editing.
- There is no definition for typical and atypical tumors.
- It Is not clear whether the authors biopsied recurrent tumors and compare the expression of oncoprotein with the initial biopsy.
- How about the non-recurrent tumors. How did they find the percentage of oncogenes expression?
Thanks.

REFEREE: Reviewer | **Revision** (0)

29 Jun 2018

Dear AE,

There are some points which should be addressed by the author:
1- Introduction is too long and needs to be truncated, deleting the general characteristic of pit adenomas, to only 2 paragraphs, mentioning the possible role of genetics in oncogenesis of pit adenoma and the aim of the research.
2- The heterogeneity of the groups compared with each other makes conclusion very difficult. It is suggested to divide the material into subgroups according to the classic classification of adenomas and show the material in tables in separate rows in addition to the characteristics of each group.
3- Instead of percentile, it is preferred to show the impact of each variable using p value via t-test.
4- The paragraph mentioning the main limitation of this research such as the retrospective nature of data collection is certainly necessary.
5- Reference list is not complete and needs to be further searched in the relevant literature.
Thanks.

REFEREE: Associate Editor | **Revision** (0) 4 Jul 2018

Dear EIC
The reviewer(s) have recommended publication, but also suggest some major revisions to the manuscript. Therefore, I invite the author to respond to the reviewer(s)' comments and revise his manuscript.
Kind regards,

REFEREE: EIC | **Revision** (0) 4 Jul 2018

Dear Author,
Please revise the manuscript according to the reviewers' comments.
Thanks.

OPEN PEER REVIEW

Revision (1)

Reply to Reviewers

Ideally, the reviewing process can significantly improve the submitted manuscripts by allowing the authors to take into account the advice of reviewers. Author(s) must reply to all reviewers' comments in a separate Word file, point by point. A "**Reply to Reviewers**" document is submitted along with revised manuscript during submission of revised files, summarizing the changes that the authors made in response to the reviewers' comments. The responses to reviewers' comments specifies how the authors addressed each comment the reviewers made.

You can read the authors' responses to the reviewers' comments in the next page.

Response to Reviewers

July 23, 2018

Prof. Zahid Hussain Khan, Editor-in-Chief of Archives of Neuroscience

Title of the paper: **Expression of Pro-apoptotic P53 Tumor Suppressor Gene in Pituitary Adenomas: Comparison with Anti-apoptotic Bcl-2 Oncoprotein**
Author: Francisco Tortosa

Author´s responses to reviewers' comments
First, I would like to thank the comments made on article. They have undoubtedly improved the manuscript. Then, I will explain all the changes introduced in the text (highlighted in yellow):

Reviewer 1:
1. It needs vigorous English editing.
Authors' answer: I have reanalyzed all the text to improve the language used on it, and so to facilitate the reader's understanding. Posteriorly, the manuscript has been checked linguistically by a native English speaker as indicated by the reviewer.

2. There is not definition for typical and atypical tumors.
Authors' answer: It has been introduced the definition for these type of tumors (p. 5).

3. It is not clear whether authors biopsied recurrent tumors and compare the expression of oncoprotein with the initial biopsy. How about the non-recurrent tumors. How did they find the percentage of oncogenes expression.
Authors' answer: In this study only primary tumors were considered; in 18 there were post-operative recurrences during follow-up, defined as reappearance of the tumor in imaging studies for nonfunctioning as functioning adenomas, as well as hormonal hypersecretion for functioning tumors. I have introduced in the text these considerations, as required by the reviewer (p. 8).

Reviewer 2:
1. Introduction is too long and needs to be truncated, deleting the general characteristic of pit adenomas, to only 2 paragraphs, mentioning the possible role of genetics in oncogenesis of pit adenoma and the aim of the research.
Authors' answer: I thank the reviewer for the comment. The "Background" section has been reformulated as suggested by the reviewer.

2. The heterogeneity of the groups compared with each other makes conclusion very difficult. It is suggested to divide the material into subgroups according to the classic classification of adenomas and show the material in tables in separate rows in addition to the characteristics of each group.
Authors' answer: The material has been divided into clinical and histopathological subgroups; p53 and bcl-2 immunoreactivities with regards to the different pituitary tumor groups are presented in Table 2.

3. Instead of percentile, it is preferred to show the impact of each variable using p value via t-test.
Authors' answer: The impact of each variable is shown using *p* value via *t*-test as suggested by the reviewer (p. 7, 8, and Table 2).

4. The paragraph mentioning the main limitation of this research such as retrospective nature of data collection is certainly necessary.
Authors' answer: I have introduced a paragraph mentioning the main limitations of this study (p. 11).

5. Reference list is not complete and needs to be further searched in the relevant literature.
Authors' answer: The following bibliographical references have been added to the manuscript (p. 10, 11 and 15).

- Moldovan IM, Susman S, Pirloq R, Jianu EM, Leucuta DC, Melincovici CS, et al. Molecular markers in the diagnosis of invasive pituitary adenomas - an immunohistochemistry study. *Rom J Morphol Embryol*. 2017;**58**(4):1357-64.
- Yin D, Tamaki N, Kokunai T, Yasuo K, Yonezawa K. Bromocriptine-induced apoptosis in pituitary adenoma cells: relationship to p53 and bcl-2 expression. *J Clin Neurosci*. 1999;**6**(4):326-31.
- Ahlbom E, Grandison L, Zhivotovsky B, Ceccatelli S. Termination of lactation induces apoptosis and alters the expression of the Bcl-2 family members in the rat anterior pituitary. *Endocrinology*. 1998;**139**(5):2465-71.

I would like to thank you sincerely for the targeted comments, which have given me the opportunity to refine the manuscript. I are looking forward to hear from you soon.

With best regards,

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Revision (1)

Here, you can see the **Reviewers**, **Associate Editors** and **EICs'** comments from the beginning to the end of the revision process.

REFEREE: Reviewer | **Revision** (1) 23 Oct 2018

Dear AE,
The study is reviewed carefully. According to comments and revisions by the author, this manuscript is accepted.
Thanks

REFEREE: Associate Editor | **Revision** (1) 24 Oct 2018

Dear EIC
Based on the authors' answers to the reviewers' comments, the reviewer(s) have recommended publication.
Kind regards.

REFEREE: EIC | **Revision** (1) 24 Oct 2018

Dear Author,
The document is reviewed carefully by the reviewers. According to their comments and your revisions as requested, this manuscript is accepted.
Thanks.