

## Format for ANSWERING REVIEWERS



August 25, 2012

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: **4446-review.doc**).

**Title:** *Molecular biomarkers of cell proliferation in ameloblastomas. A mini-review*

**Author:** Bologna-Molina Ronell, Bedoya-Borella Ana Maria, Soria-Moreira Liliana, Soría-Suárez Sandra

**Name of Journal:** *World Journal of Stomatology*

**ESPS Manuscript NO:** 4446

The answer to the reviewers are described below and are added in manuscript (highlighted in yellow).

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

Major comments:

**Reviewer suggestion:** 1) The authors discussed and summarized several molecular biomarkers of cell proliferation in ameloblastomas; however, they did not discuss the potential applications of these biomarkers for this disease in the clinic. For example: (i) What is the possibility and reliability of using these biomarkers for diagnosis of ameloblastomas in the clinic, as compared to other clinical parameters of odontogenic tumor disease activity? (ii) Whether these biomarkers can be used for monitoring response to therapy or treatment effectiveness in ameloblastomas? (iii) Whether these biomarkers can be used for monitoring disease progression and prognosis in patients with ameloblastomas?

**Authors response:** **Note that the use of these biomarkers alone are not useful for the diagnosis of ameloblastoma, the diagnosis is based on clinical and histopathologic features, but yet proliferation molecular biomarkers provide important information when predicting the prognosis of patients with ameloblastoma , so the histopathological types together with proliferation marker expression could be useful tools for evaluating the biological behavior of ameloblastomas.**

**Reviewer suggestion:** 2) Besides AgNOR and IHC mentioned in the manuscript, are there any other methods and techniques like the mitotic index, flow cytometry, western blotting, or real-time qPCR that can be used for detecting the expression or levels of these biomarkers in ameloblastoma patients? If so, which method or technique is better than others in terms of sensitivity and specificity as well as feasibility? For example, which method or technique is simpler and easier than other techniques for the diagnosis of ameloblastomas, making it a more practical method for use in primary care clinics and hospitals in developing countries, which may lack sophisticated equipment and facilities. The authors may want to discuss about these issues in this paper.

**Authors response:** **There are specific and sensitive techniques for determining the presence of these markers such proteomics techniques which allow to know what proteins are present or absent in**

these tumors. Another technique quantitative, sensitive and highly specific is the real-time PCR that allows determining the expression levels of genes in the ameloblastoma.

Both techniques are more expensive and more laborious than the immunohistochemistry technique that despite having less specificity and sensitivity has the advantage of being able to display "in situ" the presence of proteins, important data for understanding how the tumor proliferates.

Notably, all of these techniques can support the diagnosis, however, only the hematoxylin and eosin staining gives the information needed for the final histopathological diagnosis.

Minor comments:

Reviewer suggestion: All of the authors' affiliations in the paper should be in English.

**Authors response: The change was done**

Reviewer suggestion: Pay more attention to the punctuation mark throughout the manuscript.

**Authors response: The change was done**

Reviewer suggestion: The conclusion section needs to be revised. For instance, the authors should give perspective remarks on the future research of biomarkers in ameloblastomas, and whether and how these marker proteins can be potentially used as biomarkers for diagnosis and prognosis of ameloblastomas and for monitoring therapy response and disease progression in patients with ameloblastomas.

**Authors response: The change was done**

Reviewer suggestion: The authors should give a brief figure legend to Figure 1 and some brief information in the footnote of Table 1 to help the reader fully understand Figure 1 and Table 1 without referring to the text of the paper.

**Authors response: The change was done**

Reviewer suggestion: Some sentences in the manuscript are confusion. *e.g.* "MCM proteins are expressed cells in all phases of the cell cycle, ....." on page 7. The authors need to carefully edit this submission before the paper could be published in an English-language journal.

**Authors response: The change was done**

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

Sincerely yours,

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