Format for ANSWERING REVIEWERS

June 9, 2013

Dear Mr.Sheng Ma,

Enclosed you will find the revised manuscript in Word format (file name: 2616-review.doc).

Title: Expression of matrix metalloproteinases 9 and 12 in actinic cheilitis

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Name of Journal: World Journal of Experimental Medicine

ESPS Manuscript NO: 2616

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

Reviewer 1.

1. The demographic information of the patients were included in: Page 5 line 12 : Biopsies of the lower lip……. Table 1. Furthermore the demographic information is presented in table 1 page 15.
2. Histopathological information of the samples and the grade of dysplasia are presented in detail in Table 4 page 18.
3. Microphotographs of MMP-9,MMP-12 in normal lip and negative control were included in the manuscript. Figures 3,4,5 in the revised manuscript.
4. The study on MMP-9 and actinic cheilitis of Souza-Freitas (OOOOE,,2011; 112:342-348) was added in the discussion (reference no 32 in the revised manuscript)

Reviewer 2.

1. The issue that MMP-9 in actinic cheilits may have no differences in the pattern of expression in comparison with squamous cell carcinomas was raised by Hernandez-Perez M and El-hajahmad M et al in 2012. In our study we did not detect strong immunoractivity for MMP-9 in actinic lesions. However, we did not compare the actinic cheilitis samples with squamous cell carcinomas. In the manuscript (discussion page 8 line 36) the text was modified as follows:
   "Recently it has been reported that MMP-9 was strongly expressed in SCCs of the lip and moderately expressed in ACs and control samples[32]. Whereas another study detected positive expression of MMP-9 in actinic cheilitis lesions with no statistical differences in the pattern of

expression in comparison with squamous cell carcinomas[33]. Despite the above mentioned previous findings, in our study we were not able to…….”

2. I definitely agree with your suggestion that although the limitations of the zymographical techniques make difficult to interpret the data, it is the most suitable technique to analyze the MMPs. However, we have not been able to perform either Northern Blotting or gelatin zymographic assay due to financial restrictions in our school.

   Furthermore, by using zymography complexes of MMPs might complicate the analysis, such as, in the occasion of MMP-9 which can be associated with a 25-kDa protein, giving a band at 125 kDa and a dimer at 215kDa. These complexes are not dissociated in zymography. In addition by using zymography it is often not possible to discriminate different MMP-s because the substrates are usually degraded by more than one MMP. Consequently MMPs should be identified by a complementary technique such as immunohistochemistry, which is still a reliable method, for valid conclusions. (Yan SJ, and Blomme EA. 2003).
3. All minor concerns have been corrected and the manuscript was revised for minor grammatical and typographical errors.

Editorial Office

1. The Core Tip was included under the key words.
2. The Comments were included under the discussion and provided information about background, research frontiers, innovations and breakthroughs, applications, terminology, peer review.
3. References and typesetting were corrected and doi as well as PMID were included.

3 References and typesetting were corrected

Thank you again for publishing our manuscript in the World Journal of Experimental Medicine

Sincerely Yours

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