

ANSWERING REVIEWERS

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Low expression of angiotensinogen and dipeptidyl peptidase 1 in saliva of patients with proliferative verrucous leukoplakia

Reviewer 1

To the Editor and the Authors: In this study, the authors performed the salivary proteome analysis of the patients with PVL. Among thirty-one proteins which showed significant difference in relation to abundance between the control and PVL, the authors concluded that DPP1 and ATG were potential biomarkers for PVL and the authors suggested that DPP1 and ATG may be involved in mechanisms for development of PVL. The purpose, background, and results of this study are interesting and this manuscript is well written. However, this manuscript contains some critical problems. Therefore I have concerns as follows;

1) Inclusion and exclusion criteria of this study were not clearly described in the Method section.

The inclusion and exclusion criteria were included in the Material and Method Section

For example, the authors stated in the Result section that "All thirty patients were female". Were only female enrolled in this study? The authors should show their inclusion and exclusion criteria more clearly.

The sample was composed only by women because PVL affects particularly this gender. The inclusion and exclusion criteria were included in the Material and Method Section.

2) Baseline characteristics of the participants were not fully described. The authors have better to provide other information which is supposed to be risk factors of PVL, such as smoking and alcohol consumption.

These patients do not have a known risk factor. These information was included in the introduction as follow "An intriguing characteristic of this entity is the prevalence in older women with no history of exposure to known risk factors for leukoplakia, such as tobacco and alcohol consumption, suggesting the existence of active molecular events."

3) Table II is confusing. Were Cases 1, 2, and 11 taken their saliva after the treatment of PVL

No. These cases corresponding to patients with history of previous treatment for PVL lesions.

Reviewer 2

The manuscript is well written. May be accepted for publication

Reviewer 3

Interesting article

Reviewer 4

The manuscript is interesting and presents a novel diagnostic tool. I would suggest a text review by an English-speaker reviewer, as well an author review for minor errors all over the text.

The text was submitted to English review process.

It would be interesting the insertion of a figure representing the classical clinical PVL aspect.

The classical clinical figure was included.

I suggest that Table 1 presents more demographic data, other than just ages (sucha as gender...).

The additional demographic aspects were included in the Table 1.

Introduction: the “ four histological features encountered during the course of the disease” are not observed in ALL cases (not all present verrucous hyperplasia and verrucous carcinoma development) . Thus, I suggest reorganization of this paragraph and all idea presentation.

One sentence was included to explain the histopathological findings in PVL entity.