Published online 2016 June 28.

### Letter

# Application of Immunocytochemistry on Oral Smears: A Noninvasive Method for Early Detection of Cellular and Molecular Changes in High-Risk Populations

## Bita Moudi<sup>1,2,\*</sup>

<sup>1</sup>Infectious Diseases and Tropical Medicine Research Center, Zahedan University of Medical Sciences, Zahedan, IR Iran <sup>2</sup>Department of Histology, School of Medicine, Zahedan University of Medical Sciences, Zahedan, IR Iran

<sup>\*</sup> *Corresponding author*: Bita Moudi, Department of Histology, School of Medicine, Zahedan University of Medical Sciences, Zahedan, IR Iran. Tel/Fax: +98-5433295794, E-mail: bita.moodi@yahoo.com

Received 2016 May 14; Revised 2016 June 05; Accepted 2016 June 07.

Keywords: Immunocytochemistry, Chronic Disease, Noninvasive

## Dear Editor,

It has been reported that chronic diseases, are the main cause of death all over the world. The world health organization has reported that more than half of the patients with chronic diseases, reside in low and middle income countries (1). In this regard, suitable preventive programs such as early detection can improve the patient's critical condition (1-3). Nowadays, diagnostic and preventive methods use modern technologies to perform the available approaches for all patients. Such developments improve the quality of life and health of the subjects with chronic diseases. Therefore, new methods that are able to detect chronic diseases and their related-complications are of great interest (4, 5). In this regard, diagnosis can be made on the basis of oral signs and symptoms (6). It is important to develop new and non-invasive methods for early detection of the disease that are able to improve the general health of patients with chronic disease and even protect them from dangerous complications. In the recent years, important advances have been made in the development of non-invasive diagnostic methods. We should all be aware that there has been an increased effort to introduce easy and accurate diagnostic approaches to help patients with chronic diseases. The basis of such techniques is the optimal use of available clinical samples when facing a patient with chronic conditions and related complications (6).

This is regarding the research article titled "Immunocytochemical study of p53 protein in exfoliated cells of oral mucosa in patients with type 2 diabetes" by Heidari et al., 2015 Jan, vol-2(1): e24881 (6) in Gene, Cell and Tissue. The authors have skillfully investigated a non-invasive method for detection of precancerous changes using oral exfoliated cell smears. The authors provide a case-control study for analysis of the immunocytochemistry of p53 in exfoliated oral mucosal cells in patients with type 2 diabetes. They found a significant increase in p53 expression in exfoliated cells of the oral mucosa in patients compared with controls. In addition, the results showed a significant correlation between the intensity of p53 expression and the level of fasting blood sugar as well as between the percentage of p53 positive cells and fasting blood sugar.

According to these results they concluded that there was a significant overexpression of p53 in oral mucosal exfoliated cells of diabetic patients compared with the control group. They proposed that this noninvasive technique could be useful to detect premalignancy changes of oral mucosa, as well as, for early detection of malignancies.

Noninvasive simply means the body is not invaded during surgical investigations. For several decades, exploratory surgery was routinely performed to determine the source of illness. However nowadays, it is necessary to diagnose without having to perform exploratory surgery. Detection of oral lesions by exfoliated cells of the oral mucosa in patients with chronic diseases, as an example of non-invasive methods, is the best approach in that it does not involve incisions. This non-invasive detective method will become the most common method of early detection of many chronic diseases and related-triats in the future. The use of cell smears such as exfoliated cells of the oral mucosa is related to a technique that does not involve puncturing the skin, large incision in the body or entering a body cavity. Incisions can leave large wounds that are painful and take a long time to heal. The methods that use cell smears refer to detective techniques that eliminate incisions needed and so reduce wound healing time, associated pain and risk of infection (7-9).

Exfoliated cells of the oral mucosa are easily accessible

Copyright © 2016, Zahedan University of Medical Sciences. This is an open-access article distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (http://creativecommons.org/licenses/by-nc/4.0/) which permits copy and redistribute the material just in noncommercial usages, provided the original work is properly cited.

and can be the raw material for detection methods such as immunocytochemistry (ICC). Immunocytochemistry is used for tracking an antigen in cells via an antibody (10). The role of immunocytochemical staining in detection of various tumors and progression of the disease has been understood and some studies indicated that immunocytochemical techniques are reliable methods for evaluation of cancer progression (11, 12). In addition, the use of cell smears can improve the development and use of genomics and biotechnology for public health. Genomic science is largely laboratory-based and revolves around molecular studies. It has the potential to help combat infectious and chronic diseases of poverty, from genome mapping to genetic engineering, and is continuing to expand with advances in scientific research. Genetic evidences are likely to lead to the production of new diagnostics as well as treatments with which to combat disease. They can also help improve the understanding of disease pathology and so may help limit the effects of chronic and infectious diseases. In this regard it can be noted that easy access to the samples is very important. The method of the abovementioned study is not invasive and painful for patients and its implementation in disease severity can be easy and convenient. If the performance of immunocytochemistry and genetic researches on exfoliated cells of the oral mucosa obtains necessary technical improvements, we can detect cellular changes without any complex and difficult surgeries. Furthermore, altering the expression of some genes can be easily observed. A lot of useful information can be obtained with this technique.

Therefore, with regards to chronic diseases and related-oral lesions, the use of ICC, DNA extraction and exfoliated cells of the oral mucosa in diagnosis and research is a very impressive and remarkable approach. In addition, the search strategy used by Heidari et al. was reported in detail, therefore the search strategy did allow replication. In conclusion, early detection of diseases with ICC and genetic studies on convenient sampling such as exfoliated cells of the oral mucosa may provide unique information to predict disease progression at early stages and be used to choose an appropriate treatment approach.

### References

- 1. WHO. Noncommunicable diseases, Fact sheet. Geneva: World Health Organisation; 2016.
- Nojilana B, Bradshaw D, Pillay-van Wyk V, Msemburi W, Laubscher R, Somdyala NI, et al. Emerging trends in non-communicable disease mortality in South Africa, 1997 - 2010. *S Afr Med J.* 2016;**106**(5):477-84. doi: 10.7196/SAMJ.2016.v106i5.10674. [PubMed: 27138667].
- Falci I, Shi Z, Greenlee H. Multiple Chronic Conditions and Use of Complementary and Alternative Medicine Among US Adults: Results From the 2012 National Health Interview Survey. *Prev Chronic Dis.* 2016;13:61. doi: 10.5888/pcd13.150501. [PubMed: 27149072].
- Mehrotra R, Gupta A, Singh M, Ibrahim R. Retraction: Application of cytology and molecular biology in diagnosing premalignant or malignant oral lesions. *Mol Cancer.* 2012;11(1):57. doi: 10.1186/1476-4598-11-57.
- Suster S, Moran CA. Applications and limitations of immunohistochemistry in the diagnosis of malignant mesothelioma. *Adv Anat Pathol.* 2006;13(6):316–29. doi: 10.1097/01.pap.0000213064.05005.64. [PubMed: 17075297].
- Heidari Z, Sagheb HM, Rad AA, Keikhaee MA. Immunocytochemical Study of p53 Protein in Exfoliated Cells of Oral Mucosa in Patients With Type 2 Diabetes. *Gene Cell and Tissue*. 2015;2(1).
- Bolognesi C, Bonassi S, Knasmueller S, Fenech M, Bruzzone M, Lando C, et al. Clinical application of micronucleus test in exfoliated buccal cells: A systematic review and metanalysis. *Mutat Res Rev Mutat Res.* 2015;**766**:20–31. doi: 10.1016/ji.mrrev.2015.07.002. [PubMed: 26596545].
- Jara-Ettinger AC, Lopez-Tavera JC, Zavala-Cerna MG, Torres-Bugarin O. Genotoxic Evaluation of Mexican Welders Occupationally Exposed to Welding-Fumes Using the Micronucleus Test on Exfoliated Oral Mucosa Cells: A Cross-Sectional, Case-Control Study. *PLoS One.* 2015;10(8):0131548. doi: 10.1371/journal.pone.0131548. [PubMed: 26244938].
- Mohanta A, Mohanty PK, Parida G. An in vivo cytogenetic analysis of human oral squamous cell carcinoma. *South Asian J Cancer*. 2015;4(3):123–6. doi: 10.4103/2278-330X.173178. [PubMed: 26942142].
- 10. Merighi A, Lossi L. Immunocytochemistry and Related Techniques. New York: Humana Press; 2015.
- Zhao SF, Tong XY, Zhu FD. Nitric oxide induces oral squamous cell carcinoma cells apoptosis with p53 accumulation. *Oral Oncol.* 2005;**41**(8):785-90. doi:10.1016/j.oraloncology.2005.04.002. [PubMed: 15979383].
- Ravi D, Ramadas K, Mathew BS, Panikkar KR, Nair MK, Pillai MR. Apoptosis, angiogenesis and proliferation: trifunctional measure of tumour response to radiotherapy for oral cancer. *Oral Oncol.* 2001;**37**(2):164–71. [PubMed: 11167144].