Saliva protein biomarkers and oral squamous cell carcinoma

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The article by Yu et al. (1) in a recent issue of PNAS unveils potential salivary biomarkers for the early detection of oral squamous cell carcinoma (OSCC). Despite the groundbreaking findings demonstrated, the authors assert that the ongoing strategy for detecting OSCC (oral visual inspection and biopsy) is ineffective, because it has globally yielded high specificity but varied sensitivity. Here, we briefly discuss the abovementioned affirmation, taking into account the landscape of OSCC screening approaches.

First, few studies have reported population-based screening interventions for OSCC. However, to the best of our knowledge, there is a worldwide lack of policy regimes targeted toward OSCC screening and early detection. Additionally, organizations such as the US Preventive Services Task Force (2) and the WHO do not provide recommendations for OSCC screening. Likewise, professional societies (e.g., American Dental Association) only softly recommend dentists to be vigilant for early signs of OSCC on routine visual/tactile examination. Conversely, the criticism over the cost-effectiveness of visual inspection and biopsy as OSCC screening tools relies on community-based studies that are subject to dramatic sociodemographic variability.

Moreover, several barriers prevent populations from having access to oral cavity examination by trained health professionals. Thus, because the existing OSCC screening tools are generally not being implemented in primary care routine, the use of saliva protein biomarkers sounds quite distant from the current health economics state in most countries. It would probably make sense if these novel biomarkers could be used as complementary tests, instead of primary screening tools, to replace the clinical examination in developing countries. Furthermore, only a few successful biomarkers can be translated into clinical practice, because they require, at a reasonable cost, high specificity, sensitivity, positive and negative predictive values, a short time for results to be applicable in the decision-making process, and novel information currently unavailable (3).

Importantly, data from recent systematic reviews and meta-analysis have presented conflicting results. Guerra et al. (4) analyzed the diagnostic capability of salivary biomarkers for head and neck squamous cell carcinoma (HNSCC) and found a set of combined biomarkers to be potentially useful as diagnostic tools. This study has two important limitations: first, it did not include only cases of OSCC, and HNSCC is considered a highly heterogeneous disease; and, second, most studies evaluated in this review were carried out in the United States, which is unlikely to represent populations on a global scale. Gualtero and Suarez Castillo (5) observed insufficient scientific evidence to support the use of salivary biomarkers for early diagnosis of OSCC, although they could be used to discriminate between patients with and without OSCC. Lastly, a Cochrane review (6) found no eligible study investigating salivary biomarkers as potential diagnostic tests for OSCC or potentially malignant lesions.

Therefore, we cannot rule out the fact that the visual inspection of the mouth followed by biopsy remains the most reliable option for OSCC screening. Finally, it is worth mentioning that we definitely encourage research targeting noninvasive biomarkers for OSCC. Nevertheless, we emphasize that, from the public health standpoint, clinical and biological approaches are expected to work together toward obtaining better and cost-effective outcomes at the population level.

1 Yu JS, et al. (2016) Saliva protein biomarkers to detect oral squamous cell carcinoma in a high-risk population in Taiwan. *Proc Natl Acad Sci USA* 113(41):11549–11554.

2 Moyer VA; US Preventive Services Task Force (2014) Screening for oral cancer: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med* 160(1):55–60.

3 Kang H, Kiess A, Chung CH (2015) Emerging biomarkers in head and neck cancer in the era of genomics. *Nat Rev Clin Oncol* 12(1): 11–26.

4 Guerra EN, et al. (2015) Diagnostic capability of salivary biomarkers in the assessment of head and neck cancer: A systematic review and meta-analysis. *Oral Oncol* 51(9):805–818.

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5 Gualtero DF, Suarez Castillo A (2016) Biomarkers in saliva for the detection of oral squamous cell carcinoma and their potential use for early diagnosis: A systematic review. *Acta Odontol Scand* 74(3):170–177.
6 Macey R, et al. (2015) Diagnostic tests for oral cancer and potentially malignant disorders in patients presenting with clinically evident lesions. *Cochrane Database Syst Rev* 5(5):CD010276.