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Emerging Aid in Oral Cancer Diagnosis

Sachchidanand Tiwari and Pratima R. Solanki*

Special Centre for Nanosciences, Jawaharlal Nehru University, New Delhi-110067, India

Malignancies, causing oral or mouth cavity including lips, cheeks, tongue, floor of the mouth, hard and soft plate, sinuses and pharynx (throat), are known as oral cancer (OC) [1]. Squamous cell carcinoma, that develops in the tissue that lines the mouth and lips or in lining of oral mucosa, independently accounts for over 90% [2]. OC used to occur in older and middle aged individuals, but in recent years a large number of young adults are also affected worldwide [3]. Symptoms of OC are, non healing sore and patches (red and/or white) on the face, neck, mouth or lips, pain, tenderness and bleeding in mouth, loose teeth, difficulty in chewing and swallowing, and change in voice.

It is a well known fact that OC majorly occurs due to excessive consumption of tobacco, smoking and alcohol and poses 3-9 times higher risk [4]. Other factors responsible include poor nutrition, poor oral hygiene and some chronic infection caused by bacteria and viruses [3]. Social habitats and exposure to carcinogens from various sources like tobacco, alcohol and smoking are the main factors that result in molecular alterations associated with OC. Recent studies suggest that some strains of human papillomavirus (HPV) are associated with some oral and oropharyngeal cancers. However, HPV-16 and HPV-18 are found responsible for OC cases up to 22% and 14%, respectively [5]. Although numerous genes and their products are known, there is no single pathway accounting for all type of OCs. The main genes involved in predisposition of OC include p53, RAS oncogenes, c-myc, Rb, CyclinD1, CyclinA, BRCA2, p27 [6].

The proteomic and genomic studies of body fluids revealed many biomarkers related to OC progression, which make them useful candidates with tremendous potential for monitoring and diagnosis for early detection [7]. A complete description about the OC biomarkers has previously been given by many authors, including anti-oncogenes (p53, p16), growth factors (EGF, IGF and VEGF), cytokeratins (CK13, CK16), epithelial tumour factors (CYFRA-21-1) and microRNA [7-9]. With the advancement of diagnostic technologies it is possible to detect femto molar (fM) levels of cancer biomarkers in saliva and other body fluids. Saliva has an advantage over other body fluids like blood for estimation of biomarker due to non-invasive sample collection which makes it most suitable candidate for non-invasive cancer detection [7]. More recent use of saliva for detection of OC biomarkers emerged as novel and noninvasive approach. Many studies have been done in recent years to improve cancer diagnosis and prognosis throughout the body, but it has not shown similar improvement in case of OC [10]. Since five-year survival is directly related to different stages in diagnosis, prevention and early detection, efforts have the potential not only for decreasing the incidence, but also for improving the survival of those who have been infected by this disease. Unfortunately, most of the patients are diagnosed at advanced stage (stage 3 and 4) of disease. Early detection, therefore, is crucial for improved survival rate as well as access to oral health services for all mankind.

The existing conventional techniques for OC detection are visualization, biopsy, histopathology and palpation examination [10]. These methods are invasive, time-consuming, expensive, and labour-intensive. Enzyme-linked immunosorbent assay is a gold standard commercially available method with lower detection limits (LDL) near 1 pg mL−1 but is difficult to adapt to multiplexing [10,11]. Bead-based or modified immunoassays using chemiluminescence, electrochemiluminescence, or fluorescence provide LDL approaching several pg mL−1 but require high cost and high maintenance instruments for automated analyse [11]. Newly available liquid chromatography–mass spectrometry proteomics can provide multiple biomarker measurements at one spot approaching the sensitivity and detection limit, but this method of measuring biomarkers is still very expensive, labour intensive, and complex for routine diagnostics. Emerging technologies for sensitive protein biomarker measurements include biosensors based on electrochemical, optical, and nanotransistor detection.

Biosensors have many potential advantages over other conventional methods of cancer diagnosis and disease monitoring, especially low cost, sensitivity, low detection limit, involve minimal samples, increased response speed and flexibility [12]. Rapid, real-time analysis of cancer biomarkers provides instant vital information to doctors and users that can be very helpful in the planning of patient care and treatment. Biomarker based biosensors for cancer can improve the rate of earlier detection (low concentration) as well as monitoring of disease condition.

In past few years lot of efforts have been made for the development of biosensor platforms utilizing single biomarker for detection of OC [13,14]. The single biomarker based sensor cannot be utilized for all patients as the expression of biomarkers varies from patient to patient for the confirmation of positive results. Thus, a device is required that can monitor more than one biomarkers at a time to confirm positive results of disease condition. Researchers used different biomarkers secreted in body fluids to diagnose OC through biosensor in easy and rapid way, but there are very few reports available on multiplexed, non-invasive cancer detection till date. Efforts have also been made to fabricate non-invasive biosensor for oral cancer detection [12].

Future Perspectives

Biosensor is a rapidly emerging technique for diagnosis of cancer and other disease conditions worldwide. The cost effectiveness, multi analyte detection and simple handling of biosensors makes them acceptable in field of diagnostics. Non-invasive detection of cancer through body fluid such as saliva, sweat and urine provides an extra advantage to biosensor, that help to overcome it on other conventional diagnostic techniques. Saliva has been described as “mirror of body” that contains many potential information of the health condition and has been proven by proteomic studies. So the use of saliva and other

***Corresponding author:** Pratima R. Solanki, Special Centre for Nanosciences, Jawaharlal Nehru University, New Delhi-110067, India Tel: 011-26704740, 011-26704699; E-mail: partima@mail.jnu.ac.in; pratimarsolanki@gmail.com

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non-invasive body fluids for detection of Cancer and other deadly diseases for quantification of biomarkers will be effective for early and rapid detection.

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