Microarray-based gene expression profiling for early detection of oral squamous cell carcinoma

Oral squamous cell carcinoma (OSCC) is extensively recognized as the most common type of head-and-neck cancer, with a ~50% survival rate over 5 years despite various treatments and therapies available for three decades. OSCC is mainly attributed to the use of chewing betel quid with tobacco and could be preceded by clinically evident oral potentially malignant disorders (OPMDs). The OPMDs include a variety of lesions and conditions characterized by an increased risk for malignant transformation (MT) to OSCC. Leukoplakia (LPK), erythroplakia and oral submucous fibrosis (OSF) are the most common oral mucosal disorders in the regions where areca quid chewing is prevalent, such as India, Taiwan and other Southeast Asian countries.[1] The OPMDs possess many of the alterations found in cancer before the development of a malignant phenotype and those most genetic alterations occur before the phenotypic expression of malignancy. A survey showed that about 80% of oral cancers were preceded by oral precancerous lesions or conditions and between 1% and 18% of these lesions will develop into oral cancer.[2]

The histopathological features of a given lesion, especially the presence and degree of epithelial dysplasia, are generally accepted and currently the gold standard indicators of MT risk. However, histopathological assessment alone does not provide an accurate assessment of MT risk, and other features, such as clinical and molecular parameters must be taken into account. In this regard, the clinical characteristics of OPMDs can show considerable variation within the same histopathologically defined entity that may be critical to the likelihood of progression toward malignancy, thus facilitating clinical decisions for further intervention and follow-up.[3] Transformation of OPMDs to cancer has been studied in several population groups. It is very important to prevent any malignant change in

people diagnosed with OPMDs; however, the hazard ratios of various OPMDs are still not well known. Habit-related OPMDs and OSCC arise through an accumulation of genetic alterations including chromosomal alterations, DNA changes and/or epigenetic alterations due to the toxins present in betel quid and tobacco. Early detection, histopathological investigation, genetic tests and treating tobacco-related oral cancer patients, especially in their premalignant state, are the only hope in precluding the MT of this disease.[4] Different genetic pathways of progression have been reported in OSCCs, leading to the cellular and molecular subtypes with distinct clinical outcomes. Thus, emphasizes the requirement to identify the genetic alterations and the interactions between OSCC that forms multiple progression pathways. This approach may aid in a better understanding of the biology of OSCC.[5] An enhanced perceptive of the molecular biology of the OPMDs and OSCC development might lead to improved methods related to detection, assessing prognosis and novel treatments of this malignancy.

Formerly, examination of genetic events has been experimented at the single-gene level; however, "omic technologies" have made it possible for thousands of genes to be monitored simultaneously, thus guiding for a better understanding of the events characterizing the different stages of cancer development. These high-throughput technologies enable genomic analysis of changes in gene expression or chromosomal deletions/amplifications in the pathological samples to be studied.[6] Microarray, a type of novel omic technology is aimed primarily for universal detection of genes, mRNA, proteins and metabolites in a biological sample placed on a tiny chip. The crucial physicochemical process involved in microarrays is DNA hybridization.[7,8] The use of microarray technique in gene profiling for predicting MT of oral premalignant lesions

is intriguing and rapidly evolving. This technology was mainly applicable to compare the differences between normal and cancer tissues, their subtypes, prognosis, etc.[9] Microarray gene expression profiling can be used to compare the level of gene transcription in clinical conditions such as (1) identification of diagnostic or prognostic biomarkers; (2) to classify diseases of tumors with different prognosis that are indistinguishable by microscopic examination; (3) monitor the response to treatment; and (4) for understanding the mechanisms involved in the genesis of disease processes.[10]

A series of studies were carried out in the search for possible molecular biomarkers for OSCCs, where cDNA microarrays were applied to examine possible changes in gene expression and DNA copy in OSCC samples from different populations. Difference in the gene expression between tumors and normal controls has been studied to a large extent, and this has shown that many common genes and pathways are found to be associated with OSCC development. Several studies directing on different stages of OSCC progress have provided vital information about tumor classification and of oral premalignant conditions compared to OSCCs or metastasizing compared to nonmetastasizing tumors.[11] The size and complexity of these experiments often result in a wide variety of possible interpretations. The concordance between studies is low because of differences in sample number, clinical diagnosis, histological grading, microarray platforms, experimental design and analysis methods.

While advances in microarray technology have resulted in progress in genomics and transcriptomics, it is important to highlight some confines. Specifically, gene expression microarray omic strategies still provide many challenges during interpretation. The technology and the software are still developing while mapping the human proteome and metabolome is still ongoing. In many cases, analyzing expression profiling results takes far more effort than performing the initial experiments. Carefully designed experiments, accompanied by appropriate analytical techniques and statistical analyses, will assist in tackling many of these challenges, with the potential to generate liable validated data to answer important biological questions rays measure changes in mRNA abundance, not protein, and thus, there is a lack of consensus around the interpretation of microarray data.

The characterization of the timing and nature of the events happening in the early and late stages of OSCC development yields insights into head-and-neck tumorigenesis, identifies novel gene expression and regulatory pathway alterations and characterizes global transcriptional progression patterns for premalignant and malignant phenotypes. The cellular and molecular heterogeneity of oral SCC and the large number of genes potentially involved in oral carcinogenesis, and progression emphasizes the importance of studying multiple gene alterations on a global scale. A better understanding of the molecular biology of OSCC development might lead to improved methods dramatically related to detection, assessing prognosis and novel treatments of this malignancy. However, the future growth of the technologies will render the biological markers as valuable diagnostic tools in which gene expression profile will outperform all currently used clinical parameters for predicting disease outcome. Gene expression profiling of OSCC can also be valuable if it adds to the existing head-and-neck cancer staging system of OSCC to predict clinical outcomes more accurately; however, no studies to date have still not addressed this question.[12] This can also be used to provide further insight into OSCC tumorigenesis and a plethora of targets for diagnosis and therapy. In particular, these observations may be applied to early detection and chemopreventive strategies.

Conflicts of interest
There are no conflicts of interest.

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