Evolving ‘omics’ technologies for diagnostics of head and neck cancer

Nagathihalli S. Nagaraj

Abstract
Squamous cell carcinoma of head and neck (SCCHN) is the sixth most common malignancy and is a major cause of cancer morbidity and mortality worldwide. As with most solid cancers, the cure rate for SCCHN is excellent if tumors are diagnosed early in the course of the disease. Early diagnosis of cancer remains difficult because of the lack of specific symptoms in early disease as well as the limited understanding of etiology and oncogenesis. Advances in proteomics and genomics contribute to the understanding of the pathophysiology of neoplasia, cancer diagnosis and anticancer drug discovery. The powerful ‘omics’ technologies have opened new avenues towards biomarker discovery, identification of signaling molecules associated with cell growth, cell death, cellular metabolism and early detection of cancer. Analysis of tumor-specific omics profiles provided a unique opportunity to diagnose, classify, and detect malignant disease; to better understand and define the behavior of specific tumors; and to provide direct and targeted therapy. These technologies however still require integration and standardization of techniques and validation against accepted clinical and pathologic parameters. This article provides a summary of technologies, potential clinical applications, and challenges of omics in head and neck cancer.

Keywords: genomics; head and neck cancer; metastasis; omics; proteomics

INTRODUCTION
Squamous cell carcinoma of the head and neck (SCCHN) will affect nearly 55,000 new patients in the United States in 2008 and result in nearly 13,000 deaths. In head and neck cancer, tumors can be located in the oral cavity, oropharynx, nasopharynx, hypopharynx and larynx. For patients with early-stage disease (stages I and II), surgery and/or radiation therapy are pursued with curative intent. However, two-thirds of the patients are diagnosed with locally advanced or metastatic disease (stages III and IV), and in these instances multimodality therapy in combination with chemotherapy and radiotherapy has been used. Understanding the molecular basis of the biochemical pathways involved in carcinogenesis can facilitate the integration of diagnosis, anticancer drug discovery, and therapy for head and neck cancer. A realistic model of cellular regulation based on current knowledge indicates that many interacting networks operate at the epigenetic, transcriptional, translational and post-translational levels with feedback between various levels. Protein–protein and protein–DNA interactions help in defining which genes may be activated in a particular cell and whether external cues cause activation or repression. Analysis of these pathways offers new insights that promise to revolutionize clinical practice.

Efforts are focused on omics profiling, prediction of metastasis and signaling pathways and validation for head and neck cancer through the application of various omics technologies—genomics, transcriptomics, proteomics, metabolomics, peptidomics, glycomics, lipidomics—on tissue samples, cell lines and body fluids. Because of the multifactorial nature of cancer, it is very likely that a combination of several markers will be necessary to effectively detect and diagnose cancer. With the advent of new omics tools, comprehensive, systematic, and unbiased molecular analysis represent an
unprecedented approach to capture the complex cascade of events that sustain the clinical behaviour of tumors. To look for such fingerprints of cancer, it will require not only high-throughput omics profiling, but also sophisticated bioinformatics tools for complex data analysis and pattern recognition. This review focuses on the optimal use of ‘omics’ technologies as part of the new concept in head and neck cancer diagnosis and presents how such an approach can truly overcome the major bottlenecks during head and neck cancer therapy.

‘OMICS’ TECHNOLOGIES IN CANCER
Cancer genomics include examining all the genes as an entire system, in order to see how they interact and influence biological pathways and networks in organisms or cell systems. Gene-expression profiling with DNA microarrays often generates large gene-expression signatures characteristic of a particular type of tissue or cell line (Figure 1). Chung et al. [1] has explained in detail about the DNA microarray technology in head and neck cancer. Recently, we screened genes responsible for tobacco-related oral carcinogenesis using DNA microarray technology. These genes prevent the repair of carcinogen-induced DNA damage [2]. This technology is based on the selective mRNA or cDNA hybridization to the DNA probes present on an array surface. The chromatin immunoprecipitation (ChIP)–chip technique [3] offers great possibilities for broadening studies of DNA and mRNA into protein–DNA interactions. This technique represents the union of ChIP and the whole-genome DNA microarrays (ChIP–chip) allowing generation of the high-resolution genome-wide maps of the in vivo interactions between DNA-associated proteins and DNA [3]. The development of high-resolution microarray-based comparative genomic hybridization (aCGH), using cDNA, bacterial artificial chromosome (BAC) and oligonucleotide probes, is providing tremendous opportunities for translational research by facilitating detailed analysis of entire cancer genomes in a single experiment. Single-nucleotide polymorphism arrays (SNP chips) represent a type of high-density oligonucleotide–based microarrays that have been adapted for DNA copy number analyses [4] and perform comparably with traditional two-channel arrays [5]. Mapping of specific DNA copy number alterations to multiple pathways is effective in delineating markers associated with the responsiveness to targeted therapy [6]. The reproducibility and comparability within and between microarray platforms are understood better today than at the beginning of the decade as demonstrated by the emerging clinical applications.

Ultimately, proteomics aims to identify and quantify the cellular levels of each protein encoded by the genome. Fourier transform cyclotron resonance–mass spectrometry (FTICR–MS) is the highest-performing mass analyzer in terms of sensitivity, resolving power and mass accuracy available today [7]. The surface–enhanced laser desorption ionization–time-of-flight–MS (SELDI–TOF–MS) enables discovery, purification, identification and assay in the same machine. SELDI–TOF–MS is a profiling method that has been extensively used in cancer biomarker studies [8]. MS-based proteomics technology has been considered as a promising approach for the early diagnosis of cancers. Up to now, this technology has been applied to many types of cancers for biomarker discovery and diagnosis [9–11]. Recently, many new strategies have been

Figure 1: DNA microarray used for the integration of cancer signatures. By collecting, standardizing and analyzing several independent cancer signatures simultaneously, meta profiling approaches can validate and define robust cancer signatures and can also define cancer signatures representing shared biology across multiple cancer types.
developed for cancer biomarker discovery. For example, the combination of multi-dimensional liquid chromatography and 2D-gels has been applied to plasma proteomics of lung cancer [12]; 2D-gel coupled with matrix-assisted laser desorption ionization time-of-flight/time-of-flight (MALDI–TOF–TOF) can be used to screen biomarker candidates in serum samples of head and neck cancer coupling two-dimensional liquid chromatography (2DLC)/MS/MS with automated genome-assisted spectra interpretation enables the direct, high-throughput and high-sensitivity identification of biomarkers from complex biological samples [13]. To understand complex biological processes, such as cancer initiation and progression, it is important to consider differential gene and protein expression in the context of complex molecular networks. The study of such networks requires detailed study of other omics for their usefulness to shorten the time needed for biomarker discovery.

Although current work in cancer genomics and proteomics might well yield valuable information in terms of identifying novel diagnostic markers, protein- and gene-expression profiles themselves may not provide an alternative method of diagnosis. By including other omics technologies like metabolomics, peptidomics, glycomics and lipidomics, one can predict better molecular targets (Figure 2). For example, metabolomics represents the output that results from the cellular integration of the transcriptome, proteome and interactome [14] and therefore provides not only a list of metabolite components but also a functional readout of the cellular state. No matter which omics technology is used in cancer therapeutics and drug development, bioinformatics tools are required to extract the diagnostic or prognostic information from the complex data and also to identify players in cancer pathways.

To obtain reliable prognostic markers, different omics technologies may actually need to be combined (Figure 2). To fulfill the dream of individualized cancer care and treatment, we must move from the use of single omic platform to the integrated use of multiple omic platforms and to systems biology followed by the development of bioinformatics tools for integrating and mining the data from basic and clinical research [15]. In cancer research, many studies are adopting omics data-integration strategies to identify biomarkers that are associated with cancer stage, to elucidate-pathway components more fully, to conduct detailed studies of important transcription-factor mechanisms of action and activities [16, 17]. Once omics signatures are successfully validated, long-term clinical studies are also required to determine the validity of using these signatures for the prediction of patient response to chemotherapy. By using this holistic approach we can simultaneously reproduce many findings of other researchers.

**Figure 2:** ‘Omic’ data are providing comprehensive descriptions and interactions within the cancer cell. The central pathway traces the biological information flow from the cancer genome to the cellular phenotype, and the available omics data types that are used to describe these processes are indicated. DNA (genomics) is first transcribed to mRNA (transcriptomics) and translated into protein (proteomics) which can catalyze reactions that act on and give rise to metabolites (metabolomics), glycoproteins and oligosaccharides (glycomics) and various lipids (lipidomics). The molecular interactions are protein–DNA interactions in the case of transcription and protein–protein interactions in translational processes.
and thereby link changes in the transcriptome and the proteome to changes in the metabonome. By using this combined analysis, it is possible to better evaluate the importance of some changes in cancer progression.

‘OMICs’ PROFILING OF SQUAMOUS CELL CARCINOMA OF HEAD AND NECK

Despite the relative novelty of omics technology, the ability to examine tumors using DNA microarray and quantitative RT–PCR for generation of clinically relevant molecular signatures is becoming more widely accepted in cancer research. Many groups have described the heterogeneous nature and characteristics of SCCHN tumors at the molecular level using DNA microarray [18–21]. These molecular characteristics have been shown to be associated with prognosis, risk of developing metastasis and predicting outcomes in patients with SCCHN. To investigate gene-expression profiles of different stages of tumor progression, Mendez et al. [22] examined the gene-expression profiles of 26 invasive oral SCCHN, two pre-malignant lesions and 18 normal tissue samples using oligonucleotide arrays. The study provided the molecular portrait of oral SCCHN as well as statistically significant changes in gene expression between normal and invasive oral tumors. Using comparative genomic hybridization, Ashman et al. [23] identified genetic aberrations in SCCHN associated with survival and applied these genomic molecular signatures as a prognostic biomarker gene set that could potentially be used to help guide clinical trials.

Recently, Belbin et al. [24] studied molecular profiling of tumor progression in head and neck by using microarray containing 17 840 complementary DNA clones to measure gene-expression changes associated with tumor progression in nine patients with squamous cell carcinoma of the oral cavity. A distinct pattern of gene expression, with progressive up- or down-regulation of expression, is found during the progression from histologically normal tissue to primary carcinoma and to nodal metastasis. Gottschlich et al. [25] studied the molecular mechanisms causing the development of squamous cell carcinomas in the head and neck region by using microarray. The purpose of the study was to identify transcriptional alterations of apoptosis associated genes between normal mucosa and tumor tissue.

The results showed first time for the diagnostic use of microarrays in SCCHN region. Pramana et al. [26] studied the prediction of outcome after chemoradiation in advanced head and neck cancer using gene-expression analysis by using 92 biopsies from untreated head and neck cancer patients subsequently given cisplatin-based chemoradiation for advanced SCCHN.

To date, more than 20 studies incorporating microarray analysis have reported on the genetic changes associated with oral squamous cell carcinoma (OSCC). Unfortunately, many of these studies have used a variety of gene-expression arrays and platforms, and thus, it is difficult to make a direct comparison [24, 27]. In addition, none of these studies have tested their OSCC gene signature for its ability to predict OSCC using an independent validation data set. Recently, Ziober et al. [28] identified a gene-expression signature for OSCC. By analyzing microarray data from patient-matched normal and OSCC tissue and by validation at the RNA and protein level, and using several independent validation gene data sets, identified a tissue specific gene-expression signature that can predict OSCC. For example MMP-1, MMP3, MMP-11, MMP-13, STAT-1 and laminin-5 were up-regulated and they play a significant role in OSCC tumor development and progression. Among the biological pathways they identified to be prominently involved in OSCC were the JAK/STAT and IFN-γ signaling pathways. Studies have also reported Lysyl oxidase–like 2 (LOXL2) up-regulation in SCCHN and OSCC and it can be used as a new poor prognosis indicator in human squamous cell carcinomas promoting malignant transformation [28, 29]. Gene-expression studies by Kondoh et al. [30] and Chen et al. [31] confirmed that LAMC2, IFIT3, and USP18 are worthy of further investigation as predictors of the development of OSCC among patients with oral dysplasia. Kondoh et al. compared OSCC with leukoplakias, whereas Chen et al. compared OSCC with dysplastic lesions.

Epigenetics is heritable changes in gene expression that are not coded in the DNA sequence [32] and the changes have been associated with cancer-specific expression differences in human malignancies, including SCCHN. Promoter hypermethylation of p16 is a frequent event in SCCHN and this mechanism of gene silencing accounts for the low levels of expression [33]. p53 mutations, microsatellite alterations, increased mitochondrial
DNA content and TSG promoter hypermethylation variation have been demonstrated in SCCHN [34–37]. Recent study showed a significant decrease in mitochondrial DNA content in post-operative salivary rinses from patients with SCCHN [38]. The sources of free DNA have been shown to be serum (p16, MCiMT, DAP-kinase), saliva/oral rinse (p16, p14, MGMT) and urine. Hence recognition of hypermethylation pattern in both the tumor tissue and circulating free DNA has a potential clinical application in early less invasive diagnosis and tumor surveillance.

In addition to well-established gene-expression microarrays, the technology can be applied to measure other biological variables, such as copy number and SNPs [39, 40]. Genes targeted by genomic alterations in SCCHN by integrating copy number and gene-expression microarray data were investigated and further analyzed for a few selected genes by quantitative PCR or RT-PCR [18, 41, 42]. None of the studies have integrated genome-wide data in a systematic manner to achieve more accurate information about genes that are activated or inactivated by copy number alteration with focus on specific SCCHN site. Recently, Jarvinen et al. [43, 44] studied an integrated copy number and gene-expression analysis for laryngeal SCC (LSCC) and oral tongue (OTSCC) to determine genes that are regulated in association with altered copy number. They compared genetic changes between OTSCC and LSCC to evaluate similarities of these two head and neck locations with distinct patterns of tumor behavior by integrating microarray based genomic and transcriptomic data and highlighted potential genes with importance in SCCHN tumorigenesis and progression. In addition to deletions of the known tumor suppressor genes, such as FHIT, CSMD1, and CDKN2A, they identified genes with no previously reported deletion in SCCHN. These included ITGAV at 2q31–q32, PDE4D at 5q12, and IL1RAPL2 at Xq22.2–q22.3. ITGAV, which was down-regulated in association with deletion, partners with other integrin subunits to form different types of heterodimers. It recognizes components in the extracellular matrix and can promote cell proliferation and migration in SCCHN [45]. A number of homozygously deleted genes were located close or within common fragile sites such as LRP1B/FRA2F, FHIT/FRA3B and CSMD1/FRA8B [46]. Chromosomal aberrations include segments of allelic identifiable by loss of heterozygosity (LOH) at polymorphic loci, which may be used to implicate regions harboring tumor suppressor genes. By using SNP array based LOH profiling on a large panel of 40 human SCCHN cell lines, Ye et al. [47] observed that a recently identified candidate tumor suppressor gene MTUS1 may be a tumor suppressor for SCCHN. Ongoing research of the structural variations of the human genome will provide more information about variants with causative or predisposing role in disease which is also suggested by Jarvinen et al. [44]. Further investigation regarding the pathogenetic relevance of the genes located in deleted regions, studies on epigenetic modification or mutation in one allele and a deletion in another allele are required.

Proteomic technologies have been utilized to detect biologically significant differences in protein expression of SCCHN obtained from the same samples utilized in gene-expression analysis. MALDI–TOF mass spectrometry coupled with bead fractionation allows for automated protein profiling to identify peptides that distinguish biological variability [48]. MALDI–TOF technology as a discovery platform has also been used to generate biomarker panels for use in more accurate prediction of prognosis and therapeutic response [49]. Recently, Ralhan et al. [50] identified 811 non-redundant proteins in SCCHNs, including structural proteins, signaling components, enzymes, receptors, transcription factors and chaperones by using multidimensional LC–MS/MS to identify proteins that are differentially expressed in human SCCHN compared to non-cancerous head-and-neck tissues (controls) for cancer biomarker discovery. Validation of the proteins YWHAZ, stratifin, and S100-A7 confirmed their overexpression and utility as potential credible cancer biomarkers. Various SCCHN biomarker candidates have been proposed based on proteomic analysis of cancer and control surgical specimens. C-reactive protein, creatine kinase, galectin-7, heat shock proteins 27 and 60, glutathione S-transferase, cytotkeratin 6B, and others have been found to be up-regulated in oral carcinoma, while annexin 1, heat shock protein 20, and myosin show decreased expression in oral carcinoma [51–53]. The current success in identifying a number of tumor-associated proteins proved that proteomic analysis can provide rich information to help understand the pathology of a disease in an integrated way.

A molecular signature that can predict metastatic disease versus local recurrent disease would be of
As the amount and variety of the data continues to increase, bioinformatics methods can continue to be developed, refined and applied to exploit the larger datasets. The application of bioinformatics methods in cancer target discovery is starting to generate many exciting target leads for further experimental validation.

**PREDICTION OF METASTASIS AND SIGNALING PATHWAYS**

Metastasis is the principal cause of death in individuals suffering from cancer; the events leading to it are poorly understood. The presence or absence of metastases mainly determines survival from SCCHN. Identification of metastatic disease therefore has major impact in selecting the appropriate treatment plan. Distant metastases will eventually develop in a third of all patients with head and neck malignancy, with most occurring in patients who initially present with advanced disease [59]. Accumulation of genetic damage that leads to expression of a malignant phenotype is a prerequisite for metastasis formation [60]. As metastasis involves multiple steps, each of which is under the influence of regulatory mechanisms, not one single factor is probable to play the decisive role.

The data presented by Ramaswamy et al. [61] support a model in which the metastasis arise from rare cells within a primary tumor that have gained metastatic potential and the gene-expression profiling of 64 primary tumors and 12 metastatic adenocarcinomas by the same group suggests that genetic programming of metastasis exists within most, if not all, of the primary tumor at the time of diagnosis. From these primary tumors, a metastasis signature defined 17 unique genes were identified and the metastatic prediction accuracy was 83%. To determine whether metastases could be predicted from gene expression within primary SCCHN, Chung et al. [29] determined gene expression within 60 primary SCCHNs. When they used pathologic staging of nodal metastases as the supervising parameter, prediction accuracy of gene expression from the primary tumor improved significantly and further improved when the tumors were analyzed on the basis of their anatomic subsites. The study by using the first large-scale gene-expression analysis of the hypopharynx, a localization associated with particularly aggressive behavior identified genes involved in tumorigenesis, as well as gene-expression...
patterns that will distinguish tumors that will metastasize from those that will not. By use of 168 gene targets, metastatic prediction accuracy was 92% [18]. Many of these sequences could contribute to the prediction of whether a patient with hypopharyngeal cancer will develop metastases.

In addition to providing a basis for improved diagnosis and treatment, a recent study by Roepman et al. [62] is also screened for metastasis-associated genes from 82 primary SCCs of the oral cavity and oropharynx. Many of the 102 predictor genes have previously been implicated in metastasis and the overall predictive accuracy was 86%. The SCCHN predictive profile was independently validated primary tumor expression signature that can reliably detect the presence of metastases in local lymph nodes. The profile is capable of distinguishing metastasizing from non-metastasizing tumors and pivotal for treatment planning. The mir-205 a microRNA has been reported in previous studies to have variable expression across many human tissues and compared its relative expression in normal and cancerous mucosal tissues of SCCHN. The use of miRNA as biomarkers for the diagnosis of SCCHN is showing early promise. The study gave credence to the use of mir-205 as a squamous epithelial-specific marker capable of detecting occult metastatic tumor deposits. Further comparison study is needed to determine the efficacy of mir-205 relative to existing mRNA markers for the detection of SCCHN metastases. These results suggest that the metastatic prediction accuracy of gene-expression analyses for SCCHN may be improved through analyses subsites separately. Further validation of gene sets by using other ‘omics technologies is needed for reliability and this could improve current diagnosis and treatment.

It is now known that the potential of a tumor cell to metastasize, the primary tumor cell must complete a series of sequential steps, including promoting tumor-cell growth, survival, angiogenesis, invasion, detachment from other tumor cells, and proliferation at the metastatic site [67]. Each of these steps is regulated by transient or permanent changes in DNA, RNA or proteins. Recently, Hensen et al. [21] defined pathways and gene sets involved in each of these steps using the publicly available pathway databases KEGG and Biocarta, and also by researching literature on metastasis in SCCHN. They categorized these pathways in the following subgroups: survival, proliferation, differentiation, apoptosis, cell adhesion, extra cellular matrix signaling and remodeling, hypoxia and angiogenesis. The multiple microarray analyses performed by Manoli et al. [68] resulted in discriminative pathway regulation signatures that are found and validated by different laboratories and microarray analysis methods. Pathways obtained by these analyses are likely to be more robust than those generated by a single analysis on a single dataset. Hensen et al. [21] were able to identify and validate several pathways which are involved in the process of extracellular matrix remodeling (MMPs, MMP regulating pathways and the uPA system), hypoxia and angiogenesis (HIF1α regulated angiogenic factors and HIF1α regulated invasion) in SCCHN. Circulating genetic alterations specific to SCCHN has been detected in serum by identifying common mutations, promoter hypermethylation, LOH, and predicting the likelihood of developing metastatic disease [69–73]. This revealed biologically relevant similarity between results of different gene-expression studies, even if studies have used different microarray platforms with different probes.

VALIDATION AND FUTURE PROSPECTS FOR HEAD AND NECK CANCER DIAGNOSTICS

In cancer diagnostics, one major challenge for biomarker validation is the considerable molecular heterogeneity of individual cancers, even from a single tissue. Another major challenge is the low incidence of many cancers in the general population limiting the validation of the true potential of a biomarker or a panel of biomarkers. PCR, RT–PCR and protein microarray (high-throughput ELISA) technology holds promise for cancer biomarker validation. Tissue microarray (TMA) technology is emerging as a powerful tool to validate potential biomarkers. TMAs are arrays of core biopsies obtained from paraffin-embedded tissues, which can provide a method for high-throughput gene or protein-expression analysis of large cohorts of cancer patients on a single slide. After biomarkers are validated, there is much to be done before they can be used in clinical laboratories for cancer diagnostics.

Candidate biomarkers discovered by various ‘omics’ technologies must clear a number of practical
hurdles before they can be developed into a clinical diagnostic test. After biomarkers are validated, the remaining major task is how to implement these diagnostics in clinical practice. Many exciting methods are under development, for example, using electrochemical immunosensors, some tumor biomarkers (e.g. CEA, AFP, α-1-fetoprotein, and b2-microglobulin) could be detected, even with a detection limit down to 1 ng/ml [74, 75]. A very promising technology is microfluidics-based diagnostic tool. The unique capabilities of microfluidic devices in sample handling, reagent mixing, separation and detection makes it possible to create portable point-of-care (POC) medical diagnostic systems [76]. A microfluidics-based salivary diagnostic system is being developed at the University of Washington [77]. Such a system allows measurement of binding rates of analytes to surfaces in saliva in just a few minutes. In a word, these technologies have enormous potential to push ‘omics’-based cancer diagnostics into clinical implementation.

The prognosis of head and neck cancer has not changed in the past two decades. The challenge has been to reproduce prognostic gene signatures and to generate candidate markers that can be easily applied to aid the diagnosis and prognosis of SCCHN. It is surprising that only a few studies that have shown an impact on prognosis. For example, in some studies laminin was associated with tumor aggressiveness, metastasis, and poor prognosis [78, 79] and it was predicted as a prognostic factor in OSCC etiology and progression [28]. Argyrophilic nucleolar organizer region associated proteins (AgNOR) had been confirmed as relevant for prognosis in more reports than proliferation cell nuclear antigen (PCNA) or MIB1 [80]. It is also important to evaluate the combined significance of several markers and/or clinical and histological variables for their prognostic value. For example, combinations of several molecular/genetic markers [81], and molecular/genetic markers and histopathology [82, 83] have been proposed. The use of omics markers for predicting malignant transformation of oral pre-malignant lesions is intriguing and rapidly evolving. So far, these studies have not demonstrated methods that are readily applicable for routine diagnostic work. MicroRNA (miR) arrays are now being performed on SCCHN, but the interpretation of the results is still at its early phase [63]. Recently, mir-98 has been shown to be up-regulated in selected head and neck cancer lines grown under hypoxic conditions [84]. The exact function of these mir genes remains to be determined in SCCHN.

Overall, studies using DNA-based assessment have been more reproducible than those that profile using mRNA-based gene arrays. Today, there are many recommendations on standardization procedures dealing with acquisition, management and use of data on a large scale, such as the minimum information about a microarray experiment (MIAME), minimum information about a proteomics experiment (MIAPE) and systems biology markup language (SBML) [85]. The genetic analysis of cancers reached a crescendo with the completion of the Human Genome Project along with the development of high throughput genome-wide analytic techniques. These analyses have helped shape our understanding of human malignancies in general, and head and neck cancers in particular. Global genomic analyses have identified molecular subsets of SCCHN, which may have prognostic implications [86–88]. Moreover, even though they are provocative, these studies now need to be validated sufficiently to allow use in routine clinical practice.

CONCLUSIONS

The omics technologies are among the most powerful hypothesis-generating tools available today and have provided valuable new information in both basic and clinical research. Numerous biomarker studies generated from the comprehensive analyses of genetic information and their expression as DNA, RNA, proteins and metabolites can distinguish clinically relevant differences within histologically identical tumors. Metabolic and proteomic fingerprints as well as the bioinformatic analysis and modeling of all the omics data are needed to complete a comprehensive understanding of the molecular deregulation of the head and neck cancer cells in vitro and in vivo. These technologies performed on various biological samples have offered exciting opportunities in biomarker discovery and cancer diagnostics. However, important questions remain to be answered by the integration of biochemical, genetic, clinical and various omics data for obtaining the holistic molecular view of pathogenetic processes, tailoring patient therapies and developing sophisticated technologies for translating omics based diagnostics into clinical reality.
Integration of omics data have revealed a more comprehensive molecular profile of SCCHN and have opened a new era of research with substantial promises in the field of prognosis and prediction of therapeutic response. The use of omics technologies in clinics for treating head and neck cancer will depend on the appropriate design and the execution of sufficiently large validation studies to ensure that these signatures are truly worthy of clinical implementation.

Key Points
- Omics technologies can simultaneously measure the expression of genes, proteins and metabolites and have opened a new era of research with substantial promises in the field of prognosis and prediction of therapeutic response of SCCHN.
- Omics technologies have enabled us to better understand the events characterizing the different stages of SCCHN development, provided important clues to the understanding of the various gene networks implicated in head and neck carcinogenesis and may contribute to selecting molecular targets for possible diagnosis and therapy in the future.
- Predictive markers of sensitivity or resistance to treatment and use of innovative trial designs are imperative to efficiently bring promising agents to treat SCCHN and tailor patient therapy.

References


