

COMPARISON OF GLOBAL GENETIC ALTERATIONS IN ORAL SQUAMOUS CELL CARINOMA FROM DIFFERENT SITES OF THE ORAL CAVITY-A BASIS FOR FUTURE MOLECULAR TARGETED THERAPY

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INTRODUCTION

Oral squamous cell cancer (OSCC) is a common disease in Asia. Interestingly, apart from other clinical and pathological parameters, the prognosis and clinical behavior of OSCC is influenced by the site of the cancer. Previous studies demonstrated that cancers can be sub-classified based on their molecular profiles and this has significant impact on the clinical management of patients.

OBJECTIVE

We studied the gene expression of OSCC from different sites of the oral cavity to determine if there were significant differences in the pattern of gene expression which were consistent with clinical observations.

METHODOLOGY

Using 63 OSCC and 33 normal formalin-fixed paraffin-embedded tissues from matching sites (cheek, gum and tongue), we conducted microarray experiments on the DASL (Illumina) platform to compare the gene expression of OSCC from the cheek, gum and tongue. The analysis of gene expression to identify differentially expressed genes were conducted using Gene Spring and the validation of gene expression changes were performed using quantitative polymerase chain reaction (qPCR).

RESULTS

Using Principal Component Analysis (PCA), we demonstrated that OSCC from the cheek and gum can be distinctly separated based on their gene expression profiles. However, the gene expression from specimens of the tongue appears to be a lot more heterogeneous. We identified differentially expressed genes and used Hierarchical Clustering analysis and Pathway

Enrichment (DAVID) to decipher the significant pathways implicated in OSCC. Using ANOVA and the Venn Diagram we identified genes that were commonly altered in all sites and those that were exclusive to a particular site. These findings, and the role of genes

expressed at specific sites have to be validated in independent specimens and in vitro models. At present we are studying the role of a gene which is found to be up-regulated in tongue cancer in oral cancer cell lines that we established previously.