Molecular Markers of Hypoxia (CA9) and HPV (p16) in Oral Cavity Squamous Cell Carcinoma

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INTRODUCTION

The multiplicity of Oral Cavity Squamous Cell Carcinoma (OCSCC) subtypes, diversity of stages, variation in patient co-morbidity, and heterogeneity of tumour biology behavior make accurate estimation of prognostic difficult for individual patients. Furthermore these diverse factors make treatment selection challenging.

By gaining insight into the molecular characteristics of a tumour, clinicians may understand the biologic behavior and thereby tailor treatment and prognostics more accurately. It has therefore been hypothesized that molecular markers could be a useful aid in current staging systems leading to better treatment selection and more appropriate survival predictions.

Predictive biomarkers may:
1) Identify high risk tumors
2) Define tumor response to radiation and /or chemotherapy
3) Assist with selection of patients best treated surgically
4) Predict survival

Hypoxia (low oxygen) is the result of an imbalance between the supply and consumption of oxygen. Tumors are susceptible to hypoxia through a number of mechanisms including abnormally vascular architecture, limited tissue perfusion, or therapy-associated anemia. Carbonic Anhydrase 9 (CA9) warrant particular attention due to their association with HNSCC outcomes.

METHODS AND MATERIALS

This is a retrospective study of 104 patients who underwent surgical resection and neck dissection for OCSCC, treated at the Frothingham Hospital by 2 surgeons from 1995 - 2005.

All patient demographics and clinical outcomes (including disease-free survival and overall survival) if applicable, dates of death were collected by a combination of a comprehensive chart review and the Alberta Cancer Registry Information.

Tissue Microarray’s (TMA) were constructed from primary tumor, metastatic lymph node, and surrounding normal lymph node Specimens. Automated quantitative IHC (AQUA) was performed to measure the expression and distribution of CA9 and p16. This involves coining TMA blocks, staining with antibodies labeled with enzyme or fluorophore scanning using a Histofluor PM-2000 image analysis platform, and analysis of the acquired images with the AQUA analysis software (Histofluor, Inc., New Haven).

Kaplan-Meier survival analysis was used to assess the impact of CA9 and p16 on overall disease specific survival.

REFERENCES

1. Kim et al 3 proposed that tumor hypoxia may inhibit angiogenesis and lead to decreased vascular density, which can result in reduced tumor perfusion and poor clinical outcomes. Although not statistically significant, elevated stromal CA9 was associated with reduced 5-year survival, high expression vs. low expression (p<0.001).

RESULTS

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