**Cancer Research**

**Abstract 1883: Clinical and molecular genetic analysis of squamous cell carcinoma of the oral tongue**

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**Abstract**

Squamous cell carcinoma of tongue (SCCT) is a common form of head and neck squamous cell carcinoma (HNSCC) in developing countries, mainly in India. In the last few decades, a steady increase in incidence rate of SCCT has been reported across the world. More importantly, though SCCT is considered to be a tobacco-related late-onset cancer, recent reports indicate an increase in incidence of SCCT in the young and in non-smokers. We analyzed the status of known tumorigenic pathways/genes including TP53, epidermal growth factor receptor (EGFR), microsatellite instability (MSI), CDKN2A, FHIT and human papilloma virus (HPV) infection in 120 surgically resected primary oral SCCT (SCCOT) samples and correlated with clinico-pathological variables and disease specific survival. 78 of 121 (65%) samples exhibited p53 nuclear stabilization confirming earlier reports. Interestingly, p53 nuclear stabilization was more common in young (36/46; 78%) than in older (44/75; 56%) patients (p = 0.0184). Further, PCR based mutation screening of exons 5-8 (encoding the DNA binding domain of p53) revealed mutations in ten of nineteen samples (52.6%) that exhibited p53 nuclear stabilization and in three of fifteen tumors (20%) that did not. We identified a novel 33bp deletion, c.616-648del33, located in exon 5 in a p53 positive tumor from a chronic tobacco chewer. Case control analysis revealed that Proline at TP53 codon 72 increased the risk of SCCOT. Majority of samples (97/121; 80%) exhibited significant EGFR expression though HPV infection was rare (14/106; 13%). MSI was observed in 14/106 (13%) samples, a frequency higher than reported for other populations. Loss of Heterozygosity (LOH) was more frequently observed in CDKN2A (28%) and FHIT (26%). In addition, LOH at FHIT locus was significantly associated with p53 nuclear stabilization (p = 0.0508), especially in non-smokers. A significant difference in survival rate between p53 positive and negative group (p = 0.0056) (Hazard ratio 2.5595) was observed. Though associated with p53 stabilization, FHIT loss did not exhibit significant effect on patient survival. Interestingly, patients exhibiting p53 nuclear stabilization as well as FHIT loss exhibited worse survival. We performed genome-wide DNA copy number and transcript profiling in several SCCOT samples. Interestingly, there was no significant difference in extent and profile of chromosomal instability in p53 positive and negative tumors. Amplifications were detected at chromosomal regions 3q26.1 (PIK3CA), 5p, 8q22 (MYC, RUNX1T1), 11q13 (CCND1) and 20q13 (HNFα). Genome-wide transcript profiling identified novel pathways that appear to drive tumorigenesis in tumors not exhibiting p53 inactivation. Our comprehensive analysis has therefore revealed important insights into the molecular basis for SCCOT and identified prognostic indicators in patients not associated with tobacco use.

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