Differential gene expression profile of tongue and buccal cancers produce unique and shared vaccine candidates for cancer immunotherapy

R. Gupta, K. V. Paul, Nitin Mandloi V. Ramprasad, R. Vijayalakshmi,* A. Gupta and Amitabha Chaudhuri
MedGenome Inc. 953 Indiana Street, California 94107
* Department of Preventive Oncology Cancer Institute (WIA), Adayar, Chennai, India

Key findings

- Tongue and buccal cancers share similar mutation and gene expression profiles
- T-cell neo-epitopes are predominantly private in both the cancer types
- Shared neo-epitopes are contributed by differentially expressed genes

Introduction

Head and Neck squamous cell carcinoma (HNSCC) comprises of tumors arising from multiple sites of the upper aerodigestive tract. Cancers of buccal and tongue are highly prevalent worldwide and account for significant morbidity and mortality. Tobacco chewing and the use of alcohol increase the incidence of these cancers significantly. Further, in the absence of any targeted therapies the 5-year survival is <50%. Currently, inhibitors against EGFR and MET pathways are in clinical development to target tumors harboring amplification of EGFR and MET genes. In the last two years, the traditional approach of targeting driver genes in cancer has been complemented by checkpoint control inhibitors that activate host immune response to eliminate cancer cells. Several factors, including T-cell activating somatic mutations, the quality of immune cell infiltrate within the tumor, and the tumor cytokine environment determine response to these inhibitors singly or in combination.

Objectives

1. Discovery of T-cell neo-epitopes in HNSCC that can be used as potential cancer vaccines
2. Identifying shared vaccine candidates from tongue and buccal cancers

Methods

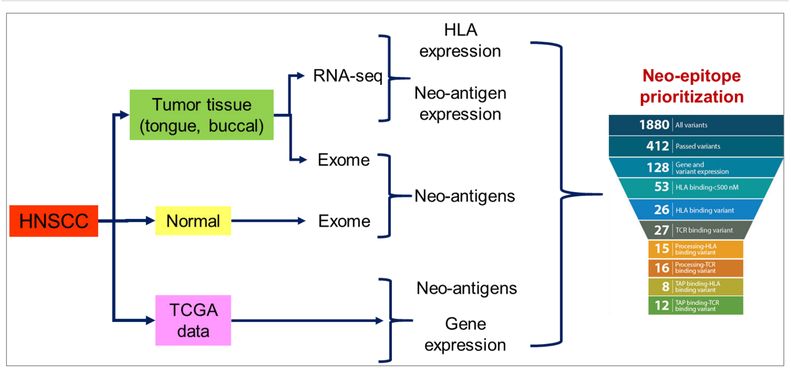
Sequencing and Data analysis

Fourteen buccal and 11 tongue tumor/normal pairs were sequenced on a panel of 344 cancer genes and somatic mutations were identified using MedGenome's proprietary variant calling pipeline VariMAT™. Gene expression analysis was performed on RNA-seq data (80-100 million reads/sample) and expressed as FPKM units. Differential gene expression was analyzed using Cuffdiff, DESeq2 and EdgeR. HLA typing was done from RNA-seq data at a 4-digit resolution using Seq2HLA.

TCGA 3-tier data for 160 tongue and 23 buccal cancers was downloaded and analyzed through our internal pipeline.

T-cell neo-epitope prediction and prioritization was done using OncoPept (Figure 1).

Figure 1. OncoPept Workflow combines exome and RNA-seq data to select T-cell neo-epitopes



Results

Table 1. Samples analyzed in this study

Study	Tissue	Samples	Data type
TCGA data	Tongue	160	Exome/RNA-seq
TCGA data	Buccal	23	Exome/RNA-seq
MG study	Tongue	11	Panel/RNA-seq
MG study	Buccal	14	Panel/RNA-seq

Figure 2. Variant classes detected in tongue and buccal cancer samples

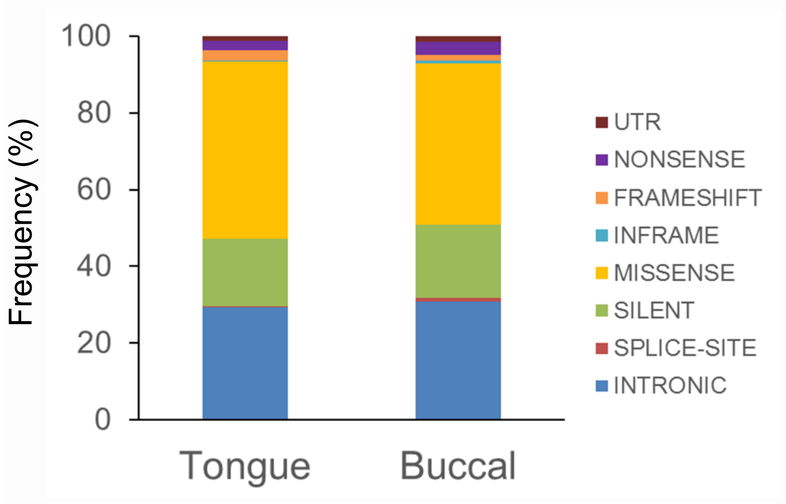


Figure 3. Frequently mutated genes in HNSCC

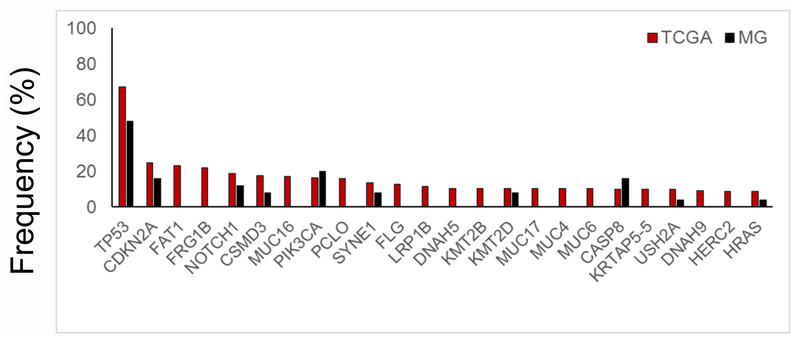


Figure 4. Frequently mutated genes in tongue and buccal cancers (TCGA data)

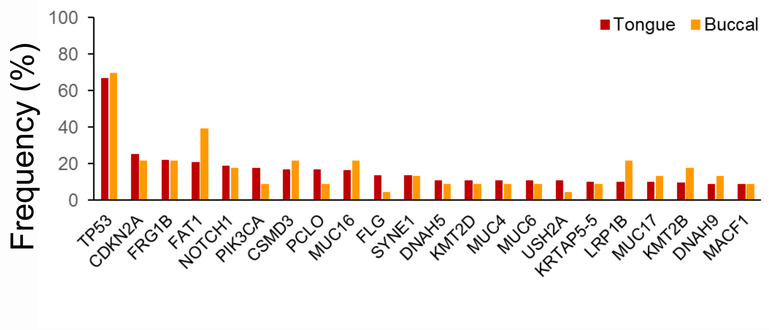


Figure 5. Mutation spectra of TP53 and CDKN2A genes in HNSCC (OncoMD data)

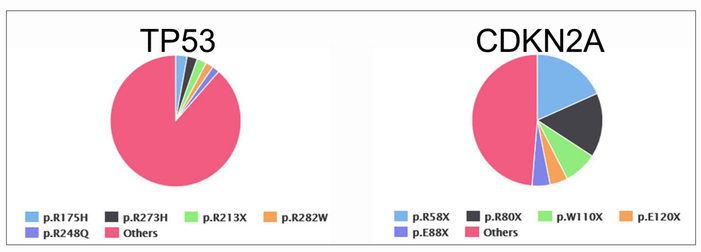


Figure 6. Mutation spectra and gene expression profile of smokers vs non-smokers

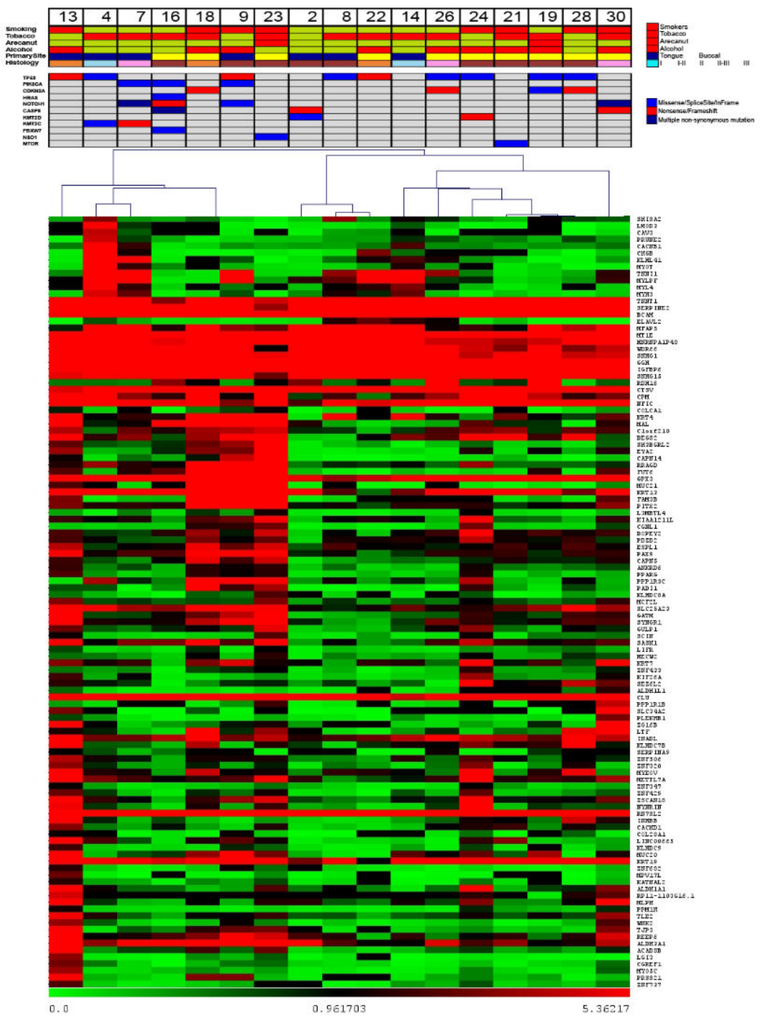


Figure 7. Tongue and buccal cancers share few T-cell neoepitopes from mutated genes

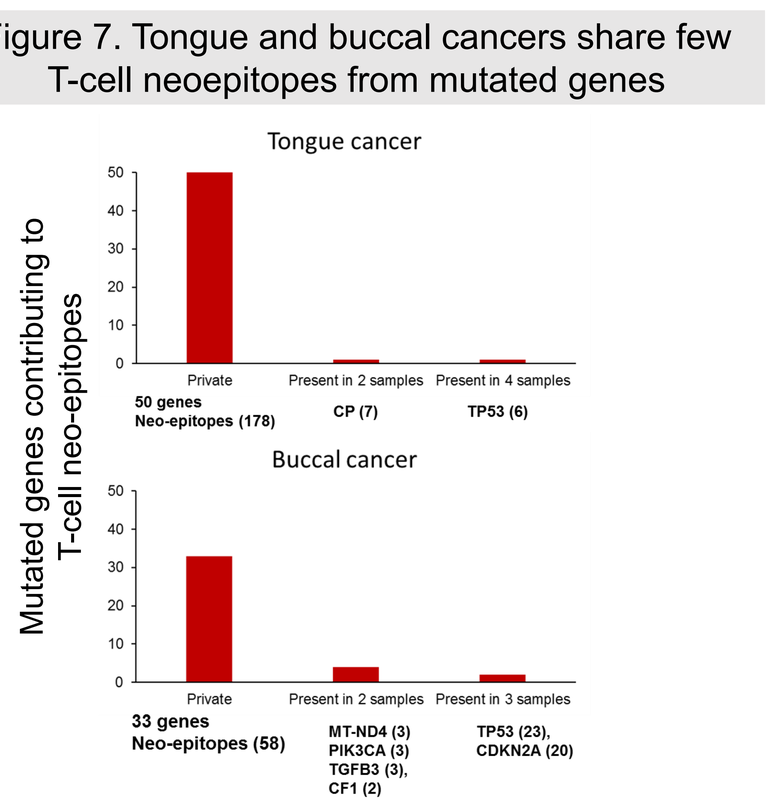


Figure 7. Expression of mutant alleles contributing to T-cell neo-epitopes

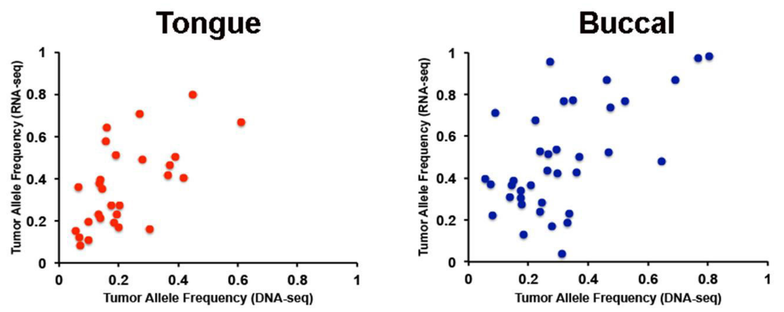


Figure 8. Differentially expressed genes contributing to T-cell neo-epitopes