Tobacco smoke causes most laryngeal squamous cell carcinoma and decreases treatment efficacy.1-3 Genetically, tobacco smoke induces mutations in several important pathways.4,5 This genetic signature can be detected using a publicly-available program through the Wellcome Trust Sanger Institute, deconstructSig.

The Cancer Genome Atlas provides whole-genome sequencing of many cancers, including laryngeal squamous cell carcinoma.

Genomes from TCGA can be analyzed using deconstructSig to determine the relative burden of tobacco-associated mutations.

Here, we compared tobacco-associated mutations with clinical outcomes in 72 laryngeal squamous cell carcinoma patients from TCGA.

### Materials and Methods

- Staging, patient characteristics, and overall survival were collected for 72 laryngeal SCCa from TCGA.
- DeconstructSig was used to characterize genetic mutations for each patient, generating 30 mutational profiles including one tobacco-induced signature.
- Total mutational burden and tobacco-induced mutations, as well as traditional staging, were used to predict overall survival.
- Univariate and multivariate analysis were performed by cox proportional hazard ratio using R statistics package. Number of pack-years was compared to number of tobacco-associated mutations by linear regression. Significance was defined as p<0.05.

### Results

#### Staging Information

| Larynx SCCa (n=72) |
|-------------------|------------------|
| T stage | N stage |
| T1 | 1 | No | 33 |
| T2 | 12 | N1 | 10 |
| T3 | 23 | N2, NO | 5 |
| T4a | 29 | N2a | 3 |
| T4b | 0 | N2b | 6 |
| Unknown | 7 | N2c | 5 |
| | | N3 | 2 |
| | | Unknown | 7 |

Table 1. Staging information for 72 TCGA patients, SCCa: squamous cell carcinoma. NO: not otherwise specified.

#### Increasing pack-years was associated with higher number of tobacco-associated mutations (Figure 1, p=0.0341).

#### Overall survival for all patients is shown in Figure 2.

### Discussion

- Increasing burden of tobacco-induced somatic mutations predicts improved overall survival among laryngeal SCCa patients in TCGA, independent of T stage, N stage, or overall number of mutations.
- Improved survival in this setting may indicate increased immune recognition of neo-epitopes generated from tobacco-induced mutations.6
- This study is limited by its small number of patients and bias toward advanced-stage laryngeal cancer patient available in TCGA.
- Studies comparing tumor immunity to tobacco-induced mutations in laryngeal cancer are warranted, and may provide insight into risk stratification for laryngeal cancer patients.

### References


