A novel biomarker for oral cancer

Tongue squamous cell carcinoma (TSCC) is the most predominant form of oral cancer in developed countries with varying incidence in developing countries wherein diverse etiological factors such as chewing betel-quid comprising betel leaf, areca nut and slaked lime forms distinct underlying genetic alterations that remain uncharacterized to date. Another unique feature of TSCC is that in about 27-40% of patients at an early stage (pT1 or pT2) nodal metastases status plays a decisive role for choice of treatment, with unmet need for prognostic biomarkers to stratify the patients who could be spared unnecessary surgery lessening morbidity and cost of treatment. While several large-scale genome-sequencing efforts of advanced stage primary oral tumors have been described, systematic efforts to catalogue somatic alterations in tobacco/ nut chewing associated early stage (pT1/2) HPV-negative tongue tumors has been lacking.

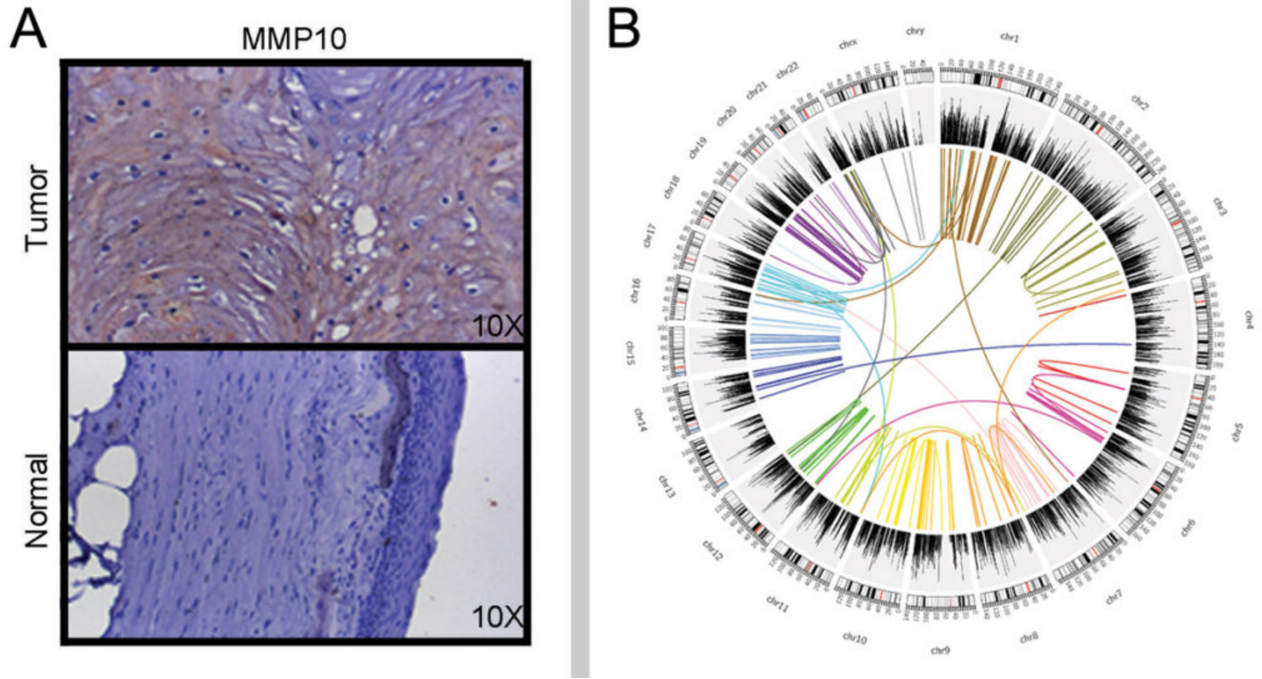

Fig. 1. A. Representative IHC stained photomicrographs from normal and tongue tumor samples stained for MMP10 are shown at 10X magnification. Brown color indicates positive expression. ; corresponding H&E stained slides are shown in the lower panel.
B. Circos plot representation of high-quality candidate fusions transcripts identified in tongue tumors using advanced sequencing technology. From outside to inside: karyotype, Gene expression (TPM) and transcript fusions. Black lines track for gene expression, fusion transcripts arc colored by their chromosome of origin.

Here, we present first and most comprehensive glance to genomic alterations and mutational signature across 57 early stage (pT1 and pT2) derived from HPV-negative early stage tongue cancer patients habitual of chewing betel nuts, areca nuts, lime or tobacco using by whole exome and whole transcriptome sequencing followed by validation using orthologous methods. We present several lines of distinct features underlie this study attributing to unique aetiology, subsite, and specific population, which have been previously described for HNSCC The mutational profile of large fraction of patients display high frequency (53%) of C:G > A:T transversion in exome sequencing data—a hallmark of tobacco usage—reflecting tobacco as the most predominant etiological agent. We present the first report to describe *EGFR* amplification in TSCC mutually exclusive to 11q13.3 (*CCND1, FGF19, ORAOV1, FADD*) amplification among HPV-negative early TSCC tumors. Most significantly, we identify gene-sets involved in EMT processes with significant overexpression of *MMP10* in 48% early stage TSCC tumors (n=50) as a potential candidate prognostic biomarker in early stage tongue cancer patients to predict nodal metastases.

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