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Abstract Title:- Transcriptomic analysis to identify potential biomarkers to demarcate tumor and non-tumor tissue in oral cancer.

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Aims:- Oral squamous cell carcinoma (OSCC) accounts for around 90% of head and neck cancers (HNSC). It is one of the most prevalent cancers in the world, especially in India as it accounts for about 30% of all cancers. Despite advancements in treatment and screening approaches, OSCC incidence has been rising and it has poor prognosis. One of the most common reasons for treatment failure and main concern with OSCC is recurrence as it is known to occur in about 60% of patients with advanced and 30% with early OSCC. To improve patient prognosis, it is important to achieve adequate margins during surgery and so a solution should be sought that can rapidly evaluate the entire resection surface.

Thus, it is important to identify effective biomarkers to demarcate tumor and non-tumor tissue.

Methods:- In this study we did RNA isolation, library preparation, next generation sequencing and finally transcriptomic analysis of 30 tumor and 26 adjacent normal oral tissue samples. We identified differentially expressed genes (DEGs) between tumor and adjacent normal oral tissue samples that can be potential biomarkers to demarcate tumor and non-tumor tissue. DEGs present in plasma membrane and matrix that were significant in HNSC were considered for the analysis.

Results:- Differential expression analysis between tumor and adjacent normal sample groups identified 704 upregulated genes, followed by gene ontology (GO) analysis to identify the ones present in the plasma membrane and matrix. It was found that 123 genes were present in the plasma membrane, 28 in matrix and there were 8 other MMP genes. Of these, 23 plasma membrane genes, 19 matrix genes and 4 MMPs were reported in HNSC database of TCGA (The Cancer Genome Atlas). Among these genes, the genes that have a greater potential of being effective biomarkers to demarcate tumor and non-tumor tissue were selected based on various analysis factors including log₂ fold change, average RPKM, ROC analysis, PPI network analysis and differential expression study in different stages of cancer as well as in individual sample pairs. These selected genes were: CA9, ADAM12, COL1A1, COL1A2, PDPN, LAMC2, MMP10, MMP13, POSTN, COL3A1, COL4A1 and COL4A2. Even among these, the genes ADAM12, PDPN, MMP10 and MMP13 had comparatively higher significant ROC value and log₂ fold change.

Conclusions:- Thus, all these significant genes have the potential to become biomarkers to demarcate tumor and non-tumor oral tissue. These biomarkers can be used for efficient margin clearance during surgery, which can help manage the concerns of high recurrence rate of OSCC and improve patient prognosis.

Keywords:- OSCC (Oral Squamous cell carcinoma), HNSC (Head and Neck Squamous Cell Carcinoma), Differentially expressed genes (DEGs), Biomarker, Margin clearance.