

**CYCLIN D1 AMPLIFICATION IN TONGUE AND
BUCCAL MUCOSA SQUAMOUS CELL CARCINOMA**

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ABSTRACT

Introduction

Oral cancer is a significant health problem worldwide with almost 300,000 new cases are diagnosed each year. Despite the numerous studies done, and even with the best treatment option utilized, more than 50% of patients with oral cancer will experience relapse. In search for better options for prognostication, researches are now focusing on the molecular biology of cancer, for instance in search of reliable tumor markers. Among the markers reported in the literatures, Cyclin D1 is actively studied protein. Cyclin D1 regulates the cell cycle progression by forming a complex with different cyclin dependant kinase. Dysregulation of cyclin D1 can result in loss of normal cell growth and tumor development. The aim of this study is to determine and compare the amplification of Cyclin D1 in buccal mucosa and tongue oral squamous cell carcinoma(OSCC) and to associate its amplification in buccal mucosa and tongue OSCC with tumor depth, tumor front, histopathological grading, pathological tumor size, lymph node status, TNM staging and survival rate.

Materials and methods

The study samples were paraffin-embedded OSCC surgical specimens obtained from the archives of the Department of Oral Pathology, Oral Medicin and periodontolgy and Oral Pathology Diagnostic Laboratory. Fifty samples of patients with primary OSCC of buccal mucosa and tongue were included in the study. The sociodemographic and clinical data were obtained from the Malaysian Oral Cancer Tumor and Database System coordinated by the Oral Cancer Research and Coordinating Centre (OCRCC), University of Malaya. There were 31(62%) female and 19(38%) male with the overall age ranging from 26 to 94 years with a mean age of 60years.

The OSCC samples were from 44(68%) Indians, 10(20%) Malays and 6(12%) Chinese. The fluorescent-in-situ hybridization (FISH) technique was used to detect the amplification of Cyclin D1 using the Vysis protocol. Fluorescence evaluation of Cyclin D1 was performed using the image analyzer where the Cyclin D1 amplification signal appears as a small spot. At least 200 nuclei were scored using a 100X objective in each defined histological area, and each nucleus was assessed for the chromosome copy number. Statistical correlations of Cyclin D1 and certain clinicopathological parameters of OSCC were analyzed using the chi-square method or Fisher's exact test

Results

The present study found positive amplification of cyclin D1 in 72% (36) of OSCC. Detection of positive amplification for cyclin D1 was observed in 88% (22) and 56% (14) of the tongue and buccal mucosa OSCC respectively where the difference was statistically significant($p=0.012$). There was a significant correlation between Cyclin D1 positivity and ethnicity for the OSCC of the buccal mucosa ($p=0.037$); larger pathological tumor greatest dimension (pT) ($p = 0.019$), higher pTNM stages ($p=0.014$), tumor depth ≥ 5 mm in tongue cases ($p<0.001$) and survival rate ($p=0.009$) for overall SCC cases and ($p<001$) for buccal mucosa SCC cases.

Conclusion

There is a significant correlation between amplification of Cyclin D1 with tumor depth and size of the tumor for tongue SCC; ethnicity and survival rate for buccal mucosa SCC .

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LIST OF ABBREVIATIONS

CCND1	Cyclin D1
CDK4\6	Cyclin dependent kinases 4 and 6
DAPI	4',6'-diamidino-2-phenylindole
EBV	Epstein-Barr virus
FISH	Florescence in Situ Hybridization
H&E	Hematoxylin and Eosin
FITC	Fluorescein Isothiocyanate
HIV	Human immunodeficiency virus
HNSCC	Head and Neck Squamous Cell Carcinoma
HPV	Human papilloma virus
IHC	Immunohistochemistry
MOCTDBS	Malaysian Oral Cancer Tumor and Database
OCRCC	Oral Cancer Research Coordinating Center
OSCC	Oral squamous cell carcinoma
pN	Pathological lymph node metastasis
pT	Pathological tumor greatest dimension
pTNM	Pathological TNM stage
Rb	Retinoblastoma
SPSS	Computer program used for statistical analysis
TNF	Tumor necrosis factor
WHO	World Health Organization
XP	Xeroderma Pigmentosum