

**ASSOCIATION BETWEEN *TNF- α* -308 G/A
POLYMORPHISM AND ORAL CANCER RISK AMONG
MALAYSIAN INDIAN AND INDIGENOUS**

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MALAYSIAN INDIAN AND INDIGENOUS
POPULATION**

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This project paper is dedicated to my family and friends to let them know how much they mean to me.

ABSTRACT

The primary role of tumor necrosis factor alpha (*TNF- α*) gene is to regulate immune cells. Dysregulation and, in particular, overproduction of this gene has been found to increase susceptibility to a variety of human diseases such as cancer. The aim of this study is to investigate the association of single nucleotide polymorphism (SNP) in *TNF- α* -308 promoter and the risk of oral cancer among the Malaysian Indian and Indigenous population. The study included 143 confirmed oral squamous cell carcinoma (OSCC) (mean age = 63.69 ± 12.84) and 79 healthy controls (mean age = 50.43 ± 16.35). The polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) was employed to analyze *TNF- α* -308 promoter polymorphism, which were confirmed by direct sequencing.

Chi-square, simple logistic regression and stratified analysis were performed using the SPSS (ver 15.0) to study the role of *TNF- α* polymorphism in modulating the risk of oral cancer. The wild-type genotype (GG) was seen in 88.8% (127) of OSCC patients in comparison to 87.3% (69) controls; while variant genotypes (GA & AA) were seen in 9.8% (14) and 1.4% (2) of cases and 11.4% (9) and 1.3% (1) of controls respectively. Also no significant association was observed between variant genotypes (GA & AA) and oral cancer risk. Polymorphism of *TNF- α* at position -308 G/A may not be a risk factor for oral cancer because we did not find a statistically significant association between the *TNF- α* -308 G/A polymorphism and oral cancer risk ($p = .710$ and $p = .946$ for GA and AA respectively).

In conclusion, no association was seen between *TNF- α* -308 G/A polymorphism and oral cancer risk among the Malaysian Indian and Indigenous population.

ABSTRAK

Peranan utama ketumbuhan necrosis faktor gen alpha (TNF- α) adalah untuk mengawal sel-sel imun. *Dysregulation* dan, khususnya, produksi berlebihan gen ini telah didapati meningkatkan risiko pelbagai penyakit manusia seperti kanser. Tujuan kajian ini adalah untuk menyiasat perhubungan polimorfisme tunggal nukleotida (SNP) dalam promoter TNF- α -308 dan risiko kanser mulut di kalangan penduduk India dan Orang Asli Malaysia. Kajian ini melibatkan 143 peserta kajian yang disahkan mempunyai sel skuamus karsinoma oral (OSCC) (umur min = 63.69 ± 12.84) dan 79 peserta kumpulan kawalan yang sihat (min umur = 50.43 ± 16.35). *Polymerase chain reaction-restriction fragment length polymorphism* (PCR-RFLP) telah digunakan untuk menganalisis polimorfisme promoter TNF- α -308 yang telah disahkan menggunakan kaedah “direct sequencing”.

Khi-kuasa dua, regresi logistic ringkas dan analisis berstrata dilakukan dengan menggunakan SPSS (ver 15.0) untuk mengkaji peranan polymorphism TNF- α -308 G / A dalam modulasi risiko kanser mulut. Genotip normal jenis (GG) dilihat dalam 88.8% (127) pesakit OSCC berbanding dengan 87.3% (69) dalam kumpulan kawalan; manakala genotip varian (GA & AA) telah dilihat dalam 9.8% (14) dan 1.4% (2) kes-kes dan 11.4% (9) dan 1.3% (1) kawalan masing-masing.

Juga tidak ada perhubungan yang signifikan telah diperhatikan antara genotip varian (GA & AA) dan risiko kanser mulut. Polimorfisme TNF- α pada kedudukan -308 G/A tidak boleh menjadi factor risiko untuk kanser mulut kerana kita tidak mendapati perhubungan signifikan dari segi statistic antara polimorfisme TNF- α -308 G/A dan risiko kanser mulut ($p = .710$ dan $p = .946$ untuk GA dan AA masing-masing).

Kesimpulannya, kajian ini mendapati tiada perhubungan dilihat antara polimorfisme hisam $\text{TNF-}\alpha$ -308 G/A dan risiko kanser mulut dalam kalangan penduduk India dan Orang Asli Malaysia.

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LIST OF ABBREVIATIONS

APC	Adenomatous Polyposis Coli
ASR	Age Standardized Rate
BLAST	Basic Local Alignment Search Tool
CARIF	Cancer Research Initiatives Foundation
cDNA	Complementary Deoxyribonucleic Acid
CI	Confidence Interval
DNA	Deoxyribonucleic acid
dNTP	Deoxy nucleoside triphosphates
EB	Ethidium Bromide
FHIT	Fragile Histidine Triad
gDNA	genomic Deoxyribonucleic Acid
HPV	Human Papilloma Virus
HSV	Herpes Simplex Virus
HWE	Hardy-Weinberg Equilibrium
IARC	International Agency for Research on Cancer
ICC	Invasive Cervical Cancer
ICD	International Classification of Diseases
ILs	Interleukins
MOCDTBS	Malaysian Oral Cancer Database & Tissue Bank System
NCBI	National Center for Biotechnology Information
NCR	National Cancer Register
OCRCC	Oral Cancer Research and Coordinating Centre

OR	Odds Ratio
OSCC	Oral Squamous Cell Carcinoma
PCR	Polymerase Chain Reaction
RBC	Red Blood Cell
RE	Restriction Enzyme
RFLP	Restriction Fragment Length Polymorphism Analysis
ROS	Reactive Oxygen Species
RR	Relative Risk
SLR	Simple Logistic Regression
SNP	Single Nucleotide Polymorphism
SPSS	Statistical Package for the Social Sciences
TNF- α	Tumor Necrosis Factor alpha
TNF- β	Tumor Necrosis Factor beta
UKM	Universiti Kebangsaan Malaysia
UM	University of Malaya
USM	University Sains Malaysia
UV	Ultra Violet
WBC	White Blood Cell
WHO	World Health Organization