ASSOCIATION BETWEEN $TNF-\alpha$ −308 G/A POLYMORPHISM AND ORAL CANCER RISK AMONG MALAYSIAN INDIAN AND INDIGENOUS

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ASSOCIATION BETWEEN TNF-α −308 G/A POLYMORPHISM AND ORAL CANCER RISK AMONG 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 menyiaskat 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 sequensing”.

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 TNF-α –308 G/A dan risiko kanser mulut dalam kalangan penduduk India dan Orang Asli Malaysia.
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<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>APC</td>
<td>Adenomatous Polyposis Coli</td>
</tr>
<tr>
<td>ASR</td>
<td>Age Standardized Rate</td>
</tr>
<tr>
<td>BLAST</td>
<td>Basic Local Alignment Search Tool</td>
</tr>
<tr>
<td>CARIF</td>
<td>Cancer Research Initiatives Foundation</td>
</tr>
<tr>
<td>cDNA</td>
<td>Complementary Deoxyribonucleic Acid</td>
</tr>
<tr>
<td>CI</td>
<td>Confidence Interval</td>
</tr>
<tr>
<td>DNA</td>
<td>Deoxyribonucleic acid</td>
</tr>
<tr>
<td>dNTP</td>
<td>Deoxy nucleoside triphosphates</td>
</tr>
<tr>
<td>EB</td>
<td>Ethidium Bromide</td>
</tr>
<tr>
<td>Fhit</td>
<td>Fragile Histidine Triad</td>
</tr>
<tr>
<td>gDNA</td>
<td>genomic Deoxyribonucleic Acid</td>
</tr>
<tr>
<td>HPV</td>
<td>Human Papilloma Virus</td>
</tr>
<tr>
<td>HSV</td>
<td>Herpes Simplex Virus</td>
</tr>
<tr>
<td>HWE</td>
<td>Hardy-Weinberg Equilibrium</td>
</tr>
<tr>
<td>IARC</td>
<td>International Agency for Research on Cancer</td>
</tr>
<tr>
<td>ICC</td>
<td>Invasive Cervical Cancer</td>
</tr>
<tr>
<td>ICD</td>
<td>International Classification of Diseases</td>
</tr>
<tr>
<td>ILs</td>
<td>Interleukins</td>
</tr>
<tr>
<td>MOCDTBS</td>
<td>Malaysian Oral Cancer Database &amp; Tissue Bank System</td>
</tr>
<tr>
<td>NCBI</td>
<td>National Center for Biotechnology Information</td>
</tr>
<tr>
<td>NCR</td>
<td>National Cancer Register</td>
</tr>
<tr>
<td>OCRCC</td>
<td>Oral Cancer Research and Coordinating Centre</td>
</tr>
</tbody>
</table>
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