

CHROMOSOMAL ALTERATIONS AND GENE  
PATHWAYS OF TONGUE AND CHEEK SQUAMOUS  
CELL CARCINOMA

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Field of Study: Oral Oncology

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## ABSTRACT

### **Introduction:**

Tongue and cheek squamous cell carcinoma (SCC) have different behaviours. In order to understand these behaviours, there is a need to look into the chromosomal alterations and gene pathways that maybe associated with oral cancer at these sites. Therefore, the objective of this study is to determine the chromosomal aberrations and gene pathways involved in tongue and cheek SCC using high resolution array based comparative genomic hybridization (aCGH).

### **Methodology:**

A genome wide screening with array CGH (SurePrint G3 CGH 1x1M microarray) was performed using gDNA from 20 snap frozen fresh tissues consisting of 12 tongue and 8 cheek SCC (samples from the Malaysian Oral Cancer Database and Tumour Bank System [MOCDTBS] coordinated by OCRCC-UM). Cytosure Software was used to detect the chromosomal aberrations and candidate genes related to the selected regions. Pathway analysis was done using MetaCore™ software for selected genes.

### **Results:**

The mean number of chromosomal aberrations per tumour for tongue SCC ( $22.75 \pm 26.58$ ) was higher than cheek SCC ( $8.63 \pm 11.89$ ). The most common amplified regions in tongue SCC were 8q24.22 (33.33%), 8q24.3 (33.33%), 11q13.2 (33.33%), 12q13.13 (33.33%), 14q32.33 (33.33%) and for cheek SCC the most common amplified region was 22q12.3 (25%). For the deleted regions, the most common for tongue SCC were 2q21.1 (16.67%), 6q21 (16.67%) and for cheek SCC were 2q22.1 (25%), 7q35

(25%), 19q13.33 (25%). The most significant pathway involved in tongue SCC was cell adhesion extracellular matrix (ECM) remodelling pathway, while for cheek SCC; it was cadherin-mediated cell adhesion pathway.

**Conclusion:**

This study showed that the sites of oral cancer origin have a great influence over the variations in chromosomal aberrations and gene pathways. Nevertheless, the identified chromosomal aberrations genes and their interactive pathways revealed from the present research are worth for further investigations on oral carcinogenesis. (Acknowledgment: Grant of UMRG085/09HTM and PS017/2010A)

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## Table of Contents

<b>Title Page</b>	<b>i</b>
<b>Original Literary Work Declaration</b>	<b>ii</b>
<b>Abstract</b>	<b>iii</b>
<b>Acknowledgements</b>	<b>v</b>
<b>Table of Contents</b>	<b>vi</b>
<b>List of Appendices</b>	<b>ix</b>
<b>List of Figures</b>	<b>ix</b>
<b>List of Tables</b>	<b>ix</b>
<b>List of Abbreviations</b>	<b>x</b>
<b>List of Symbol</b>	<b>xi</b>
<b>1.0 Introduction</b>	<b>1</b>
<b>2.0 Literature Review</b>	<b>7</b>
<b>2.1 Epidemiology of oral cancer</b>	<b>7</b>
<b>2.1.1 Incidence</b>	<b>7</b>
<b>2.1.2 Gender, Ethnic and Age distribution</b>	<b>8</b>
<b>2.2 Clinical and Histological characteristics of oral cancer</b>	<b>10</b>
<b>2.2.1 Subsites of oral cancer (ICD-10)</b>	<b>10</b>
<b>2.2.2 Clinical appearance</b>	<b>11</b>
<b>2.2.3 Histological appearance</b>	<b>11</b>
<b>2.3 Etiological factors</b>	<b>12</b>
<b>2.3.1 Tobacco smoking</b>	<b>12</b>
<b>2.3.2 Excessive alcohol consumption</b>	<b>13</b>
<b>2.3.3 Betel quid chewing</b>	<b>14</b>
<b>2.3.4 Human Papillomaviruses Virus (HPV)</b>	<b>15</b>
<b>2.3.5 Genetic Susceptibility</b>	<b>16</b>
<b>2.3.6 Diet and Nutrition</b>	<b>17</b>
<b>2.3.7 Mouthwash</b>	<b>18</b>
<b>2.4 Genetic Alteration</b>	<b>19</b>
<b>2.5 Chromosomal Instability (CIN)</b>	<b>20</b>

<b>2.6 Oncogene and Tumor Suppressor Gene</b>	<b>22</b>
<b>2.6.1 Oncogenes</b>	<b>22</b>
<b>2.6.2 Tumor Suppressor Genes</b>	<b>24</b>
<b>2.7 Carcinogenesis</b>	<b>26</b>
<b>2.8 Hallmarks of Cancer</b>	<b>28</b>
<b>2.8.1 Self-sufficiency of growth signals</b>	<b>28</b>
<b>2.8.2 Insensitivity to growth-inhibitory signals</b>	<b>29</b>
<b>2.8.3 Evasion of programmed cell death</b>	<b>29</b>
<b>2.8.4 Immortality or unlimited replicative potential</b>	<b>30</b>
<b>2.8.5 Sustained angiogenesis</b>	<b>30</b>
<b>2.8.6 Tissue Invasion and Metastasis</b>	<b>31</b>
<b>2.9 Model of oral squamous cell carcinoma (OSCC)</b>	<b>33</b>
<b>2.10 Conventional Cytogenetic</b>	<b>36</b>
<b>2.11 Molecular Cytogenetic</b>	<b>36</b>
<b>2.11.1 Comparative genomic hybridization (CGH)</b>	<b>36</b>
<b>2.11.2 Florescent in situ hybridization (FISH)</b>	<b>43</b>
<b>2.12 Omic Profiling</b>	<b>45</b>
<b>2.12.1 Array CGH</b>	<b>46</b>
<b>3.0 Methodology</b>	<b>52</b>
<b>3.1 Study Design</b>	<b>52</b>
<b>3.2 Sample selection</b>	<b>52</b>
<b>3.2.1 Demographic characteristics of the samples</b>	<b>52</b>
<b>3.2.2 Sample Criteria</b>	<b>53</b>
<b>3.3 Sample Preparation of DNA</b>	<b>53</b>
<b>3.3.1 Cryosection on Frozen tissue</b>	<b>53</b>
<b>3.3.2 DNA Extraction</b>	<b>53</b>
<b>3.3.3 Quantification of DNA measurement</b>	<b>54</b>
<b>3.4 Technique to be employed for Array CGH.</b>	<b>54</b>
<b>3.4.1 Sample Preparation (Defragmentation Method) for aCGH</b>	<b>55</b>
<b>3.4.2 Sample Labeling for aCGH</b>	<b>55</b>
<b>3.4.3 Probe Purification for aCGH</b>	<b>56</b>
<b>3.4.4 Microarray Hybridization</b>	<b>56</b>
<b>3.4.5 Washing Preparation for aCGH</b>	<b>57</b>
<b>3.4.6 Microarray Scanning using Agilent Scanner Control</b>	<b>57</b>

## **and Feature Extraction (FE)**

<b>3.5 Analysis</b>	<b>58</b>
<b>3.5.1 Data Analysis</b>	<b>58</b>
<b>3.5.2 Population analysis</b>	<b>58</b>
<b>3.5.3 Pathway Analysis</b>	<b>59</b>
<b>4.0 Result</b>	<b>61</b>
<b>4.1 Demographic characteristic of the study samples</b>	<b>61</b>
<b>4.2 Chromosomal alterations (aberrations) detected using array CGH and genes involved</b>	<b>62</b>
<b>4.2.1 Chromosomal aberrations detected genes involved in tongue SCC</b>	<b>62</b>
<b>4.2.2 Chromosomal aberrations detected genes involved in cheek SCC</b>	<b>67</b>
<b>4.3 Significant signaling pathways analysis from data sets of chromosomal aberrations in tongue SCC and cheek SCC</b>	<b>70</b>
<b>4.3.1 Significant signaling pathways of tongue SCC</b>	<b>70</b>
<b>4.3.2 Significant signaling pathways of cheek SCC</b>	<b>73</b>
<b>5.0 Discussion</b>	<b>76</b>
<b>5.1 Chromosomal aberrations (alterations) in tongue and cheek SCC using array CGH</b>	<b>78</b>
<b>5.2 Significant pathways involved in tongue and cheek SCC using pathway analysis software</b>	<b>84</b>
<b>5.3 Study Limitation</b>	<b>89</b>
<b>6.0 Conclusion and recommendations</b>	<b>90</b>
<b>References</b>	<b>93</b>
<b>Appendices</b>	<b>128</b>



## LIST OF APPENDICES

Appendix 2.1: Reprinted from Argiris *et al.* (2008) with permission. 128

### List of figures:

Figure 1: Hypothetical model of oral carcinogenesis. 34

### List of Tables:

Table 4.1: Demographic characteristics of study samples. 61

Table 4.2: Details of the amplified regions for each chromosome in 12 tongue SCC. 63

Table 4.3: Details of the deleted regions for each chromosome in 12 tongue SCC cases. 67

Table 4.4: Details of the amplified regions for each chromosome in 8 cheek SCC cases. 68

Table 4.5: Details of the deleted regions for each chromosome in 8 cheek SCC cases. 69

Table 4.6: Significant biological pathway associated with amplified genes from  
tongue SCC. 71

Table 4.7: Significant biological pathway associated with deleted genes from  
tongue SCC. 73

Table 4.8: Significant biological pathway associated with amplified genes from  
cheek SCC. 74

Table 4.9: Significant biological pathway associated with deleted genes from  
cheek SCC. 75

## List of Abbreviations

aCGH: Array Comparative Genomic Hybridization  
AJCC: American Joint Committee on Cancer  
ASR: Age-Standardized rate  
AURKA: Aurora kinase A  
BM: Buccal Mucosa  
BRCA1: Breast Cancer 1  
CAMs: Cell adhesion molecules  
CDKN2A: Cyclin-Dependent Kinase Inhibitor 2A  
CGH: Comparative Genomic Hybridization  
CHK1: Checkpoint kinase 1  
CHK2: Checkpoint kinase 1  
CIN: Chromosomal Instability  
Cy3: Cyanine 3  
Cy5: Cyanine 5  
DNA: Deoxyribonucleic acid  
ECM: Extracellular matrix  
EGFR: Epidermal Growth Factor Receptor  
EMT: Epithelial-mesenchymal transition  
F: Female  
FHIT: Fragile Histidine Triad  
FISH: Fluorescent *in situ* hybridization  
gDNA: Genomic Deoxyribonucleic acid  
GLOBACAN: Global Burden of Cancer  
H&E: Hematoxylin and Eosin  
hTERT: human Telomerase  
IACR: International Agency for Research on Cancer  
ICD: International Classification of Disease  
IFN: Interferon  
M: Male  
MAPK: Mitogen activated protein kinase  
Mb: Million basepairs  
MIN: Microsatellite Instability  
MMPs: Matrix metalloproteinases  
MNCR: Malaysian National Cancer Registry  
NNK: 4-(methylnitrosoamino)-1-(3-pyridyl)-1 butanone  
NNN: Nitroso-nor-nicotine  
OCT: Optimal Cutting Temperature  
OSCC: Oral squamous cell carcinoma  
PAH: Polycyclic aromatic hydrocarbons  
PDGFR: Platelet-Derived Growth Factor Receptors  
PI3K- Phosphatidylinositol 3-kinase  
RB1: Retinoblastoma 1  
ROS: Reactive Oxygen Species  
T: Tongue  
TSG: Tumor suppressor gene  
VEFG: Vascular Endothelial Growth Factor

## List of Symbols:

$\mu$ l: Microliter

ng: nanogram

bp: Basepairs

$\alpha$ : Alpha

$\beta$ : Beta