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DETECTION OF p53 GENE MUTATION IN ORAL SQUAMOUS CELL CARCINOMA PATIENTS USING MULTIPLEX LIGATION-DEPENDENT PROBE AMPLIFICATION IN MALAYSIAN POPULATION

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ABSTRACT

P53 gene mutations observed at about 50 to 60 % in oral squamous cell carcinoma (OSCC). Until now, most of the studies were focused on exon 5 to 8 of p53 gene instead of the whole exons and it becomes a trend for p53 gene mutation study. However, the site of p53 gene mutation is still in controversy as available techniques showed different results. More importantly, using the same technique the reports demonstrated inconsistence mutation sites. The objective of the present study is to examine the status of p53 gene mutation in all exons (1 to 11). Recently, Multiplex Ligation-dependent Probe Amplification (MLPA) technique has proven to be reliable and efficient for the detection of mutation. Therefore, present study used Multiplex Ligation-dependent Probe Amplification (MLPA) to examine p53 gene mutation from exons 1 to 11. DNA specimens from 58 OSCC patients and 10 healthy (controls) were used in this study. Our results demonstrated that 31% of OSCC patient have p53 gene mutation. Among them 56% of mutation occurred in exon 3, followed by exon 4 which was 50%. Our study strongly indicated that exons 3 and 4 could be reliable and positive markers of OSCC development and progression. To our knowledge, this study for the first time showed that exon 3 is the hot spot region for p53 gene mutation in OSCC.

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CHAPTER ONE
INTRODUCTION

1.1 BACKGROUND OF THE STUDY

Cancer was the second leading cause of death after heart disease in developing and developed countries in 2004 (World Health Report, 2005). However, in 2010 cancer had replaced heart disease as the overall leading cause of death worldwide (Cancer Facts and Figures, 2013), accounting for one in eight deaths. In Malaysia, cancer was the third leading cause of death after septicemia and heart disease in 2007 (*National Cancer Registry Report*, 2007).

Cancer is a genetic disease where a single cell in the body undergoes genetic transformation into cancer cell (Croce, 2008). According to the Oxford Dictionary of Biology, cancer is defined as any disorder of cell growth that can cause damage to healthy tissues by abnormal cells (Robert, 2007). It can originate from almost everywhere in the body, from the skin to bloodstream. There are different kinds of cancer, which are carcinomas, sarcoma, leukemia and lymphoma, depending on where it originates (Cooper, 2000).

Cancer is a complex genetic disease that can be caused either by external or internal factors. External factors include radiation from sunlight, chemicals from our environment, carcinogens present in our foods or water and viruses. Internal factors include heredity, hormones and individual's immune conditions (Kademani, 2007). Cancer of the head and neck accounts for almost 3% of worldwide cases. More than 95 % of head and neck cancers are oral squamous cell carcinoma (OSCC), which is the sixth most common cancer worldwide (Tsantoulis *et al.*, 2007). There are about 300,000 to 400,000 individuals worldwide diagnosed annually with oral cancer and nearly 90% of them are diagnosed with OSCC (Kademani, 2007; Knobloch *et al.*,2011). In South-Central Asia, (Pakistan, India, Bangladesh, Iran, Afghanistan, and the Central Asian Republics) OSCC is the most common malignancy found in men (Parkin *et al.*, 1999). In India, OSCC is the leading malignancy diagnosed in men and the third most common cancer (Sen *et al.*, 2002). In Malaysia, it is prevalent among Indians and Indigenous people of Sabah and Sarawak. It is the fourth most