UNIVERSITI TEKNOLOGI MARA

DEVELOPMENT OF A GENETIC TEST FOR DETECTION OF POLYMORPHISM OF HUMAN EPIDERMAL RECEPTOR-2 (*HER-2*) GENE

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ABSTRACT

The aim of this study is to develop a genetic test using specific primers to defect the polymorphism of the Human Epidermal Receptor (HER-2) gene. PCR is used to amplify a specific region of DNA in order to produce a large number of nearly identical copies. The method uses a heat stable DNA replication enzyme called a DNA polymerase, the four deoxynucleotide building blocks of DNA and two small single-stranded DNA segments called primers. Polymerase Chain Reaction using first set of primers was done to amplify the specific sequence of HER-2 gene while the second set of primers was used to amplify the allele specific polymorphism site of HER-2 gene. Both have different fragment size. The PCR products were analyzed using the gel electrophoresis to determine the DNA fragment produced. The bands are observed via gel imaging using the ultra violet (UV) light. The required bands were compared to the standard ladder or marker with known fragment size. Result showed one band indicate homozygous while two bands indicate heterozygous gene. However, for further confirmation, the product that was obtained in this study should be sent for sequencing.

CHAPTER 1

INTRODUCTION

1.1 Research Background

A single nucleotide polymorphism (SNP) at codon 655, resulting in a guanine to adenine transition (Val655Ile) in the transmembrane domain-coding region of this gene has been identified (Papewalis *et al.*, 1991). A population-based, case control study of this polymorphism was reported recently, and the Val allele was found to be associated with an increased risk of breast cancer, particularly among younger women. However, there is little information on the population distribution of this SNP (Xie *et al.*, 2000).

This is an important issue in the context of statistically significant ethnic differences in the incidence of breast cancer and of other solid tumors. Alterations of this gene are found in more than 20% of breast tumors and have been shown to be associated with steroid hormone receptor–negative tumors, higher nuclear and histologic grades, tumor aneuploidy, and higher rates of proliferation, a reduced response to chemotherapy and hormonal therapy, and poor prognoses (Baselga *et al.*, 1998).