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DETECTION OF 484C>G MUTATION IN PEROXISOME PROLIFERATOR ACTIVATED RECEPTOR ALPHA (PPARA) IN HUMAN DNA USING ALLELE-SPECIFIC POLYMERASE CHAIN REACTION

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TABLE OF CONTENTS

ACKNOWLEDGEMENT ii

TABLE OF CONTENT iii

LIST OF TABLES vi

LIST OF FIGURES vii

LIST OF ABBREVIATIONS viii

ABSTRACT ix

CHAPTER ONE 1

INTRODUCTION 1

1.1 Background Of Study 1

1.2 Problem Statement 2

1.3 Objectives 2

1.4 Hypothesis 2

1.5 Significance Of Study 3

CHAPTER TWO 4

LITERATURE REVIEW 4

2.1 Peroxisome proliferator-activated receptor alpha (PPARA) 4

2.2 PPARA gene chromosomal location and structure 5

2.3 PPARA functions 6

2.3.1 Lipid metabolism 6

ABSTRACT

PPARA is encoded by *PPARA* gene and offers the highest affinity for fatty acids binding. Genetic mutation or polymorphism of this gene in human DNA may results in greater defects on the human normal lipid metabolism. Hence, genetic mutation detection of this gene could be significant in determining the appropriate drug therapy for an individual patient especially for the lipid lowering drug therapy. The purpose of the study is to detect the mutation of 484C>G in PPARA in human DNA. Previous detection of this gene is done by using polymerase chain reaction-restriction fragment length polymorphism (PCR-RFLP) as the detection method. Four samples of human DNA were tested for the detection of the presence or absence of the mutation using an allele-specific polymerase chain reaction (PCR) method in a thermocycler. The results were obtained by running the PCR product under gel electrophoresis using 1.5% of agarose gel. First run of PCR produced amplicons of the DNA of interest while the second run of PCR produced amplicons of both wild type and mutant alleles. All samples were found to be heterozygous as the results showed that the wild type and mutant allele are present.

CHAPTER ONE

INTRODUCTION

1.1 BACKGROUND OF STUDY

Peroxisome proliferator-activated receptors (PPARs) belongs to the nuclear receptor superfamily and exist in three isoforms or subtypes in human; PPAR-alpha, PPAR-gamma and PPAR-beta/delta (Volcik, Nettleton, Ballantyne, & Boerwinkle, 2008). PPARs are responsible for the expression control of various types of genes involved in metabolic processes such as lipid metabolism, energy combustion, glucose metabolism and inflammation (Pyper, Viswakarma, Yu, & Reddy, 2010). All PPARs are activated via heterodimerization with the retinoid X receptor (RXR) as well as binding to the peroxisome proliferator response element (PPRE) of target genes (Robitaille et al., 2004). This study focus on one of the subtypes, PPAR-alpha which encodes by *PPARA* gene that offers the highest affinity for the binding of fatty acids. Thus, genetic mutation or polymorphism of PPARA may results in greater defects on the human normal lipid metabolism.

Any changes or modifications of a gene will lead to mutation or polymorphism in which it may alter the normal body physiological functions. The alteration however may or may not be harmful to the person depending on the functions altered. PPARA polymorphism increase risk factors of dyslipidemia (Gu, Guo, Zhou, Hu, & Wu, 2014), breast cancer (Golembesky et al., 2008) and cardiovascular risk such as myocardial