UNIVERSITI TEKNOLOGI MARA

THE IDENTIFICATION OF SNP 29209 IN EXON 10 OF LOW DENSITY LIPOPROTEIN RECEPTOR (LDLR) GENE USING ALLELE-SPECIFIC PCR (AS-PCR) METHOD

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Dissertation submitted in partial fulfilment of the requirements

for the degree of

Bachelor of Pharmacy (Hons.)

Faculty of Pharmacy

2014

ACKNOWLEDGEMENTS

Foremost, I would like to express my sincere gratitude to my supervisor, Dr. John Shia Kwong Siew for his guidance, advice, patience and support throughout the time of research and completion of this thesis. I would also like to thank the Director of Integrative Pharmacogenomics Institute (iPROMISE), Prof. Dr. Mohd Zaki Salleh and Prof. Dr. Teh Lay Kek for their insightful comments and encouragement. My special thanks also go to the staffs and post-graduate students in iPROMISE especially Mdm. Siti Nooraishah Husin, Miss Bibi Aishaiahjan Selamat, Miss Ismanura'in Ibrahim, Miss Nur-Jalinna Abdul Jalil, Miss Rose Iszati Ismet Nayan and Miss Noor Syakilla Azman for the advice and assistance they provided at all levels of the research project. Lastly, I would like to express my heart-felt gratitude to my family and friends for their continuous support.

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ABSTRACT

Familial hypercholesterolemia (FH) is a genetically inherited autosomal dominant disease. Individuals with FH show an elevation in their blood cholesterol level. Polymorphism in LDLR gene is associated with the occurrence of FH. SNP 29209 A>G is one of the polymorphisms found in exon 10 of this gene. It is a synonymous SNP. The objective of the present study was to detect the presence of SNP 29209 A>G using the allele-specific PCR (AS-PCR) method which is a more rapid and cost-effective approach of SNP detection. All ten subjects tested in this study were found to carry the mutated G allele in which 50% were heterozygous mutant and another 50% were homozygous mutant. The frequency of A allele and G allele in the studied subjects were 16.0% and 84.0% respectively. The G mutant allele appears to have a protective effect against high LDL level. For future plan, AS-PCR method using higher number of subjects should be carried out to determine a more accurate allelic frequency of this SNP. Further studies are needed to provide a more significant relationship between the targeted SNP and FH.

CHAPTER 1

INTRODUCTION

1.1 Background of Study

Autosomal dominant hypercholesterolemia (ADH) is a condition that can develop due to genetic inheritance. It is associated with a high plasma level of low density lipoprotein (LDL). Among the most common genetic diseases that fall under ADH are Familial Hypercholesterolemia (FH) and Familial Defective Apolipoproteins B-100 (FDB) (Motazacker et al., 2012). FDB cannot be clinically distinguished from FH but its manifestation of hypercholesterolemia is shown to be less severe compared to that of in FH (Whitfield et al., 2004). FH is caused by mutation in the LDLR gene. This mutation can affect the cholesterol uptake and plasma clearance of cholesterol giving rise to an elevated level of low density lipoprotein cholesterol (LDL-C) in the circulation (De Castro-Orós et al., 2010). The disease is classified into heterozygous FH and homozygous FH.

It is reported that the presence of high LDL level in plasma is an important risk factor of cardiovascular disease (CVD). This is because the condition may lead to the development and progression of atherosclerotic plague on the arterial wall (Alonso et al., 2008). Studies on mutation of LDLR gene leading to FH have been widely conducted in