

Title : Analysis of Gene Variation in the Middle Region of Melanocortin 4 Receptor Gene in Obese Thai Individuals

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ABSTRACT

At present, obesity is a growing health problem both globally and in Thailand, with a remarkable impact on health and economy. Assessment of the risk and the tendency of individual to become obese by analyzing specific gene variations is therefore an important option. In this study, the middle region of the melanocortin 4 receptor (*MC4R*) gene was analyzed in obese Thais to investigate the impact of nucleotide variations on the occurrence of obesity. The obtained data can be used as a database for the prognosis and the prevention of obesity. The *MC4R* gene encodes a receptor protein of the leptin-melanocortin pathway, which is involved in regulating appetite and energy expenditure in the body. Firstly, DNA was extracted from the hair roots of forty four Thai volunteers aged between 18-60 years old with a body mass index (BMI) of more than 25.0. The middle region of *MC4R* gene (position 5,555-6,166) was then amplified by polymerase chain reaction (PCR). PCR products were analyzed by agarose gel electrophoresis and single specific PCR product of 612 base pairs was obtained. Concentrations of PCR product were adequate for the nucleotide sequence analysis by Big Dye Terminator technique. All PCR products were sent to APICAL SCIENTIFIC SDN. BHD. (Malaysia) for nucleotide sequence analysis using the MC4R-F1 primer. In the final step, the nucleotide sequences of the middle region of the *MC4R* gene of Thai volunteers were compared with the reference nucleotide sequence from the National Center for Biotechnology Information (NCBI) to identify single nucleotide polymorphisms (SNP). DNA analysis of 44 samples identified two heterozygous SNPs at G5726A and T6100C. The odds ratio for G5726A was 10.77, indicating that individuals with this SNP have a 10.77 times greater likelihood of developing obesity compared to those without SNP. The G5726A mutation causes a valine to isoleucine substitution at codon position 103 (V103I) in the *MC4R* gene. As it is a conservative missense mutation, the chemical properties and the function of the protein is supposedly not significantly affected. In contrast, the T6100C is silent mutation, meaning it does not alter the amino acid sequence or protein function. This finding provides information that could assist a better understanding about the correlation between gene variations and obesity, which may facilitate an obesity risk assessment and prognosis, and help establishing suitable prevention strategies for the Thai population in the future.

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