EFFECTS OF *PCSK1* GENETIC VARIANTS ON OBESITY AMONG THAI CHILDREN AND THEIR FAMILY MEMBERS: IN RELATION TO HEALTH RISK, AND BIOCHEMICAL AND ANTHROPOMETRIC PARAMETERS

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Abstract. Single nucleotide polymorphisms (SNPs) in *PCSK1*, namely, rs6234, rs6235, and rs271939 have been linked to obesity in European population; and rs3811951 has also been connected to type 2 diabetes and obesity parameters in Chinese population. In this family-based case-control study, we analyzed links between *PCSK1* genetic variants and obesity in Thai children and their families. Eleven obese children with a percent weight for height ≥140 who had family history of obesity and 69 family members were recruited. SNPs rs6234, rs6235, rs3811951, and rs271939 of *PCSK1* were analyzed using PCR and gene sequencing methods. DNA of 200 normal weight subjects was used as control. Participants with variant genotypes in the rs6234-6235 pair are at significantly more risk of being obese [OR = 2.44 (1.35-4.43), $p = 0.003$], and also at increased risk of being severely obese (obese class III) [OR = 3.03 (1.20-7.66), $p = 0.015$]. Variant rs3811951 showed no association with being obese, but is significantly linked to an increased risk of being severely obese [OR = 3.59 (1.42-9.08) $p = 0.005$]. Moreover, high density lipoprotein (HDL)-C levels between normal and variant rs3811951 group differed considerably, with patients with variant genotype having a lower HDL-C level ($p = 0.037$). Thus, Thais carrying SNPs rs6234-5 are at increased risk of being obese, and the risk of severe obesity increases when carrying both rs6234-5 and

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rs3811951, but not with rs271939. Furthermore, patients with genetic variations at rs3811951 are at risk of having low HDL-C levels.

Keywords: *PCSK1* gene, genetic variant, obesity, BMI