Genetics and Molecular Research

Exome sequencing in Thai patients with familial obesity

S. Kaewsutthi[1], J. Santiprabhob[2], B. Phonrat[3], A. Tungtrongchitr[4], P. Lertrit[5] and R. Tungtrongchitr[1]

[1]Department of Tropical Nutrition and Food Science, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand
[2]Division of Endocrinology and Metabolism, Department of Pediatrics, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand
[3]Department of Clinical Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Bangkok, Thailand
[4]Department of Parasitology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand
[5]Department of Biochemistry, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Corresponding authors: R. Tungtrongchitr / P. Lertrit
E-mail: rungsunn.tun@mahidol.ac.th / patcharee.ler@mahidol.ac.th

Genet. Mol. Res. 15 (2): gmr.15028311
Received August 8, 2015
Accepted November 26, 2015
Published July 15, 2016
DOI http://dx.doi.org/10.4238/gmr.15028311

ABSTRACT. Obesity is a major worldwide health issue, with increasing prevalence in adults and children from developed and developing countries. Obesity causes several chronic diseases, including cardiovascular and respiratory diseases, osteoarthritis, hypertension, stroke, type II diabetes, obstructive sleep apnea, and several types of cancer. Previous genome-wide association studies have identified several genes associated with obesity, including *LEP*, *LEPR*, *POMC*, *PCSK1*, *FTO*, *MC3R*, *MC4R*, *GNPDA2*, *TMEM18*, *QPCTL/GIPR*, *BDNF*, *ETV5*, *MAP2K5/SKOR1*, *SEC16B*, *SIM1*, and *TNKS/MSRA*. However, most of these variants are found in the intronic

or intergenic regions, making it difficult to elucidate the underlying mechanisms. Therefore, in this study, we performed a whole exome sequencing of the protein-coding regions in the total genome (exome) of two obese and one normal subject belonging to the same Thai family to identify the genes responsible for obesity. We identified 709 functional variants that were differentially expressed between obese and normal subjects; of these, 65 were predicted to be deleterious to protein structure or function. The minor allele frequency of 14 of these genes (*ALOX5AP*, *COL9A2*, *DEFB126*, *GDPD4*, *HCRTR1*, *MLL3*, *OPLAH*, *OR4C45*, *PRIM2*, *RXFP2*, *TIGD6*, *TRPM8*, *USP49*, and *ZNF596*) was low, indicating causal variants that could be associated with complex traits or diseases. Genotyping revealed *HCRTR1*, *COL9A2*, and *TRPM8* to be associated with the regulation of feeding behavior and energy expenditure. These genes constituted a network of pathways, including lipid metabolism, signaling transduction, immune, membrane transport, and gene regulation pathways, and seemed to play important roles in obesity.

Key words: Exome sequencing; Variants; Gene; Obesity; Thailand; Body mass index

