ASSOCIATION OF UCP1 -3826A/G AND UCP3 -55C/T GENE POLYMORPHISMS WITH OBESITY AND ITS RELATED TRAITS AMONG MULTI-ETHNIC MALAYSIANS

Objective: Our study investigated the association of UCP1 -3826A/G and UCP3 -55C/T single nucleotide polymorphisms (SNPs) with obesity and its related traits among multi-ethnic Malaysians.

Participants: A total of 447 (225 males; 46 Malays, 339 ethnic Chinese, 62 ethnic Indians; 111 obese) participated.

Methods: Demographic and anthropometric data were collected, and genotyping was performed by polymerase chain reaction-restriction fragment length polymorphism.

Results: The minor allele frequencies (MAFs) for UCP1 according to Malay/Chinese/Indian ethnicities were .61/.55/.52 and .32/.55/.38, respectively. UCP3 genotype and allele distribution was significantly associated with ethnic and waist-to-hip ratio (WHR), but among non-obese and Chinese participants only, respectively, after stratified analysis. Chinese participants with T allele had significantly lesser risk to be centrally obese [odds ratio = 0.69 (CI = .48, 1.00); P = .04], and also had significantly lower WHR compared to those with C allele. The UCP1 or UCP3 SNPs were not associated with obesity/BMI and total body fat (TBF), but combinatorial genotype analysis revealed that those having the AA and CC genotype for the former and latter SNPs had significantly highest BMI and TBF compared to other genotype combinations.

Conclusions: UCP3 -55C/T SNP was associated with central obesity among Malaysian participants of Chinese descent. Combinatory genotype analysis showed that BMI and TBF were significantly different among UCP1 -3826A/G and UCP3 -55C/T genotype combinations, suggesting the existence of a gene interaction between UCP1 and UCP3 in influencing obesity and adiposity. (Ethn Dis. 2015;25[1]:65–71)

Key Words: Uncoupling Protein 1, Uncoupling Protein 3, Single Nucleotide Polymorphism, Obesity, Malaysia

INTRODUCTION

The prevalence of obesity is rising at an alarming rate worldwide including Malaysia, where the latest global meta-analysis reported the combined prevalence of overweight and obesity at 43.8% and 48.6% among men and women aged >20 years, respectively. Obesity is a multifactorial disorder that involves an imbalance between genetic and environmental factors, causing an imbalance between energy intake and expenditure. There are more than 120 candidate genes that have been linked with obesity-related phenotypes, and uncoupling proteins (UCPs) genes are a family of them.

Uncoupling proteins, with approximately 32 kDa mitochondrial transporters present in the inner membrane of mitochondria, play an important role in allowing protons to reenter the mitochondria without using energy, thus, energy is released by heat. Three distinct UCPs namely UCP1, UCP2 and UCP3 have been identified. UCP1, an integral component of the mitochondrial inner membrane solely expressed in brown adipose tissues, plays a role in increasing thermogenesis that contributes to energy expenditure in humans. On the other hand, UCP3 is predominantly found in skeletal muscles, and plays a role in energy homeostasis and substrate oxidation.

The relationship between UCP loci and susceptibility to obesity and its related traits has been investigated in a number of human genetic studies and particular attention has been focused on the -3826A/G (rs1800592) polymorphism in the promoter region of UCP1 gene and the -55C/T (rs1800849) polymorphism in the promoter region of UCP3 gene. The results of these studies are inconsistent, with some of them demonstrating associations between one or both of these polymorphisms with obesity and related traits such as type 2 diabetes, while others failed to detect any association.

Therefore, our study aimed to determine the association of UCP1 -3826A/G and UCP3 -55C/T SNPs with obesity (assessed by BMI), overall adiposity (assessed by total body fat percentage – [TBF]) and central adiposity (assessed by waist-to-hip ratio [WHR]) in a representative sample of the multi-ethnic Malaysian population.

METHODS

Participants

Convenience sampling was conducted from Oct–Dec 2008 and Feb–

Our study aimed to determine the association of UCP1 -3826A/G and UCP3 -55C/T SNPs with obesity, overall adiposity and central adiposity in a representative sample of the multi-ethnic Malaysian population.

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Ethnicity & Disease, Volume 25, Winter 2015