RELEVANCE OF PEROXISOME PROLIFERATOR-ACTIVATED RECEPTOR-GAMMA IN OBESITY

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ABSTRACT

The peroxisome proliferator-activated receptor gamma (PPAR-γ) plays an important role in the regulation of the transcription of several genes involved in adipocyte differentiation, lipid oxidation, glucose and lipid metabolism, insulin sensitivity, angiogenesis and inflammation. The Pro12Ala polymorphism in PPAR-γ2 is frequently associated with type-2 diabetes while its association with obesity in different populations are contradictory. Its association with obesity among Caucasians, Mediterranean and Asian population are widely studied; however, no study was conducted among the Malaysian Malays. This study investigates the influence of Pro12Ala missense mutation of PPAR-γ on the risk of obesity and obesity-related phenotypes in Malaysian Malays which include effects of dietary fat intake and the level of physical activity with BMI. We recruited 40 obese and 40 lean individuals aged from 18 to 65 years old and conducted anthropometrical examinations for the calculation of Body Mass Index (BMI) and waist-hip ratio (WHR). Body fat mass as well as fat percentage was also measured using bioelectrical impedance analyser TANITA® SC-330 (TANITA Corp, Japan). Indication for the level of physical activity was derived from self-administered long form International Physical Activity Questionnaire (IPAQ) while 24-hour dietary recall was conducted by trained dieticians for the calculation of dietary fat intake. The Pro12Ala polymorphism was assessed using Allele-specific PCR. Seven (8.75%) obese subjects and two (2.50%) lean subjects had Pro/Ala genotype while the others had Pro/Pro genotype. Individuals with the Pro/Ala genotype was found to have significantly higher waist-hip ratio (p=0.029) compared to those with the Pro/Pro genotype. There is however no significant association between the Pro12Ala polymorphism and obesity (p=0.154) at 95% CI that could be due to small sample size.

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CHAPTER 1

INTRODUCTION

1.1   General background

World Health Organization (WHO) defines overweight and obesity as abnormal or excessive fat accumulation that presents a risk to health (WHO 2012). It is a multifactorial disease with many complications of metabolic disorders such as diabetes and cardiovascular disease. Unfortunately, obesity has become a major problem globally, in many developed and developing countries including Malaysia. Although obesity is frequently associated with environmental factors such as diet and lifestyle, previous studies had proven that genetic factors also play an important role in the development of obesity (Loos et al., 2003). One of the genes that have been associated with obesity is the peroxisome proliferator-activated receptor gamma (PPAR-γ) gene. From previous literatures, Pro12Ala polymorphism in the PPAR-γ gene was shown to be associated with obesity. A recent study by Prakash, J., et al., 2012, showed that the Pro12Ala polymorphism of PPAR-γ is associated with obesity among Asian Indians in the metropolitan cities in north India while a study conducted among Korean subjects suggest that the Pro12Ala mutation in PPAR-γ is not associated with obesity and may not be an important determinant of obesity in Korean subjects (Oh, et al., 2000). The differences in findings with regards to the difference in study population has encouraged us to further study on the association of the Pro12Ala polymorphism of PPAR-γ gene with obesity in Malaysia.