Identification of a Regulatory Single Nucleotide Polymorphism in the Adiponectin (APM1) Gene Associated with Type 2 Diabetes in Han Nationality

MIN YANG⁵, CHANG-CHUN QIU⁷, WEI CHEN⁵, LING-LING XU¹, MIAO YU⁵, AND HONG-DING XIANG⁵,²

¹Department of Endocrinology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences, Beijing 100730, China; ²National Laboratory of Medical Molecular Biology, School of Basic Medicine, Peking Union Medical College, Institute of Basic Medical Sciences, Chinese Academy of Medical Sciences, Beijing 100005, China

Objective To identify the genetic defects of the adiponectin (APM1) gene that contribute to the development of type 2 diabetes (T2DM) and determine the functional single nucleotide polymorphisms (SNPs) in the APM1 gene associated with T2DM in Han nationality. Methods The APM1 gene 5’-UTR was screened by direct sequencing to identify common polymorphisms. Identified SNPs were genotyped in 585 nondiabetic controls, 278 subjects with impaired glucose intolerance (IGT) and 212 patients with T2DM. The functions of SNPs in the regulatory region were assessed by reporter gene assay. Possible association between SNPs and plasma APM1 levels or metabolic parameters was statistically assessed. Results Three SNPs were identified in the APM1 gene 5’-UTR. A case-control study revealed that SNP -11377 G/C had significant differences in allele frequencies between T2DM patients and nondiabetic controls (G 0.314/C 0.686 vs. G 0.265/C 0.735, P = 0.03). Haplotype analysis of three SNPs in the APM1 gene showed that no significant association of haplotypes with T2DM. IGT was detected in the present study. Reporter gene assay showed that SNP did not influence the transcription efficiency in the 3T3-L1 cell line. Conclusion SNP -11377 G/C in the proximal promoter region of the APM1 gene contributes to the development of T2DM in Han nationality but may not be a functional SNP in the APM1 gene.

Key words: Diabetes; Adiponectin; Single nucleotide polymorphism; Reporter gene; Promoter

REFERENCES


(Received December 5, 2007  Accepted July 2, 2008)