Abstract

Pleiotropic effects of single nucleotide polymorphophisms of EDIL3 gene: Association with cancer, obesity, and type 2 diabetes

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Background: Genetic variants are being increasingly recognized to be associated with the comorbidity of cancer, obesity, and type 2 diabetes. Laboratory studies show that Epidermal growth factor-like repeats- and discoidin I-like domains-containing protein 3 (EDIL3) is expressed in some forms of cancers and human cancer cell lines, and over expression of EDIL3 may promote cancer growth, progression, invasion, and recurrence. Genomic copy number variation survey found that genetic variants of EDIL3 might also be associated with metabolic diseases such as obesity. We examined genetic association of single nucleotide polymorphisms (SNPs) in EDIL3 with cancer and metabolism-related diseases including obesity and type 2 diabetes. Objectives: The purposes of this study were to investigate the association of EDIL3 SNPs with cancer, obesity, and type 2 diabetes. Methods: The subjects are from the publicly available data of the Marshfield sample which is a Genome-Wide Association Study on Cataract and HDL. Cases of cancer were defined as any diagnosed cancer excluding minor skin cancer. Obesity was determined as a body mass index (BMI) $\geq$ 30. We examined the genetic associations of 79 SNPs with cancer (1,442 cancer cases and 2,122 controls), obesity (1,442 obese and 2848 non-obese), and type 2 diabetes (878 diabetes and 2686 non-diabetes). Multiple logistic regression models, adjusted for age and sex, were performed using PLINK software (version 1.07). The odd ratios (ORs) and 95% confidence intervals (CIs) were calculated. Results: Within the EDIL3 gene, we identified nine SNPs statistically significantly associated with cancer risk (top SNP rs350477 with p = 1.28×10^{-5}). Furthermore, we also found five SNPs significantly associated with obesity (top SNP rs3776901 with p = 6.09×10^{-4}) and five SNPs associated with type 2 diabetes (top SNP rs1159734 with p = 3.7×10^{-3}). In addition, haplotype analyses showed that the C-G haplotype from rs2269290 and rs350477 revealed significant associations with cancer (p = 1.28×10^{-5}). Conclusions: These findings provide first evidence of common genetic variants in the EDIL3 gene influencing the comorbidity of cancer, obesity, and type 2 diabetes. These findings offer the potential for new insights into the pathogenesis of 3 conditions.

Chronic disease management and prevention Clinical medicine applied in public health Epidemiology Public health or related research