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A multifactor dimensionality reduction model of gene polymorphisms and an environmental interaction analysis in type 2 diabetes mellitus study among Punjabi, a north India population

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The effects of any single genetic variation for a common complex disease such as T2DM may be dependent on other genetic variations (gene-gene interactions) and environmental factors (gene-environment interactions). Multifactor Dimensionality Reduction (MDR) method helps in detection and characterization of susceptibility in common complex multifactor disorders like Type 2 Diabetes Mellitus (T2DM). Unfortunately, negligible studies are available with this model approach to detect the status of T2DM in north Indian population. Hence, the major objectives of the present study were to investigate the association of ENPP1 K121Q (rs1044498), TCF7L2 G>T (rs12255372) and GYS1 XbaI (A1>A2) (rs8103451) gene variants with T2DM in the north Indian population; and to determine whether significant gene-gene and gene-environment (risk factors related to obesity and cardiovascular diseases) interactions exist between these selected genes in affecting type 2 *diabetes mellitus* using MDR analysis. A total of 500 participants consisting of 250 type 2 diabetes mellitus (T2DM) and 250 healthy subjects were recruited for this study. Genotyping was performed by PCR-RFLP method. Anthropometric and physiometric variables such as height, weight, waist circumference (WC), hip circumference (HC), SBP and DBP, were measured using standard protocol. The odds ratio and *Hardy- Weinberg equilibrium* deviation analyses were performed. The gene-gene and gene-environment interactions were performed by multifactor dimensionality reduction (MDR) analysis. In results it was observed that two genes ENPP1 and TCF7L2 are associated with T2DM. However, an insignificant association of the XbaI (A1>A2) polymorphism in GYS1 gene with T2DM was demonstrated. The gene-gene interactions revealed that all the three SNPs have a synergistic effect with each other. The MDR method for gene-environment interactions showed all interaction models first to ninth order interactions for T2DM patients as significant for susceptibility of obesity. The results showed that both the genes ENPP1 and TCF7L2 interacting with WHR and WC increase the susceptibility of obesity many folds among T2DM patients and non-diabetic controls. In conclusion, it is suggested that pathogenesis of T2DM, obesity and hypertension involves interplay of a variety of susceptibility alleles and environment. The gene-gene and gene-environment interactions are not only possible, but, are probably ubiquitous in determining the susceptibility of complex human diseases. Further studies on epistatic interactions are warranted to elucidate their possible underlying role in pathogenesis of T2DM.

Biography

Raman Kumar has his expertise in Genetic Epidemiology and Molecular Biology. His PhD thesis evaluated the cardio-vascular risk factor and familial aggregation of blood pressure with respect to anthropometric variables in a scheduled caste population in Punjab. It was the first of its kind from northern India. He is well versed with modern molecular biology techniques. He has a passion for gaining knowledge as much as possible from various fields.

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Notes:

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