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Genetic association of TNF-α, IL-10, NPY and IL-1β polymorphisms with susceptibility to type 2 diabetes mellitus: A case-control study of Gujarat population

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Type 2 diabetes mellitus (T2DM) is a metabolic disorder arising from complex interaction between genes and environment. Elevated concentrations of cytokines and acute-phase proteins have been associated with the development of T2DM. Tumor Necrosis Factor-α (TNF-α) inhibits insulin receptor signaling. IL-10 plays a role in repression of proinflammatory cytokines such as TNF-α, interleukin-1β (IL-1β) and has pleiotropic effects in immunoregulation and inflammation. IL-1β induces biosynthesis and release of neuropeptide-Y (NPY) leading to impaired insulin secretion, decreased beta cell proliferation, and apoptosis. In the present study, we evaluated the association of TNF-α, IL-10, IL-1β and NPY polymorphisms with T2DM subjects from Gujarat population. We have investigated five polymorphisms i.e., -238 (G/A; rs361525), -308 (G/A; rs1800629), -857 (C/T; rs1799724), -863 (C/A; rs1800630) and -1031 (T/C; rs1799964) at the promoter region of the TNF-α involving 315 patients and 525 controls using polymerase Chain Reaction-Restriction Fragment Length Polymorphism (PCR-RFLP) technique. Overall, the distribution of the genotype and allele frequencies of TNF-α polymorphisms (TNF-α-238: $p<0.0001$ and $p<0.0001$, TNF-α-308: $p<0.0001$ and $p<0.0001$, TNF-α-857: $p=0.025$ and $p=0.040$, TNF-α-863: $p<0.0001$ and $p<0.0001$, and TNF-α-1031: $p=0.012$ and $p=0.037$) were significantly different between patients and controls which suggests that these polymorphisms may be a genetic risk factor for T2DM. Genetic association analysis of IL-10 promoter polymorphisms: -819 C/T (rs 1800871), -592 C/A (rs 1800872), -1082 G/A (rs 1800896) is being attempted. Investigation of NPY exon2 T/C (Leu7Pro; rs16139), NPY promoter T/C (rs16147) and IL-1β C/T (rs16944) polymorphisms was carried out by PCR-RFLP technique involving 456 T2DM patients and 989 controls. Our results report significant association of both exon 2 T/C and promoter T/C polymorphisms of NPY ($p=0.0002$) in patients with T2DM. Interestingly, IL-1β C/T polymorphism also showed significant association ($p<0.0001$) with T2DM. Our results suggest that the well documented structural as well as promoter polymorphisms of NPY and promoter polymorphisms of IL-1β and TNF-α may have crucial role in susceptibility to T2DM.

Biography

Rasheedunnisa Begum has completed her Ph.D. at the age of 28 years from A.M. University, Aligarh, India and postdoctoral studies from National Institute of Immunology, New Delhi, India. She is a professor in Department of Biochemistry at the M. S. University of Baroda, Vadodara, India. She has published more than 35 papers in reputed national and international journals and serving as reviewer for peer reviewed international and national Journals. She is a member of various selection committees at reputed institutes of India. She is Scientific Consultant of Indian Red Cross Society, India.

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