Diabetes and Our Genes

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Type 1 diabetes (T1D) and T2D which affect approximately 200 million adults worldwide are diseases characterized by hyperglycemia. Diabetes results from metabolic consequences of beta cell dysfunction and/or the inability of insulin to properly regulate levels of blood glucose. Approximately 90% to 95% of the affected individuals are afflicted with T2D. Although T1D and T2D have some common clinical features, these diseases are the results of different biological mechanisms. T1D, which is the result of autoimmune destruction of the beta cells of the pancreas, typically presents in childhood. Human leukocyte antigen locus is the major susceptibility locus for T1D. T2D which occurs by reduced insulin secretion due to abnormalities in pancreatic beta cell function or decreased beta cell mass, typically presents in adults older than 40 years of age. Although there are some genetic similarities that exist between T1D and T2D, studies support the fact that these are two distinct diseases. Also, there is another type of diabetes existing: latent autoimmune diabetes in adults. Environmental and genetic factors play role in the etiology of diabetes. There is a strong evidence for the genetic contribution that includes concordance rates that are higher in monozygotic twins when compared to dizygotic twins. It has been proven to be more challenging to identify the genes for T2D. But emerging of non-hypothesis-driven molecular genetics techniques such as Genome-Wide Association Studies and next generation sequencing have given great opportunity to find disease related loci. Maturity-onset diabetes of the young (MODY) which is a special form of diabetes occasionally seen in patients before the age of 25 and is inherited in an autosomal dominant fashion. The prevalence of MODY has been estimated to be 2-5% of all diabetes cases. The patients in this group have mutations in the limited number of the genes such as *HNF1A* and *GCK*. As a result, diabetes has different subtypes all of which have different genetic backgrounds.

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Approach to Monogenic Diabetes

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Stefan S Fajans has described the diabetes mellitus and well-controlled metabolic syndrome with the help of sulfonylurea in non-obese children and adolescents with the mild symptoms for the first time in 1960. In spite of the unapparent difference between type 1 diabetes mellitus (T1DM), all of the clinical findings of this newly described DM would have clarified after 15 years and it has been identified as 'Maturity Onset of Diabetes of the Young' (MODY). After the last classification done by American Diabetes Association and World Health Organization, MODY has been put in the 'beta cell genetic dysfunction' group. They constitute 2-5% of all diabetes. In recent studies, the prevalence is 45/1 000 000 in children and 100/1 000 000 in adults. 80% of the cases have been shown to take either T1DM or T2DM diagnoses mistakenly. The description of genetic subgroups is vitally important for the response achieved after the treatment. Monogenic diabetes is the diabetes resulted after either one or more mutations at a single gene. Mutation could have either occurred *de novo* or could have been inherited dominantly or recessively. There are more than 40 genetic subtypes of MODY. The diagnosis could be made with molecular testing with 1-2% rate. In childhood, almost all of the monogenic diabetes would occur with the gene mutations controlling beta cell functions and very seldom with the mutations resulting in insulin resistance. Most important approach is to think monogenic diabetes as a diagnosis. Because it is an autosomal dominant disease, a detailed anamnesis is vitally important. Monogenic diabetes should always be in mind for the cases having a diagnosis inconsistent with their current clinical situations: 1) Whatever the age of the diabetic patient, all of the diabetic patients having a diagnosis within 6 months, 2) Unprogressive, moderate fake bad scale elevations, 3) Patients with clinical findings inconsistent with T1DM; a) diagnosis <6 months, b) family history with affected mother or father, c) not having achantosis nigrigans. There are 6 reported MODY genes, however, up to 13 types (very rare) has been described in recent years.

Key word: Monogenic diabetes