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THE ASSOCIATION OF GENETIC POLYMORPHISMS WITH DIABETES MELLITUS TYPE 1

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One of the most common endocrine disorders in children and adolescents, Diabetes mellitus (DM), is a chronic, polygenic and complex illness. Based on etiology, DM can be divided into two basic groups: Diabetes mellitus type 1 (DMT1) and Diabetes mellitus type 2 (DMT2). DMT1 is a disease mediated by immune mechanisms based on the autoimmune destruction of insulocyte by immunoreactive T cells and antibodies which leads to insulin resistance and hyperglycemia syndrome.

Several different molecular mechanisms contribute to the destruction of β-cells of Langerhans islets, such as: the production of autoantibodies directed against antigens on insulocytes, lysis of Langerhans islets mediated by cytotoxic CD8+ T lymphocytes, local production of cytokines (TNF and IL-1) by macrophages that damage insulocytes and delayed hypersensitivity reactions mediated by CD4+ Th1 lymphocytes.

The most important genes that show a high degree of association with DMT1 are found in the region which encodes MHC (major histocompatibility complex) of molecules class I and II. However, there is very strong evidence of association of other genes (outside of the MHC gene domain) with the expression of DMT1. These are: insulin gene (INS), Cytotoxic T-Lymphocyte Associated Protein 4 (CTLA4), Protein Tyrosine Phosphatase Non-Receptor Type 22 (PTPN22), Protein Tyrosine Phosphatase Non-Receptor Type 2 (PTPN2), C-type lecithin gene (CLEC16A, KIAA0350), interleukin 2 receptor α gene (IL2RA/CD25), interferon-induced helicase gen domain (IFIH1), Potassium Voltage-Gated Channel Subfamily J Member 11 (KCNJ11), Platelet and T Cell Activation Antigen 1 (CD226), vitamin D receptor gene (VDR), tumor necrosis factor gene (TNF) and lymphotoxin-α (LTA). In addition to these genes, researchers are still searching for other genes that are associated with the appearance and expression of DMT1.

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