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Prevention of Type 1 Diabetes by Regulation of the Immune System

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Abstract

Immune mediated beta cell destruction is one of the major causes for type1 diabetes mellitus, which makes immune system a primary target for intervention for prevention of type1 diabetes. This review is done to know the immunological interventions for T1DM prevention viz immunosuppressive agents, Antigen Specific Immunotherapy, Anti-CD3 Antibodies and Anti CD20 antibodies.

Keywords: Diabetes mellitus; Immunosuppressive agents; Anti CD3 Antibodies

Introduction

Diabetes mellitus is a metabolic disorder characterized by hyperglycemia due to absolute and relative insulin deficiency. Type 1 diabetes mellitus also known as insulin dependent diabetes mellitus accounts for 5-10% of all causes of the syndrome, is a T-cell–mediated autoimmune disease that begins, in many cases, three to five years before the onset of clinical symptoms, continues after diagnosis, and can recur even after islet transplantation.1-3 Theeffector mechanisms which is responsible for the destruction of beta cells involves the action of cytotoxic T cells as well as soluble T-cell products [1,2].

Immunological Intervention for Treatment of Diabetes Mellitus Type 1 Immunosuppressive Agent

These are the agents which decreases the destruction of pancreatic beta cells. One of the example for the immunosuppressive agent is Cyclosporin A which blocks cytokine production by all T cells thus limiting production of the T-cell, it also prevents the secretion of cytokines, which is animportant direct mediators of beta cell destruction, these includes Interferon C (IFN-c) and Tumor Necrosis Factor a (TNF-a) [3,4]. Cyclosporine A, hasbeen reported to decrease destruction of beta cells [5]. Although Cyclosporin A targeted cytokine production, other broadspectrum immunosuppressive regimens also may be effective in preventingthe loss of insulin production [6]. These immunosuppressive agents are nephrotoxic and have other side effects making it highly inappropriate for long term uses [6].

Antigen Specific Immunothreapy

These strategies are based on the factthat a response to antigen is affected by many factors which include the antigenic signal strength, co-stimulation, and the cytokine environment. Therefore, by modulating these parameters, it is possible to divert pathogenic responses of the antigens into a protective, nonpathogenic response [4,6]. In addition to modifying the strength of the T-cell receptor signal with altered ligands or adjuvants, the prevention of antigen can be altered [7,8,9]. By this way type 1 Diabetes Mellitus can be prevented by inducing immune regulation to the administrated antigen.

Anti-Cd3 Antibodies

Anti CD 3 molecules contain FcR- binding portion which is responsible for T-Cell activation signals and other effects of T-Cells, thus by eliminating FcR binding portion of Anti CD3 molecule type 1 diabetes mellitus can be prevented. It has been reported that non-FcR binding antibody induces previously activated T-Cells but naïve cells were unaffected. Also, the other inhibitory effects were limited to the previously activated T-helper cells- which are involved and are present in pancreas of subjects with type1 diabetes mellitus. Anti CD 3 antibody molecule may induce tolerance to autoimmune destruction of pancreatic beta cells preventing diabetes mellitus type1. The non FcR binding antibodies activates signal to T cells resulting in release of Interleukin 10 (IL 10). The conventional Anti CD3 Antibodies release IFN-c [10-13].

An Anti-Cd20 Antibody

These molecules inhibits B cells, it has been reported that anti CD 20 Antibodies also provoke C-peptide responses. Through their action prevents type1 diabetes but long term action have not been studied in detail [4].

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