

Rebooting the immune system: The science behind type 1 diabetes innovations¹

Rakaesh Goyal*

Department of Pharmacology, Delhi Pharmaceutical Sciences and Research University, New Delhi, India

Introduction

Type 1 diabetes (T1D), an autoimmune disease where the immune system attacks insulin-producing beta cells in the pancreas, is a condition that has been challenging to treat. Unlike Type 2 diabetes, which primarily involves insulin resistance, Type 1 diabetes results in complete insulin deficiency. Traditionally, managing T1D has required lifelong insulin injections, glucose monitoring, and a careful balance of diet and exercise. However, recent advances in immunotherapy and regenerative medicine are offering new hope for a "reboot" of the immune system, potentially revolutionizing the treatment and even offering a cure [1].

T1D typically begins in childhood or adolescence and occurs when the body's immune system erroneously identifies the insulin-producing beta cells in the pancreas as harmful invaders. This immune attack, driven by autoantibodies and immune cells like T-cells, gradually destroys beta cells, resulting in the body's inability to produce insulin. Without insulin, glucose cannot enter the cells, leading to high blood sugar levels. Over time, this can cause severe complications such as kidney damage, neuropathy, and cardiovascular issues [2].

Unlike some autoimmune diseases where the immune system's errant activity can be suppressed or modulated with medications, Type 1 diabetes has posed a particular challenge because the immune system's attack on beta cells is not easily reversible. However, recent breakthroughs in understanding the mechanisms behind this immune response and the development of novel therapies are offering promising alternatives to current insulin therapy [3].

One of the most promising areas of research in T1D treatment focuses on immunotherapy. Researchers aim to stop or slow the immune system's attack on beta cells by modulating the immune response without compromising the body's ability to fight infections. There are several strategies under investigation [4].

This approach seeks to retrain the immune system to stop attacking the pancreas. One method involves using a modified version of the target antigen (in this case, a component of the beta cell) to "teach" the immune system to recognize it as harmless. Clinical trials, such as those using **teplizumab**, an anti-CD3 monoclonal antibody, have shown some success in

delaying the progression of T1D by preventing further damage to beta cells. Teplizumab works by selectively modulating T-cells, which are primarily responsible for the autoimmune attack [5].

Researchers are exploring vaccines designed to prevent the immune system from attacking beta cells. These vaccines would ideally work by boosting the immune system's tolerance to insulin-producing cells. One example is the **DiaPep277** vaccine, which has shown potential in slowing the progression of T1D by promoting immune tolerance [6].

Since B cells produce antibodies that target beta cells, therapies aiming to deplete or alter the function of B cells could also prevent autoimmune attacks. Certain monoclonal antibodies, such as **rituximab**, have been studied for their ability to deplete B cells and prevent the destruction of beta cells [7].

In addition to targeting the immune system, regenerative medicine is another exciting frontier in the treatment of Type 1 diabetes. The idea is to restore the body's ability to produce insulin by regenerating or replacing the lost beta cells. This could be done through several approaches. Stem cells have the potential to differentiate into various types of cells, including insulin-producing beta cells. Several research teams are working on techniques to generate functional beta cells from stem cells in the lab. For example, scientists have successfully derived beta-like cells from human pluripotent stem cells. These cells have shown the ability to secrete insulin in response to glucose. Although clinical use is still years away, stem cell therapy offers a long-term solution by potentially reversing the loss of insulin production [8].

A more established technique, though still in its early stages for widespread clinical use, is the transplantation of islet cells from a donor pancreas into a patient with T1D. While this method has had success in certain cases, it is hampered by the limited availability of donor organs and the need for lifelong immunosuppression to prevent rejection [9].

Gene editing technologies, such as CRISPR, offer the potential to modify a patient's cells to produce insulin. Researchers are exploring the possibility of inserting a functional copy of the insulin gene into a patient's cells, effectively "reprogramming" them to produce insulin. While this approach is still in its infancy, it represents a potential future avenue for a cure.

*Correspondence to : Rakaesh Goyal, Department of Pharmacology, Delhi Pharmaceutical Sciences and Research University, New Delhi, India. E-mail: rkesh@goyal

Received: 30-Aug-2024, Manuscript No. AADY-25-158379; Editor assigned: 02-Sep-2024, PreQC No. AADY-25-158379 (PO); Reviewed: 11-Sep-2024, QC No. AADY-25-168379; Revised: 16-Sep-2024, Manuscript No. AADY-25-158379; Published: 25-Sep-2024, DOI: 10.36841/aady-8.5.225

Alongside immunotherapies and regenerative medicine, advancements in artificial intelligence (AI) are transforming how T1D is managed. AI algorithms are being used to improve insulin delivery systems, such as insulin pumps and continuous glucose monitors, by enabling more precise and dynamic control of blood sugar levels. These smart systems can anticipate blood sugar fluctuations and adjust insulin delivery accordingly, minimizing the risks of hyperglycemia and hypoglycaemia [10].

Conclusion

While Type 1 diabetes remains a challenging and complex disease, the progress made in understanding its underlying immunological causes and developing innovative treatments is truly transformative. Immunotherapies that target the autoimmune process, coupled with regenerative medicine approaches that aim to restore insulin production, offer the potential to change the lives of millions of individuals living with T1D. These innovations, along with advancements in AI and personalized medicine, may soon provide a future where Type 1 diabetes is no longer a lifelong burden but a manageable, and perhaps even reversible, condition.

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