

Review

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Review

Novel Treatment Modalities of Type 1 Diabetes Mellitus: Opportunities and Challenges

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Abstract: Despite the effectiveness of insulin injections in managing hyperglycemia in Type 1 Diabetes, they fall short in addressing autoimmunity and regenerating damaged islets. This review aims to explore the potential of various treatment modalities for T1DM, including mesenchymal stem cells (MSCs), MSC-derived exosomes, gene therapy, islet allotransplantation, and pancreatic islet cell transplantation. **Results:** MSCs demonstrate efficacy in T1DM treatment through immunomodulation and tissue regeneration, although further research is warranted to optimize their therapeutic potential. Gene therapy presents a promising approach despite challenges such as donor shortage and immune rejection. Pancreatic islet cell transplantation emerges as a viable option, albeit with associated risks including graft rejection and the need for immunosuppression. Teplizumab, an FDA-approved humanized monoclonal antibody, revolutionizes the treatment landscape of Type 1 Diabetes by significantly delaying its onset, offering a paradigm shift since the discovery of insulin. **Conclusion:** Ongoing studies and technological advancements in T1DM management offer a promising outlook for improved treatments and possibly even eradication on a global scale. MSCs, MSC-derived exosomes, gene therapy, and pancreatic islet transplantation hold considerable potential.

Keywords: type1 diabetes mellitus; mesenchymal stem cells; gene therapy; pancreatic islet cell transplantation; teplizumab

1. Introduction

Diabetes mellitus (DM) stands as a chronic metabolic disorder increasingly prevalent worldwide. It is marked by either a partial or complete deficiency in insulin secretion, leading to persistently elevated blood glucose levels. This condition often manifests with an array of complications, including macrovascular issues like coronary heart disease and hypertension, as well as microvascular complications such as diabetic foot, diabetic encephalopathy, and diabetic kidney injury. These complications significantly diminish patients' quality of life and decrease their chances of survival. The global impact of diabetes is substantial, imposing a significant economic and systemic burden on healthcare systems. It is estimated that diabetes affects approximately 422 million people worldwide, the majority living in low-and middle-income countries, and 1.5 million deaths are directly attributed to diabetes each year [1]. Type 1 diabetes, affecting five to ten percent of diabetes cases [2], has historically been dubbed "juvenile diabetes" or insulin-dependent diabetes due to its early onset. It is a chronic condition in which the pancreas produces little or no insulin by itself. For people living with diabetes, access to affordable treatment, including insulin, is critical to their survival. Specifically, both the number of cases and the prevalence of diabetes have been steadily

increasing over the past few decades. Management requires life-long insulin replacement with multiple daily insulin injections, insulin pump therapy, or the use of an automated insulin delivery system. In addition to insulin therapy, glucose monitoring with a continuous glucose monitor (CGM) and a blood glucose monitor if a CGM is unavailable is recommended. Furthermore, self-management education and support should incorporate training in glucose monitoring, insulin administration, ketone testing when necessary, nutritional guidance on carbohydrate counting, physical activity, and strategies for preventing and treating hypoglycemia [3].

However, despite the effectiveness of insulin injections in managing hyperglycemia, they fall short in addressing autoimmunity and regenerating damaged islets, which are crucial in Type 1 diabetes management. T1DM is a T-cell-mediated, organ-specific autoimmune disorder which is characterized by beta-cell destruction and decreased insulin production [4]. The pathogenesis of T1D involves the destruction of insulin-releasing pancreatic beta cells, with cellular invasion by both CD4+ and CD8+ T cells, resulting in the reduction of beta cell mass [5]. Environmental exposures, in conjunction with genetic predispositions, play pivotal roles in transitioning from islet autoimmunity to full-fledged T1DM. Although researchers have identified more than 50 genetic loci associated with the disease, HLA polymorphisms contribute substantially, accounting for 40-50% of T1D cases [6,7].

The escalating prevalence of Type 1 Diabetes on a global scale has spurred significant advancements in its treatment over the past two decades. This trend has been particularly driven by two key factors: a focus on improving the quality of life for individuals with T1D and the growing recognition of the potential of regenerative medicine approaches to transform diabetes treatment.

Among these, progress has been achieved in areas such as mesenchymal stem cells (MSCs), gene therapy, pancreatic islet cell transplantation and new drug Teplizumab, leveraging immune modulation strategies, beta cell regeneration, and enhancing engraftment success rates.

This review aimed to explore the emerging landscape of innovative treatment modalities for Type 1 Diabetes Mellitus (T1DM), shedding light on both their opportunities and challenges. By offering actionable recommendations to stakeholders in healthcare, research, and policy domains, our goal is to catalyze progress in the field and improve outcomes for individuals living with T1DM.

2. Materials and Methods

A comprehensive literature search was conducted utilizing PubMed, UpToDate, and Google Scholar electronic databases for pertinent English-language articles based on recent updates in the treatment of Type 1 Diabetes Mellitus. The search criteria incorporated specific keywords, such as: ("Novel" OR "Recent" OR "Updates") AND ("Treatment" OR "Management" OR "Medications") AND ("Type 1 Diabetes Mellitus" OR "Diabetes Mellitus" OR "Diabetes Mellitus Type 1"). Following the removal of duplicates, the obtained results were organized using citation management tools (Zotero). The articles published in the last 5 years were given preference.

3. Results and Discussion

Standard Treatment by Insulin

The current standard treatment for Type 1 Diabetes Mellitus (T1DM) is lifelong insulin replacement therapy. Insulin therapy is aimed to mimic the normal physiological secretion of insulin in response to meals and maintain blood glucose levels within a normal range.

The different types of insulin that can be used for T1DM, include rapid-acting, short-acting, intermediate-acting, and long-acting insulin. The insulin type and regimen chosen depend on several factors, including the patient's blood glucose control, lifestyle, and individual needs. Another essential constituent of T1DM is self-monitoring of blood glucose (SMBG). This involves testing blood glucose levels regularly, usually, multiple times per day, to help adjust insulin doses and monitor blood glucose control.

Additionally, managing Type 1 Diabetes Mellitus (T1DM) involves implementing lifestyle modifications, such as adopting healthy eating habits and maintaining regular physical activity. It is recommended that individuals with T1DM consume balanced meals with an appropriate

carbohydrate intake, timed alongside insulin doses, and incorporate physical activity into their routine. Moreover, education about diabetes and providing support are crucial aspects of T1DM management. Comprehensive education and training on self-management of T1DM, including insulin administration, self-monitoring of blood glucose (SMBG), adopting healthy dietary patterns, engaging in regular physical activity, and effectively managing hypo and hyperglycemia, should be provided to patients and their families [3]. This holistic approach empowers individuals with T1DM to effectively manage their condition and improve their overall quality of life.

Despite significant advancements in insulin, insulin delivery, and glucose monitoring technology, many people with type 1 diabetes still do not achieve their glycemic goals. The substantial burden of type 1 diabetes on patients and their families must be acknowledged. Major challenges include calculating and timing prandial insulin doses, often from foods with unknown carbohydrate content, adjusting food and insulin during exercise, and managing the cost of therapy. The extensive impact of type 1 diabetes can lead to long-term complications, decreased life expectancy, reduced quality of life, and significant financial strain. Additionally, the psychological stress of acute management and the potential for chronic complications further contribute to the burden. This warrants education programs and regular monitoring for "diabetes burnout," which are essential for everyone with type 1 diabetes.

Future perspectives in insulin replacement therapy including the use of artificial pancreas, immune modulation, stem cell mobilization, β cell encapsulation, and incretins could improve graft survival rate and revascularization in transplanted islets. In certain situations, additional medications, such as GLP-1 receptor agonists or SGLT2 inhibitors, are added to insulin therapy to improve blood glucose control and reduce the risk of complications. However, insulin therapy remains the mainstay of T1DM management [2,8].

Mesenchymal stem cells:

The future of diabetes treatment is centered around promoting beta cell regeneration, achievable through self-replication or differentiation from progenitor cells via stem cell therapy. This approach not only tackles autoimmunity but also enhances endogenous insulin production. Multipotent Stem Cells (MSCs) emerge as a promising tool for these strategies, found primarily in the bone marrow but also in various other tissues [9]. MSCs possess the capability for in vitro differentiation into insulin-secreting cells, alongside immunomodulatory effects and the secretion of growth factors and cytokines [10]. They have demonstrated the ability to differentiate into multiple cell types, including islet cells, depending on specific signaling pathways. Notably, MSCs exhibit hypo-immunogenicity and can be home to injured tissue, making them efficient carriers for therapeutic proteins [11].

Traditionally, combating Type 1 Diabetes (T1D) involves depleting antibodies against T-cells, but this method lacks specificity and may lead to complications. MSCs offer an alternative approach by secreting soluble factors that modulate immune responses, providing greater selectivity in targeting hyper-reactive T cells [12]. Clinical trials have shown reduced levels of islet cell antibodies after MSC treatment, suggesting potential immunomodulatory effects. MSCs also induce the production of regulatory T cells, restoring immune balance and protecting beta cells against damage [13,14].

While the direct transformation of MSCs into beta cells remains unclear, systemic treatment with MSCs has been shown to increase beta cell mass and reverse hyperglycemia in streptozotocin-induced diabetic rats [15]. These findings suggest the potential of MSCs in promoting beta cell regeneration and improving glucose metabolism, offering promise for T1D treatment.

Several successful attempts have been made to generate insulin-producing cells in vitro through the trans-differentiation of MSCs. The first report in 2004 showcased the in vitro trans-differentiation of rat MSCs into functional insulin-producing islet cells, effectively controlling blood glucose levels in diabetic rats [16]. The transcription factor Pdx-1 played a pivotal role in facilitating the efficient trans-differentiation of MSCs into beta cells [9,17,18].

Other studies have elucidated the roles of various transcription factors such as paired box gene 4 (PAX4), neurogenin 3 (Ngn3), forkhead box protein A2 (FOXA2), hepatocyte nuclear factor 6

(HNF6), glucagon-like peptide-1 (GLP-1), and epidermal growth factor (EGF) in promoting beta cell regeneration [9,19–22]. Additionally, MSCs have been proposed as a potential source of 'artificial' human islets in vitro due to their ability to differentiate into glucagon and somatostatin-expressing cells [9,23]. Subsequent studies have further demonstrated the formation of islet-like clusters in vitro from MSCs with appropriate stimulation [7,22,23]. These findings underscore the potential of MSCs in generating insulin-producing cells and advancing the field of diabetes treatment. Recent advancements in tissue engineering have highlighted the potential necessity of a biocompatible scaffold for the in vitro generation of artificial islets with functional vasculature from stem cells [26]. However, it is crucial to approach these reports with caution due to the challenges encountered, including the failure to generate functional islets as a whole. This failure can disrupt the balance between insulin and glucagon, potentially leading to complications. Additionally, there have been concerns regarding the tumorigenicity of genetically modified insulin-producing cells [9]. Hence, while tissue engineering holds promise for the development of artificial islets, further research is warranted to address these challenges and ensure the safety and efficacy of such approaches in diabetes treatment.

Despite its potential, the use of MSCs in Type 1 Diabetes therapy poses certain challenges that warrant further investigation. Firstly, MSC therapy, while promising, may not sufficiently address the autoimmune aspect of T1D, necessitating additional immunosuppressive factors to prevent acute autoimmunity. Secondly, the lack of clarity regarding appropriate homing factors towards the pancreas presents an obstacle for MSCs to effectively target desired sites. Additionally, concerns related to the potential contamination of MSCs and the maintenance of stem-cell-like properties to prevent tumorigenicity add complexity to large-scale manufacturing processes. Lastly, the cost-effectiveness of MSC therapy must be carefully evaluated and compared with traditional immunosuppressive therapies to ensure optimal outcomes. Further research is crucial to address these limitations and fully harness the therapeutic potential of MSCs in T1D treatment [9].

Moreover, Mesenchymal Stem Cell Exosomes (MSC-Exos) emerge as another promising approach for managing Diabetes Mellitus. These extracellular vesicles, possessing the same bi-lipid cell membrane as MSCs, have demonstrated effectiveness in various studies focused on tissue repair, including spinal cord, kidney, liver, cardiovascular, and skin injuries [27–29]. Primarily involved in processes such as angiogenesis, cell proliferation, and immune regulation, MSC-Exos exhibit low immunogenicity and offer advantages such as easy storage and transport. Their regenerative properties closely resemble those of MSCs, rendering them suitable for repairing a wide range of organ damage associated with DM [27]. Further research into MSC-Exos holds the potential for advancing therapeutic approaches to manage DM effectively. Additionally, MSC-Exos exhibits the capacity to leverage the duodenal homeobox 1 pathway, thereby promoting the regeneration of pancreatic beta cells and enhancing insulin secretion [30].

Additionally, they possess the ability to attract pancreatic tissue. Further research has indicated their effectiveness as therapeutic and regenerative agents in Type 1 Diabetes (T1D) by modulating levels of regulatory T cells, interleukin (IL)-4, IL-10, and transforming growth factor β (TGF- β), consequently improving the autoimmune response in diabetic mice [27,31–33]. Moreover, MSC-Exos has demonstrated efficacy in addressing complications associated with diabetes, such as diabetic wounds, nephropathy, and retinopathy [27].

Gene Therapy

Human Gene Therapy, which involves the transfer of engineered genetic material into human cells via viral transduction for disease treatment, employs various techniques to achieve therapeutic outcomes. The process of transferring exogenous DNA to cells and tissues can be accomplished using two main methods: viral and non-viral methods [34]. In the context of Type 1 Diabetes treatment, several delivery vehicles are utilized, each with its advantages and disadvantages. These vehicles include viral vectors such as adenovirus, adeno-associated virus (AAV), and lentivirus, as well as non-viral vectors like plasmid DNA, liposomes, and polymeric nanoparticles. Each delivery vehicle offers unique characteristics that make it suitable for specific applications in gene therapy. However,

they also come with limitations such as immunogenicity, size constraints, and efficiency of gene transfer. Careful consideration of these factors is necessary when selecting the appropriate delivery vehicle for gene therapy in Type 1 Diabetes.

Given knowledge of the desired target whose function needs to be suppressed, the suppression of gene expression, along with gene replacement or augmentation, is beneficial for achieving the endpoint of gene therapy. Nucleic acids as recombinant plasmid DNA and replication-defective viruses have been the leading vectors in gene therapy trials [35]. Recent techniques involve the combination of small interfering RNA (siRNA) and peptide nucleic acids (PNAs) with nucleic acids [36]. In addition to these mainstays, protein duction domains, naked oligonucleotides and liposome formulations have been utilized in gene therapy. However, viral vectors have been extensively used in gene therapy studies for diabetes mellitus type 1 to engineer islets, beta cell surrogates, immune cells, or specific anatomical sites [37].

Gene therapy holds significant promise as a therapeutic approach for Type 1 Diabetes (T1D), particularly through immunomodulation, transplantation, and the development of surrogate beta cells. The autoimmune response targeting beta cells in T1D suggests that certain factors from these cells could be harnessed to regulate the immune system. Beta cell-restricted proteins have been identified as potential autoantigen triggers for T cells, indicating a possible avenue for intervention [37]. Additionally, introducing genetically modified or non-modified immune cells has shown promise in halting the progression of diabetes, highlighting the potential for immunomodulation in T1D therapy [37,38]. Clinical studies have demonstrated the effectiveness of various approaches, including the use of TGF- α , soluble IFN- γ receptor, viral vectors encoding IL-4 & IL-10, regulatory T-cells CD4⁺ CD25⁺, NK-T, and CD8⁺ CD282 cells, in reducing the progression of T1D by suppressing auto-reactive T-cells and amplifying regulatory T-cells [37,39–44]. Transplantation of intact islet Langerhans cells, once considered impractical due to the need for multiple donors and lack of long-term control over blood sugar levels, has been revisited [37,45]. By locally expressing immunoregulatory genes and trophic factors such as VEGF and NGF, islet transplants can create a conducive environment for engraftment, while the expression of free-radical scavenging proteins and anti-inflammatory agents by islet cells can enhance graft survival [37]. Moreover, surrogate beta cells offer a promising approach by transferring glucoregulatory genes into tissues less susceptible to autoimmune attacks, such as hepatocytes, skeletal muscle cells, intestinal K cells, and hypothalamic-pituitary cells [37,46]. Transcription factors like PDX-1 and adenoviral vectors encoding betacellulin or PAX-4 have been shown to generate functional beta cells, leading to diabetes reversal [33,47,48]. Gene therapy can also modify non-beta cells like mesenchymal stem cells and hematopoietic stem cells into beta cell lineage, offering potential surrogates [49,50]. While immortalized beta cells have been successful, concerns about oncogenic transformation persist [39]. Continued research into cell cycle control in beta/neonatal islet cells may uncover critical insights for promoting in vivo growth, maintenance, and lifespan extension, further advancing gene therapy as a treatment for T1D [39].

Gene therapy for T1DM offers a promising route to achieving near-normal blood glucose levels and potentially curing the disease. However, it is accompanied by several adverse effects and challenges that need to be carefully managed and mitigated. These include risks of insertional mutagenesis, host immunogenicity, toxicity, autoimmune reactions, off-target effects, variable efficacy, long-term safety concerns, technical and delivery challenges, and ethical considerations. Continued research and optimization are essential to improve the safety, efficacy, and acceptance of gene therapy as a viable treatment for T1DM.

Pancreatic Islet Cell Transplantation

Over the past thirty years, pancreatic islet isolation and transplantation techniques have turned from a rare, experimental procedure to a routine clinical procedure with predictable efficacy for selected patients with type 1 diabetes mellitus [51]. The treatment is offered only for selected patients with unstable T1DM and hypoglycemia unawareness, severe hypoglycemic episodes, and glycemic lability who cannot be stabilized successfully with intensive insulin, pumps, and/or continuous glucose monitoring therapies [53]. This minimally invasive procedure can now routinely result in

long-term glycemic control with near normalization of HbA1c in the absence of severe hypoglycemic episodes [54].

Islet cell transplantation involves extracting pancreatic islet cells from deceased donors and implanting them into the liver of the recipient. The process entails careful isolation of islet cells from the pancreas, using enzyme mixtures to separate islets from exocrine tissues, and subsequent implantation into the liver via a cannula inserted into the pancreatic duct [55].

Despite the progress made in islet transplantation, significant challenges persist. The microenvironment of transplanted sites, encompassing factors like vascularization, extracellular matrix composition, and tissue-resident immune cells, remains poorly understood, hampering efforts to identify optimal transplantation locations. Current research endeavors focus on developing tailored hydrogel-based materials and microdevices to create transplantation spaces, shield grafts from the immune system, and promote angiogenesis. However, achieving normal glycemia with cadaveric human islets or those derived from stem cells remains elusive, and the long-term survival of transplanted islets varies across transplantation sites, influenced by factors like aging and other health conditions. Moreover, uncertainties surround the effectiveness and safety of biomaterials used to encapsulate artificial islets created from stem cells, with concerns about post-implantation trans-differentiation, teratoma formation, or graft migration requiring careful consideration. To enhance the long-term efficacy and safety of islet cell treatment for diabetes patients, efforts must concentrate on improving islet graft survival and functionality in highly vascularized, nutrient- and oxygen-rich environments [56].

While the intrahepatic percutaneous trans-hepatic portal vein approach to islet transplantation is generally regarded as reliable and safe, several associated risks persist. These include the potential for bleeding and portal venous thrombosis, as well as the risk of accidentally puncturing the gallbladder during the procedure. Additionally, mild increases in levels of liver enzymes like alanine transaminase and aspartate transaminase may occur in up to half of patients' post-procedure, typically resolving within one month without intervention. Furthermore, transient discomfort or modest pain at the site of catheter insertion, often accompanied by referred pain at the right shoulder tip due to diaphragmatic irritation, may affect around half of patients. Fortunately, these symptoms can be effectively managed with standard analgesic medications, with resolution usually occurring within 24 to 48 hours in most cases [54,55].

Teplizumab:

Teplizumab is a humanized monoclonal antibody that delays the onset of Diabetes Mellitus type 1. This was approved by the FDA in 2022. Teplizumab is the first treatment, which changes the course of Diabetes Mellitus type 1 since the discovery of insulin in 1922. Teplizumab became the first drug to be approved to delay any autoimmune disease before clinical onset. This drug specifically delays the onset of clinical type 1 diabetes in stage 3 in adults and children aged 8 years and above, but the use of intravenous teplizumab on newly diagnosed type 1 diabetes is questionable [57]. Teplizumab is a humanized immunoglobulin G1 monoclonal antibody and it has a high affinity to bind with the c chain of CD3. Teplizumab was first explored for treating acute transplant rejection and psoriatic arthritis[58]. Concurrently, studies in both spontaneous and chemically induced diabetic mouse models demonstrated its potential in reversing or preventing autoimmune diabetes and promoting immune tolerance. Unlike previous immune therapies, continuous administration was unnecessary [59].

Teplizumab leads to decreased insulin use in diabetes patients and the area under the curve (AUC) of the c peptide is much higher. It does not have any effect on Hb1c levels [57]. There is improvement in total and early insulin secretion rates, which identifies a functional as well as a quantitative improvement in insulin release. In addition to quantitative decreases in C-peptide AUC, studies have identified qualitative abnormalities in beta cell secretory kinetics, with loss of early insulin secretion reflecting beta cell dysfunction prior to the onset of T1D [60]. In summary, Teplizumab treatment changes the biologic course of the disease by enhancing beta cell function reflected by the quantitative and qualitative improvements in insulin secretion. These changes were associated with modulation of the frequency and function of memory CD8+ T cells [60].

The primary adverse events observed are lymphopenia, rash, and headache, with most cases occurring during and shortly after the initial weeks of teplizumab treatment. These effects typically resolved on their own without requiring any intervention, reflecting a safety profile marked by temporary adverse events following one or two courses of teplizumab therapy [59].

The study leading to FDA approval for teplizumab was conducted by the TrialNet network, supported by funding from the National Institutes of Health. It aimed to evaluate the impact of a single 14-day infusion course on the progression from stage 2 to stage 3 of type 1 diabetes. Although the trial was relatively small, with 44 participants in the placebo group and 32 in the treatment group, initial findings reported in 2019 indicated that teplizumab infusion delayed the onset of stage 3 type 1 diabetes by a median duration of 24 months. An updated analysis in 2021 revealed that this median delay had extended to 32.5 months [61].

The risks of immunosuppression, side effects, potential long-term safety issues, variable efficacy, high cost, and the need for regular monitoring must be carefully considered when deciding on its use. Ongoing research and long-term studies are essential to fully understand the benefits and drawbacks of Teplizumab and to optimize its use in clinical practice.

5. Conclusions

The potential of Mesenchymal Stem Cells (MSCs) in diabetic therapy is promising, given their attributes as effective immunotherapy and anti-autoimmunity agents. Despite some considerations before widespread application, continued research in biotechnology and regenerative medicine could lead to the incorporation of MSCs into future Type 1 Diabetes treatments. Additionally, Mesenchymal stem cell exosomes offer another avenue for diabetic therapy, although further clinical trials and studies are needed before their adoption as therapeutic agents.

Gene therapy holds promise for maintaining normoglycemia over the long term through islet allotransplantation, which faces challenges such as a lack of cadaveric donors and immune rejection. Stem cells from various sources offer potential solutions to these obstacles, and it's time for human safety testing to explore these modalities further.

Pancreatic islet cell transplantation is a viable treatment option, particularly for individuals experiencing hypoglycemia unawareness. While the procedure presents risks such as bleeding and rejection, it has demonstrated significant success rates in curing severe hypoglycemia and improving glucose control.

Teplizumab represents a revolutionary advancement in the treatment of DM1, which received approval in 2022 by the FDA as the first therapy to alter the course of the disease since the discovery of insulin.

Overall, the future of Type 1 Diabetic therapy appears promising with these innovative approaches. To effectively address the opportunities and challenges presented by novel modalities in Type 1 Diabetes Mellitus (T1DM), collaboration and concerted action among stakeholders across various domains are imperative. Healthcare professionals should prioritize comprehensive education and training programs to adeptly utilize emerging treatments and technologies. Collaboration among researchers, clinicians, industry partners, and patient advocacy groups is crucial to accelerate the development and evaluation of novel modalities. Policymakers should advocate for streamlined regulatory pathways to ensure timely approval and access to these treatments. Additionally, stakeholders should prioritize patient-centered care by involving patients and caregivers in decision-making processes. Adequate funding and resources are essential to support research and development efforts in this field, and fair pricing and reimbursement policies should be established to enhance affordability and accessibility. Robust surveillance systems are needed to monitor safety and efficacy post-market, and raising public awareness about the benefits of novel T1DM treatments is vital. Embracing digital health solutions can further improve treatment delivery and monitoring. By collectively addressing these opportunities and challenges, stakeholders can advance novel modalities in T1DM management and improve outcomes for individuals living with this condition. Continued clinical studies and technological advancements may lead to

refinements in these treatments, potentially ushering in an era where Type 1 Diabetes can be effectively managed or even eradicated on a global scale.

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