Review Article

Emerging Cellular Therapies for Pancreatic Regeneration in Type 1 Diabetes Mellitus: Biological Foundations, Experimental Models, and Clinical Perspectives

Kevin Vargas Tenorio[1*], Diana Patricia Vargas Víquez[2], Lola Dive Chagnon[3], Katherin Durán Chavarría[4], Sofía Segreda Castro[5]

[1]Medical Doctor, San Juan de Dios Hospital, San José, Costa Rica
[2]Medical Doctor, Poder Judicial, Heredia, Costa Rica
[3, 4]Medical Doctor, Independent Researcher, Heredia, Costa Rica
[5]Medical Doctor/ Nutritionist, San Rafaela de Alajuela Hospital, Alajuela, Costa Rica
[*]Corresponding author email: **kmega100@gmail.com**

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Abstract

Type 1 diabetes mellitus is a chronic autoimmune disease characterized by the selective destruction of pancreatic beta cells, resulting in absolute insulin deficiency and lifelong dependence on exogenous insulin therapy. Although advances in insulin delivery and glucose monitoring have improved glycemic control, these approaches do not address the underlying autoimmune pathology or restore endogenous insulin production. Growing evidence indicates that pancreatic damage in type 1 diabetes mellitus arises from a complex interaction between autoreactive immune cells, pro-inflammatory cytokine networks, and intrinsic beta-cell stress responses, while the endocrine pancreas retains a limited but clinically relevant regenerative capacity. This biological context has driven increasing

interest in cellular therapies aimed at pancreatic regeneration. Recent advances in stem cell biology have enabled the generation of insulin-producing cells from embryonic stem cells, induced pluripotent stem cells, and adult progenitor populations, offering scalable alternatives to donor islet transplantation. In parallel, cellular reprogramming and transdifferentiation strategies, including alpha-to-beta cell conversion and epigenetic modulation, have demonstrated the ability to restore insulin secretion in experimental models. These approaches are supported by sophisticated in vitro systems, such as pancreatic organoids and three-dimensional culture platforms, as well as diverse animal models that enable functional, metabolic, and immunological evaluation of regenerative therapies. Despite encouraging preclinical results and early-phase clinical trial data showing safety and preliminary efficacy, major challenges remain. Recurrent autoimmunity, graft survival, tumorigenicity risk, and the need for immunosuppression continue to limit long-term success. Emerging immune protection strategies, including hypoimmune cell engineering, encapsulation technologies, and immune tolerance induction, represent critical avenues for improving durability and safety.

Key words

Autoimmune diabetes; beta-cell loss; cellular reprogramming; stem cell differentiation; immunoprotection; translational medicine.

Introduction

Type 1 diabetes mellitus is an autoimmune disorder defined by the progressive destruction of pancreatic β-cells, which results in absolute insulin deficiency and persistent hyperglycemia [1, 2]. The disease affects approximately 0.4%–0.5% of the global population and is associated with a substantial burden of chronic co-morbidities, including retinopathy, nephropathy, and cardiovascular disease, which significantly contribute to morbidity and mortality. Despite major advances in insulin formulations, delivery systems, and glucose monitoring technologies, type 1 diabetes mellitus remains a lifelong condition, and patients continue to face severe long-term complications, among which life-threatening hypoglycemia represents one of the most critical clinical challenges [2].

Although insulin therapy is indispensable for survival and effective for glycemic control, it does not address the underlying autoimmune etiology of the disease and therefore does not constitute a curative approach. Moreover, long-term insulin use is associated with recurrent hypoglycemic episodes and a measurable reduction in quality of life, reflecting the difficulty of achieving stable and physiological glucose regulation through exogenous insulin alone. Technological innovations such as artificial pancreas systems have partially improved glycemic outcomes; however, these systems still struggle to accurately replicate the dynamic, glucose-responsive insulin secretion of native β-cells, underscoring the intrinsic limitations of replacement strategies that do not restore endogenous pancreatic function [2, 3].

In this context, pancreatic regeneration and β-cell replacement have emerged as promising disease-modifying strategies aimed at restoring endogenous insulin production and achieving long-term metabolic control. Regenerating or replacing functional β-cells offers the potential for a more durable therapeutic solution by reestablishing physiological insulin secretion rather than relying exclusively on external supplementation [3, 4]. Importantly, contemporary cellular therapies are designed not only to replenish β-cell mass but also to interact with the immune system, seeking to mitigate or reshape the autoimmune response that drives β-cell destruction in type 1 diabetes mellitus [1, 4].

Among these approaches, stem cell–derived β-cells have attracted significant attention. Human pluripotent stem cells and induced pluripotent stem cells are being differentiated into β-like cells capable of insulin production, offering a theoretically unlimited and scalable source of replacement cells for transplantation [3, 5, 6]. Clinical studies using human embryonic stem cell–derived β-like cells have yielded encouraging results, including cases in which patients achieved partial or complete insulin independence [5]. Nevertheless, important challenges persist, particularly regarding the attainment of full functional maturation, long-term stability, and precise control of graft size following transplantation [6, 7].

Parallel to cell replacement strategies, regulatory cell therapies have been developed to address the autoimmune component of the disease. Interventions based on regulatory T cells, mesenchymal stem cells, and dendritic cells aim to modulate immune responses and protect residual or newly generated β-cells from immune-mediated destruction. Early clinical interventions using these immunomodulatory approaches have demonstrated mild but measurable efficacy, especially in individuals who retain a higher residual β-cell mass at the time of treatment, suggesting that immune-based strategies may be most effective when applied early in the disease course [1].

Gene-editing and cellular engineering technologies are being explored as complementary tools to enhance β-cell regeneration and improve immune evasion. CRISPR/Cas-based approaches have been proposed to modify β-cells or stem cell–derived progenitors to increase their resilience to autoimmune attack, although concerns regarding safety and off-target effects remain significant barriers to clinical translation [3]. More recently, hypoimmune pluripotent stem cells have been engineered to evade immune recognition, demonstrating promising results in preclinical models and highlighting the potential of immune-evasive cellular products as a future therapeutic avenue in type 1 diabetes mellitus [2].

The objective of this article is to comprehensively examine emerging cellular therapies for pancreatic regeneration in type 1 diabetes mellitus, integrating current knowledge on their biological mechanisms, experimental validation, and clinical perspectives, to evaluate their potential to restore endogenous insulin production and overcome the limitations of conventional insulin-based therapies.

Methodology

The present manuscript was conceived as a narrative review aimed at contextualizing emerging cellular therapies for pancreatic regeneration in type 1 diabetes mellitus. Rather than adhering to a rigid or systematic methodological framework, the work was developed through the organization of available evidence around biologically and clinically relevant questions, including the mechanisms underlying beta-cell loss, the regenerative potential of the endocrine pancreas, and the translational relevance of cellular and gene-based therapeutic strategies in contemporary practice.

The narrative synthesis was informed by recent peer-reviewed literature published between 2021 and 2026 and indexed in PubMed, Scopus, and Web of Science. Source selection prioritized studies that contributed substantively to the understanding of pancreatic beta-cell destruction, immune-mediated mechanisms, stem cell–based regeneration, immunomodulatory cellular therapies, experimental models, and early clinical applications. Publications lacking peer review, presenting redundant or incomplete data, or not directly relevant to pancreatic regeneration or therapeutic innovation in type 1 diabetes mellitus were not included. Search terms were applied flexibly to capture key concepts related to Autoimmune diabetes; beta-cell loss; cellular reprogramming; stem cell differentiation; immunoprotection; translational medicine.

Information derived from the selected literature was interpreted and integrated using a qualitative approach that emphasized biological plausibility and clinical relevance rather than formal methodological categorization. Core themes, including immune–beta-cell interactions, regenerative capacity of the pancreas, therapeutic efficacy, safety considerations, and translational limitations, were examined in parallel to reflect the complexity of real-world therapeutic development. Artificial intelligence–assisted tools were employed exclusively as supportive resources for thematic organization and conceptual clarity, without influencing the interpretation of evidence. This narrative methodology enabled the development of a coherent and integrative synthesis, highlighting emerging cellular therapies as potential disease-modifying strategies in the management of type 1 diabetes mellitus.

Biological Basis of Pancreatic Damage in Type 1 Diabetes Mellitus

Type 1 diabetes mellitus is defined by the immune-mediated destruction of pancreatic beta cells, a process predominantly driven by autoreactive T lymphocytes that recognize beta cells as foreign targets and initiate their elimination [8, 9]. This pathogenic mechanism is not solely imposed by the immune system; rather, beta cells actively participate in their own destruction by expressing stress-associated molecules that enhance immune cell recruitment and activation, thereby amplifying local inflammatory responses within the pancreatic islets [10].

Within this autoimmune cascade, autoreactive T cells, particularly CD8+ cytotoxic T lymphocytes, play a central role by directly inducing beta-cell death through antigen-specific recognition and cytotoxic effector mechanisms [11]. In parallel, B cells contribute to disease perpetuation by producing autoantibodies and functioning as antigen-presenting cells, which sustain T-cell activation and reinforce the autoimmune loop [12]. This coordinated cellular response is further intensified by complex cytokine networks, in which pro-inflammatory mediators such as interleukin-1β, tumor necrosis factor-alpha, and interferon-gamma exacerbate beta-cell stress, impair cellular function, and promote apoptosis, thereby accelerating the progression of beta-cell loss [13].

Despite this hostile immunological environment, the endocrine pancreas exhibits a degree of intrinsic plasticity that underpins interest in regenerative strategies. The islets of Langerhans are characterized by marked cellular heterogeneity, with multiple endocrine cell types contributing to pancreatic function and metabolic regulation. This heterogeneity is thought to influence the regenerative capacity of the pancreas and its ability to adapt to injury. Importantly, beta cells themselves are not a uniform population; they display functional and transcriptional diversity, which may affect both their vulnerability to autoimmune attack and their potential to participate in regenerative processes [8].

Consistent with this concept, evidence suggests that beta-cell turnover and neogenesis can occur in the adult pancreas, although these processes are generally limited in magnitude. Nevertheless, this residual regenerative capacity is considered highly relevant for therapeutic strategies aimed at restoring beta-cell mass in type 1 diabetes mellitus [14]. Experimental studies indicate that under specific conditions, such as attenuation of immune-mediated damage or enhancement of growth factor signaling, beta-cell regeneration can be stimulated, supporting the feasibility of regeneration-focused interventions [15].

At the molecular level, pancreatic regeneration involves signaling pathways associated with cell growth and survival, including those mediated by insulin-like growth factor and transforming growth factor-beta, which promote beta-cell proliferation and resistance to stress-induced apoptosis [15]. In addition, the involvement of pattern recognition receptors expressed by beta

cells highlights their capacity to sense inflammatory signals and modulate immune responses. This innate immune signaling may influence both beta-cell survival and regenerative potential, further underscoring the dynamic interaction between immune mechanisms and pancreatic regeneration in type 1 diabetes mellitus [10].

Stem Cell Sources for Pancreatic Regeneration

Embryonic stem cells possess the intrinsic capacity to differentiate into pancreatic progenitors and, subsequently, into insulin-producing beta cells, making them a compelling platform for regenerative strategies in type 1 diabetes mellitus. Differentiation protocols have been developed to direct embryonic stem cells through sequential developmental stages, including definitive endoderm specification and pancreatic progenitor formation, ultimately yielding functional beta cells capable of glucose-responsive insulin secretion [16, 17]. This stepwise recapitulation of embryonic pancreatic development has provided critical insights into beta-cell ontogeny and has established embryonic stem cells as a robust experimental and therapeutic resource. One of the principal advantages of this approach lies in the theoretically unlimited supply of cells, which could overcome the persistent limitations associated with donor tissue availability. Nevertheless, the clinical translation of embryonic stem cell–based therapies remains constrained by ethical concerns surrounding the use of human embryos and by safety issues, particularly the risk of teratoma formation following transplantation [18, 19].

In parallel, induced pluripotent stem cells have emerged as a promising alternative that circumvents several ethical and immunological barriers associated with embryonic stem cells. These cells are generated through the reprogramming of somatic cells, enabling the development of patient-specific therapeutic products that may reduce the risk of immune rejection. Induced pluripotent stem cell technology allows for the differentiation of insulin-producing cells tailored to individual patients, thereby aligning regenerative therapy with the principles of personalized medicine [16, 20]. Despite these advantages, significant challenges persist, particularly with respect to genetic stability and immunogenicity. Reprogramming processes and prolonged in vitro expansion can introduce genetic or epigenetic abnormalities, which may compromise safety and therapeutic efficacy in clinical applications [20].

Beyond pluripotent stem cell platforms, adult stem and progenitor cells have also been investigated for their potential role in pancreatic regeneration. Mesenchymal stem cells and pancreatic ductal progenitors represent key adult cell populations of interest, given their capacity to differentiate into various pancreatic lineages and to support tissue repair mechanisms. These cells have demonstrated regenerative potential not only through direct differentiation but also via indirect mechanisms that influence the pancreatic microenvironment. In particular, mesenchymal stem cells are characterized by pronounced paracrine and immunomodulatory properties, which enable them to attenuate inflammation and promote tissue repair. Through the secretion of bioactive factors, mesenchymal stem cells can enhance the survival, engraftment, and functional performance of transplanted cells, thereby reinforcing their therapeutic relevance in regenerative strategies for type 1 diabetes mellitus [21].

Cellular Reprogramming and Transdifferentiation Strategies

The conversion of non-beta pancreatic cells into insulin-producing cells has emerged as a promising strategy to restore endogenous insulin secretion while bypassing the limitations associated with donor islet availability. Among these approaches, alpha-to-beta cell transdifferentiation has attracted considerable attention, as alpha cells share a common

developmental origin with beta cells and retain a degree of plasticity. Experimental studies have demonstrated that alpha cells can be reprogrammed into insulin-producing cells through the targeted expression of key transcription factors, such as pancreatic and duodenal homeobox 1 and MafA. This reprogramming is commonly achieved using viral vectors that deliver these factors selectively to alpha cells, resulting in the acquisition of beta-like phenotypes and the correction of hyperglycemia in diabetic experimental models [22].

In parallel, stem cell–derived insulin-producing beta-like cells have been developed to address the persistent shortage of donor islets for transplantation. These engineered cells have shown the capacity to reverse diabetes in animal models, highlighting their functional relevance and therapeutic potential. However, despite these encouraging results, significant challenges remain, including issues related to uncontrolled graft growth and long-term stability following transplantation, which continue to limit their clinical translation [6].

Beyond direct cellular conversion, genetic and epigenetic modulation has been identified as a critical component of effective reprogramming strategies. MicroRNAs play an important regulatory role in the differentiation and maturation of insulin-producing cells, with specific microRNAs, such as miR-375, miR-7, and miR-145, being closely involved in beta-cell development. Modulation of these microRNAs has been shown to influence stem cell fate decisions and promote maturation toward insulin-secreting phenotypes [23]. Complementing this regulatory layer, epigenetic modifications, including DNA methylation and histone alterations, are essential for establishing and maintaining beta-cell identity. These epigenetic changes reshape gene expression programs required for the functional conversion of non-beta cells into beta-like cells [24].

Central to these reprogramming processes is the coordinated activity of transcription factors and signaling pathways that govern beta-cell identity and function. Transcription factors such as pancreatic and duodenal homeobox 1, MafA, and Nkx6.1 are fundamental for sustaining insulin expression and beta-cell–specific gene networks and are therefore commonly employed in cellular reprogramming strategies [25]. In addition, multiple signaling pathways, often modulated by small molecules, contribute to the orchestration of phenotypic conversion and the maintenance of engineered cells as functional insulin producers. Together, these pathways ensure not only the acquisition of beta-like characteristics but also the long-term functionality of reprogrammed cells [24].

Experimental Models for Evaluating Pancreatic Regeneration

In vitro models have become essential tools for investigating pancreatic regeneration and for evaluating emerging cellular therapies in type 1 diabetes mellitus. Among these, pancreatic organoids derived from human pluripotent stem cells have gained prominence due to their ability to recapitulate key aspects of pancreatic architecture and function. These three-dimensional structures provide a versatile platform for studying pancreatic development, disease modeling, and therapeutic testing, as they can be directed toward either endocrine or exocrine lineages. Current efforts focus on enhancing cellular maturation and functional competence, with the aim of improving their applicability in diabetes-oriented regenerative strategies [26]. Complementary to organoid systems, three-dimensional culture platforms based on self-assembling peptide hydrogels have been shown to support the long-term culture and functionality of human pancreatic islets. By preserving islet morphology and insulin-secretory capacity, these systems offer a controlled microenvironment that has demonstrated the potential to restore normoglycemia in diabetic experimental settings [27].

A critical component of in vitro modeling involves the functional assessment of insulin secretion, which is primarily conducted by evaluating the glucose responsiveness of stem cell–derived beta-like cells. These functional assays are fundamental for determining the therapeutic relevance of engineered cells prior to in vivo application. Pharmacological interventions, such as treatment with bleomycin, have been shown to enhance insulin secretion while selectively reducing the proliferation of undesired progenitor populations, thereby improving the functional quality of stem cell–derived beta-like cells [6]. In parallel, advances in biophysical characterization have enabled the non-invasive assessment of pancreatic organoids, allowing for the identification and pre-selection of functionally competent constructs based on physiological parameters. This approach enhances the efficiency and translational value of organoid-based platforms in both research and therapeutic contexts [28].

In addition to in vitro systems, animal models remain indispensable for evaluating the regenerative potential and therapeutic efficacy of cellular interventions in type 1 diabetes mellitus. Both chemically induced and autoimmune diabetic models are widely used; however, alternative organisms with intrinsic regenerative capabilities have provided unique insights. The axolotl salamander, for example, has been employed to study beta-cell regeneration due to its remarkable ability to regenerate tissues, offering perspectives on physiological and molecular mechanisms that are largely absent in conventional mammalian models [29]. In mammalian systems, the development of neo-islets composed of mesenchymal stromal cells and islet cells has demonstrated promising outcomes, including successful engraftment and functional insulin secretion without the need for anti-rejection therapy. These constructs have been shown to restore euglycemia in diabetic animal models and can be retrieved if necessary, highlighting their potential safety and therapeutic flexibility [30].

The evaluation of engraftment, survival, and metabolic control is a central endpoint in animal studies assessing cellular therapies. Successful transplantation is typically determined by the ability of transplanted cells to restore and maintain normoglycemia while sustaining endogenous insulin production over time. Notably, bioengineered tissues such as induced pluripotent stem cell–derived vascularized endocrine pancreas constructs have demonstrated effective engraftment and robust insulin secretion in diabetic mice, underscoring the translational potential of complex, vascularized pancreatic tissues [31]. Complementing in vivo studies, microphysiological systems in vitro have been employed to maintain the viability and functionality of pancreatic organoids under dynamic conditions. These systems support long-term culture and metabolic regulation, bridging the gap between static in vitro models and whole-animal physiology, and thereby strengthening the preclinical evaluation of regenerative therapies for type 1 diabetes mellitus [32].

Immunological Challenges and Immune Protection Strategies

Recurrent autoimmunity represents a major obstacle to the long-term success of cell replacement therapies in type 1 diabetes mellitus, as the underlying immune mechanisms that drive the disease may continue to recognize and destroy newly transplanted beta cells. Even when functional insulin-producing cells are successfully engrafted, persistent autoimmune activity can compromise graft survival and limit sustained therapeutic benefit [33]. To address this challenge, emerging strategies have focused on the development of genetically engineered hypoimmune cells, which are designed to evade immune surveillance and thereby reduce the likelihood of renewed autoimmune attacks against transplanted beta-cell populations [2].

In parallel with cellular engineering approaches, immunoisolation devices and encapsulation technologies have been developed to provide

physical protection to transplanted cells. These strategies aim to create a semipermeable barrier that allows the diffusion of nutrients, oxygen, and insulin while preventing direct contact between the graft and the host immune system, thereby reducing immune-mediated rejection [34, 35]. Advances in biomaterials science and nanotechnology have enabled the refinement of encapsulation techniques, including the use of conformal nanocoatings and polyethylene glycol–based encapsulation systems. These innovations have improved biocompatibility, reduced fibrotic responses, and enhanced the functional performance of encapsulated islets, supporting their potential role in regenerative therapies for type 1 diabetes mellitus [2, 34].

Beyond physical immunoprotection, immune tolerance induction and gene-editing approaches have gained increasing attention as complementary strategies to promote long-term graft survival. Gene-editing technologies, particularly CRISPR-Cas9, have been applied to generate hypoimmune pluripotent stem cells by selectively eliminating or modifying immune recognition markers, thereby diminishing immune activation following transplantation [2]. Concurrently, immune tolerance induction strategies, such as the incorporation of immunomodulatory biomaterials and the co-transplantation of accessory cells with regulatory properties, seek to establish a local immune environment that supports graft acceptance and function. Together, these approaches aim to shift host immune responses toward tolerance rather than rejection, enhancing the durability and clinical feasibility of cellular therapies in type 1 diabetes mellitus [36].

Translational and Clinical Perspectives

Current and ongoing clinical trials have begun to translate advances in cellular therapies for type 1 diabetes mellitus into human applications, with early-phase studies primarily focused on evaluating safety, feasibility, and preliminary efficacy. Several of these trials have investigated the transplantation of stem cell–derived beta-like cells in patients with type 1 diabetes mellitus and have reported encouraging initial outcomes. Notably, some participants have achieved partial or complete insulin independence, supporting the clinical potential of these regenerative approaches [5, 18]. In this context, Vertex Pharmaceuticals has reported a landmark case in which a patient with type 1 diabetes mellitus attained insulin independence following the transplantation of stem cell–derived islet cell clusters, underscoring the feasibility of stem cell–based beta-cell replacement in a clinical setting [6].

Beyond proof-of-concept, early-phase clinical trials have generally demonstrated an acceptable safety profile, with only mild adverse events reported to date, alongside early signs of therapeutic efficacy. The most favorable outcomes appear to be observed in patients with a shorter duration of disease and a greater residual beta-cell mass at the time of intervention, suggesting that patient selection may play a critical role in maximizing therapeutic benefit [1]. Nevertheless, important challenges remain unresolved, including the risk of uncontrolled graft growth and the persistence of proliferative cell populations within stem cell–derived clusters, which may compromise both safety and long-term efficacy [6].

The clinical advancement of these therapies is further shaped by regulatory, manufacturing, and ethical considerations that must be addressed to enable widespread implementation. The production of stem cell–derived therapeutic products requires strict adherence to Good Manufacturing Practice standards to ensure consistency, quality, and safety. This includes precise control of differentiation protocols and rigorous quality assurance measures to minimize the presence of undesired proliferative cells within the final product. In parallel, long-term safety remains a central concern, particularly with respect to tumorigenicity associated with residual proliferative cells. To mitigate this risk, strategies such as the pharmacological ablation

of proliferative cell populations are being actively explored as part of product optimization and safety assurance efforts [6].

In addition to technical and regulatory challenges, ethical and socioeconomic implications continue to influence the development and deployment of cellular therapies for type 1 diabetes mellitus. The use of stem cells, especially embryonic stem cells, raises ethical questions regarding cell sourcing and potential exploitation, which necessitate transparent governance and ethical oversight. Furthermore, the high cost associated with the development, manufacturing, and delivery of these advanced therapies may limit patient access, thereby raising concerns about equity and socioeconomic disparities in healthcare availability [37].

Limitations, Knowledge Gaps, and Future Directions

The development and clinical translation of cellular therapies for type 1 diabetes mellitus continue to face substantial technical and biological barriers that limit their widespread application. One of the most significant constraints is donor scarcity, as the availability of cadaveric islet donors remains limited, and the process of islet isolation is technically demanding and resource intensive. These factors collectively restrict the scalability of conventional islet transplantation and underscore the need for alternative cell sources [38]. In this context, pluripotent stem cell–derived beta cells have emerged as a promising solution due to their potential to provide an unlimited supply of insulin-producing cells. However, translating these cells into fully functional and mature beta cells that closely replicate the physiological behavior of native pancreatic beta cells remains a major scientific challenge [39].

Beyond cell sourcing, successful engraftment and long-term survival of transplanted cells represent additional hurdles. Ensuring that implanted cells integrate effectively within the host tissue, establish appropriate vascularization, and maintain sustained insulin secretion requires continued advancements in differentiation protocols, biomaterials, and delivery technologies. Without reliable engraftment and survival, the therapeutic impact of even highly optimized cell products may be limited [40].

The need for robust long-term efficacy and safety data further complicates the clinical adoption of these therapies. Although early clinical trials have demonstrated encouraging outcomes, including the detection of endogenous C-peptide production as evidence of functional insulin secretion, comprehensive long-term data assessing durability of glycemic control and sustained safety are still lacking [40]. In addition, the reliance on chronic immunosuppressive therapy in some transplantation protocols introduces significant risks, such as increased susceptibility to infections and malignancies, highlighting the necessity of developing approaches that minimize or eliminate the need for long-term immunosuppression [38].

In response to these challenges, increasing attention has been directed toward the integration of cellular therapies with immunomodulatory strategies. Approaches such as cell encapsulation and genetic engineering are being explored to protect transplanted cells from immune-mediated destruction, thereby reducing dependence on systemic immunosuppression and improving graft longevity. Macroencapsulation devices have been designed to physically shield implanted cells from the host immune system while allowing the exchange of nutrients, oxygen, and insulin. These devices aim to enhance cell viability and functional performance, representing a critical step toward achieving durable and clinically viable regenerative therapies for type 1 diabetes mellitus [38].

Conclusions

Type 1 diabetes mellitus results from a complex autoimmune process that destroys beta cells, yet

the pancreas retains limited regenerative capacity that supports the rationale for regenerative therapies.

Stem cell–derived and reprogrammed insulin-producing cells show strong experimental and early clinical potential, although issues related to functional maturation, graft control, and long-term stability persist.

The clinical translation of pancreatic regenerative therapies will require overcoming immune-mediated rejection, ensuring long-term safety, and integrating immunoprotective strategies to achieve durable therapeutic effects.

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