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Regenerative Medicine "From Science Fiction to Reality: the Rise of Regenerative Medicine"

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ABSTRACT

Regenerative medicine, what was once thought to be science fiction back in the day is now growing to become the most significant advancements made in the field of medicine and clinical studies. Regenerative medicines are medicines that help in repairing and replacing damaged tissue and re-establish organ function impaired by disease, trauma, or congenital abnormalities. Stem cells play a key role in the advancements of regenerative medicine. Stem cells are undifferentiated, meaning they don't have a specific function and structure like skin cells or muscle cells. But they do have the potential to develop into various specialized cells. They have the ability to regenerate and replace damaged tissue and organs in our body. For example, the lining of the intestines is replaced every four days by the stem cells present beneath it [1]. Stem cells are essential for understanding how the body works and for the development of new therapies for diseases [2].

Regenerative Medicine (RM) overcomes limitations of conventional therapies in settings like myocardial infarction, vascular disease, limb loss, and organ failure by harnessing innate repair mechanisms. Studies in zebrafish—a model capable of regenerating hearts, fins, retina, and spinal cord—reveal key processes: cardiomyocyte dedifferentiation, proliferation, and pathways such as Notch, Wnt, FGF, BMP, and microRNAs [17], [19]. Translating these insights, RM approaches now include bioengineered scaffolds, decellularized extracellular matrices, stem cell transplantation, miRNA modulation, nanomedicine-based treatments, and the creation of 3D organoids [7]. A recent milestone: vascularized cardiac and liver organoids developed by Stanford using patterned growth-factor protocols replicate embryonic vasculature and beat like early hearts—offering scalable disease models and future transplant prospects [8]. Continued exploration in vertebrate models will build an understanding of genetic, epigenetic, and mechanobiological cues—essential for harnessing regeneration in human tissues and organs, promising transformative therapies for life-threatening conditions [1], [19].

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1. HEMATOPOIETIC STEM CELL TRANSPLANTATION IN TYPE I DIABETES MELLITUS (T1D)

INTRODUCTION

Diabetes Mellitus is a metabolic disease that is a major health concern. It results from a deficiency of insulin production in type 1 diabetes mellitus or an inability to utilize insulin as occurs in type 2 diabetes. Globally more than 400 million people have suffered from Diabetes mellitus in the year 2014 compared to 1980 [108 million] [17]. If this trend continues then it is predicted that the number may increase to more than 600 million by 2045. For type 1 Diabetes, the administration

of exogenous insulin is the main treatment for the patients [17]. While the maintenance of appropriate glycemic control is possible with insulin therapy, it fails to prevent microvascular complications in many subjects. Furthermore, inaccurate insulin delivery results in a lack of glycemic control. We can also consider islet transplantation as it can provide an effective treatment. However, the essential problem with islet transplantation is the need for immunosuppression and the scarce donor supply. Alternatively, stem cell-derived insulin-producing cells can provide an unlimited supply [12], [13].

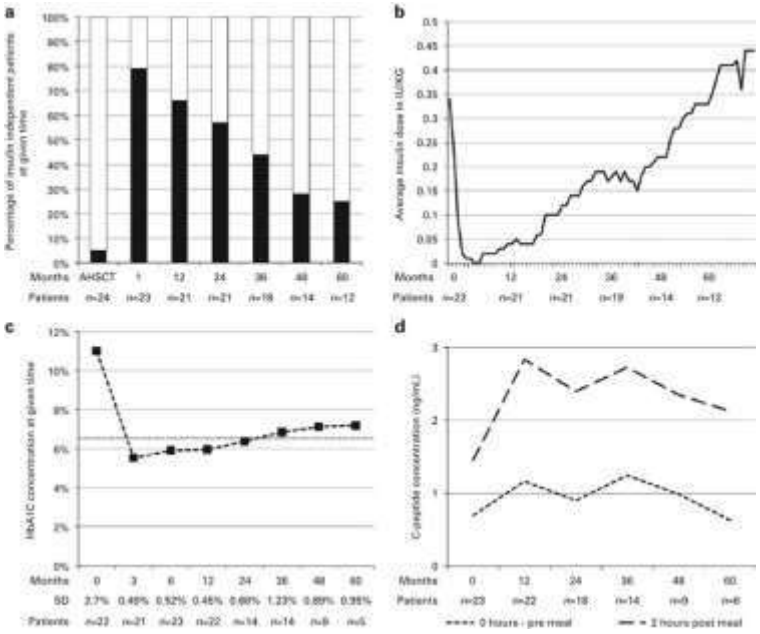
Before we get into how hematopoietic stem cells play an important role in treating T1D, let us first understand the different types of stem cells.

Stem cells are mainly classified into three types. They are Totipotent cells, Pluripotent cells, Multipotent cells, and Unipotent stem cells. The potency of these stem cells decreases from totipotent to unipotent cells. Totipotent stem cells have the ability to differentiate into any type of cells be it red blood cells or epidermal cells. Pluripotent stem cells particularly, Embryonic stem cells(ESCs) and induced pluripotent stem cells(iPSCs), have grasped the attention for their ability to differentiate into any cell and have the ability to repair and regenerate. However, due to ethical concerns and the risk of the formation of a tumor have limited their clinical application [2].

1.1. HEMATOPOIETIC STEM CELLS

Hematopoietic stem cells are multipotent stem cells originating from several sources including bone marrow, peripheral blood, or umbilical cord blood. Having differentiation and self-renewal properties, HSCs can differentiate into various lineages of blood cells which is called hematopoiesis [3], [10].

Since 1996, autologous hematopoietic stem cell transplantation has been performed for severe and refractory autoimmune diseases, with two-thirds of the patients achieving durable remissions, in spite of high morbidity and mortality rates related to transplantation or relapse and progression of the autoimmune diseases. Based on the beneficial effects of moderate immunosuppression during the course of T1D, in 2003, a Brazilian group, led by Professor Julio Voltarelli from the Ribeirao Preto School of Medicine of the University of Sao Paulo, pioneered an unprecedented study that involved a severe immunosuppression protocol ("immunological resetting") followed by autologous transplantation of hematopoietic stem cells in patients recently diagnosed with T1D [3]. The 23 patients who participated in the study (aged between 12 and 35 years) retained residual beta-cell mass and displayed a significant increase in C-peptide secretion for periods ranging from 6 to 47 months [3], [4].



This figure summarizes results from Voltarelli et al.'s study on autologous hematopoietic stem cell transplantation (AHSCT) in newly diagnosed type 1 diabetes. After AHSCT, most patients initially became insulin-independent, but over time this benefit declined—by 60 months, only about 20% remained insulin-free [3]. Correspondingly, average insulin doses dropped sharply post-transplant, then gradually increased again. HbA1c levels also improved significantly at first, reflecting better glycemic control, but slowly rose over the years [4]. C-peptide concentrations (a marker of β-cell function) increased after treatment, peaked at 12–24 months, and then declined, suggesting partial recovery of insulin secretion that diminished with time. Overall, the study showed that AHSCT can temporarily preserve β-cell function and reduce insulin needs, but most patients eventually resumed insulin therapy [3], [4].

In 2009, a Group from the University of Florida in the United States presented results of transplanting a mixture of umbilical cord, placenta, and peripheral blood cells into 15 children diagnosed with T1D. This group observed an improvement in the loss of endogenous insulin in these patients but not in the levels of C-peptide [3]. This result may

be associated with the increase in the number of regulatory T cells involved in the autoimmune process. In 2010, another group infused autologous MSCs from subcutaneous fat associated with bone marrow stem cells into 11 immunosuppressed patients. An increase (3X) in c-peptide levels and a 40% reduction in the daily insulin dose requirement were observed [11].

In 2012, another group reported the use of T lymphocytes from T1D patients cocultured with umbilical cord stem cells from a healthy donor [11]. In this study, 15 patients were diagnosed and divided into three groups, namely:

1. Newly diagnosed diabetic patients with basal insulin-producing pancreatic beta cells (n=6)
2. Diabetic patients in an advanced stage of the disease without the presence of metabolically normal pancreatic beta cells(n=6)and
3. Control (untreated) patients (n=3). These authors reported that this therapy was effective in both experimental groups, leading to increased C-peptide levels, and suggesting increased beta cell function.

T1D is characterized by a loss of self-tolerance and an aberrant immune response against self-tissue. This research group proposed to pharmacologically enhance the beta cell function by ex-vivo modulation of the immune-regulatory and trafficking properties of hematopoietic stem cells with small molecules to provide a safer and more efficacious treatment option for patients with T1D and other autoimmune disorders. They reported a reduced lymphocytic infiltration of pancreatic beta cells and inhibited the activity of auto-reactive T cells, demonstrating reversion of autoimmune diabetes in NOD mice [19].

Few clinical trials have already demonstrated the beneficial effects of hematopoietic stem cell infusion have been partially successful in slowing down or reverting T1D, while the durability of the effect is yet to be established. Some protocols involving autologous hematopoietic stem cell infusion have been partially successful in slowing down or reverting T1D progression in patients, emerging as an option to be explored.

The table below shows systematic reviews & meta-analyses on hematopoietic stem cell (HSC) therapy in type 1 diabetes (T1D) [10], [11]. It is the collected data from many studies to see the overall effect, rather than just single small trials.

Review & Year	Included Patients	Insulin Independence (%)	Duration	Mortality	Key Notes
Systematic Review 2019	487 patients	~9.6 per 100 patient-years became insulin-free	~15.6 months	~3.4%	Adding mesenchymal stem cells (MSCs) to HSCs improved biomarker effect
Systematic Review 2022	491 patients	168 became insulin-free; others reduced insulin dose	Median ~16 months	Rare deaths	MSC+HSC co-transplantation reduced insulin need but didn't boost insulin-free rates
Meta-analysis (CD34+ HSC)	524 patients	About 59% reached insulin independence	~16 months	0 deaths reported	Best outcomes in adults, early after diagnosis, and those without diabetic ketoacidosis (DKA)

2. CURRENT PROGRESS IN STEM CELL THERAPY FOR TYPE I DIABETES MELLITUS (T1D)

The efforts to treat T1D began with the discovery and use of insulin, which has enhanced the life span of T1D patients [17]. The success of whole pancreas and islet transplantation to treat brittle diabetic patients has provided direct evidence for the feasibility of re-establishing beta cells production to treat T1D [7], [16]. However, due to the shortage of pancreas from organ donors, researchers have searched for new sources of beta cells, generating IPCs (IPCs) from and even whole pancreas (bio-artificial pancreas), in vitro from adult stem cells, ESCs, and iPSCs. Studies involving the immune mechanism of T/B cell destruction in T1D have made break-throughs, and gene therapy, although its safety still needs to be confirmed in humans, has shown great promise as a potential treatment for T1D patients [12], [13], [20].

Extensive studies have been conducted for generating IPCs, or islet organoids the sources for this generation include mainly ds, in-vitro for application in Regenerative Medicine.

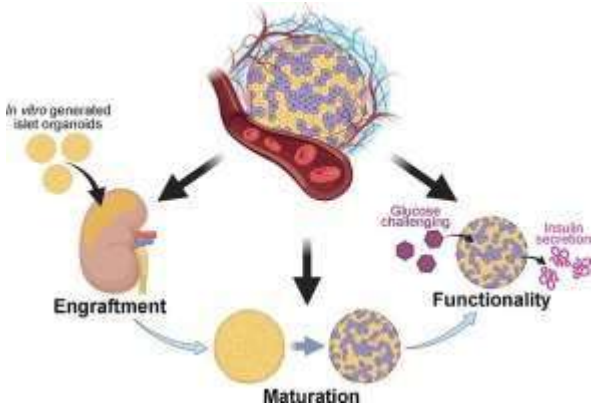
The sources for this generation include mainly hESCs (human embryonic stem cells, or hESCs and human-induced pluripotent stem cells, or hiPSCs), adult stem cells, and differentiated cells from mature tissues that can be trans-differentiated into IPCs. Current strategies for generating IPCs are mainly based on approaches that mimic normal pancreatic development. The generation of IPCs from ESC or iPSC has undergone significant improvements and refinements in the last few years, with several protocols successfully designed for the generation of IPCs or islet organoids in-vitro [6].

The importance of 3D interactions and reciprocal coordination of different types of islet cells for glucose homeostasis has already been shown. Among all 3D methods, organoids are gaining more and more prominence since they constitute a mimicked and simplified version of the organ in-vitro [12], [20]. Organoids are three-dimensional Mini-organs grown in the lab from stem cells, progenitor cells, or pluripotent cells (including induced pluripotent stem cells).

They have the remarkable ability to self-organize, meaning the cells spontaneously group, sort, and differentiate to form structured clusters that mirror the architecture of real organs. These clusters often include multiple organ-specific cell types and can perform one or more specialized functions—such as contracting like heart tissue, filtering like kidneys, or secreting hormones like endocrine glands [6], [8].

Beyond their self-organization and functional capabilities, organoids also:

1. Exhibit cellular polarization, where cells orient themselves along defined axes (e.g., apical–basal), creating features like crypts in intestinal organoids or retinal layers.
2. Show emergent behaviors—complex patterns that arise naturally from cell–cell interactions—recapitulating tissue architecture without external templates .
3. Can be genetically engineered (e.g., via CRISPR-Cas9) to study disease mechanisms, model organ development, or test therapies.
4. Are powerful tools for disease modeling, drug screening, personalized medicine, and regenerative therapies, as they faithfully reproduce the genotypes, phenotypes, and functions of their source tissues.



In summary, organoids are self-organizing, multi-cellular, functional micro-organs that bridge the gap between traditional cell cultures and living organs.

In 2016, Kim et al. developed islet-like organoids from human induced pluripotent stem cells (hiPSCs) using 3D culture techniques. These endocrine cells spontaneously clustered into uniform spheroids measuring 50–150 µm within a day. The resulting endocrine cell clusters (ECCs) exhibited significantly enhanced insulin secretion in response to glucose and potassium stimulation in vitro. Moreover, when transplanted into diabetic mice, these organoids promoted survival and partially normalized blood glucose levels for over 40 days [5]. Building on this, Wang et al. (2017) successfully generated islet organoids from human embryonic stem cells (hESCs) using biomimetic 3D scaffolds. These organoids contained all major pancreatic cell types—α, β, δ, and PP cells—with most insulin-producing β-cells expressing key maturity markers like Pdx1, Nkx6.1, MafA, Glut2, and C-peptide, without co-expressing other hormones (monohormonality). Functionally, these scaffold-grown organoids showed strong glucose-stimulated insulin secretion, reflecting their elevated cellular maturity and therapeutic potential in diabetes treatment [6].

Comparative data

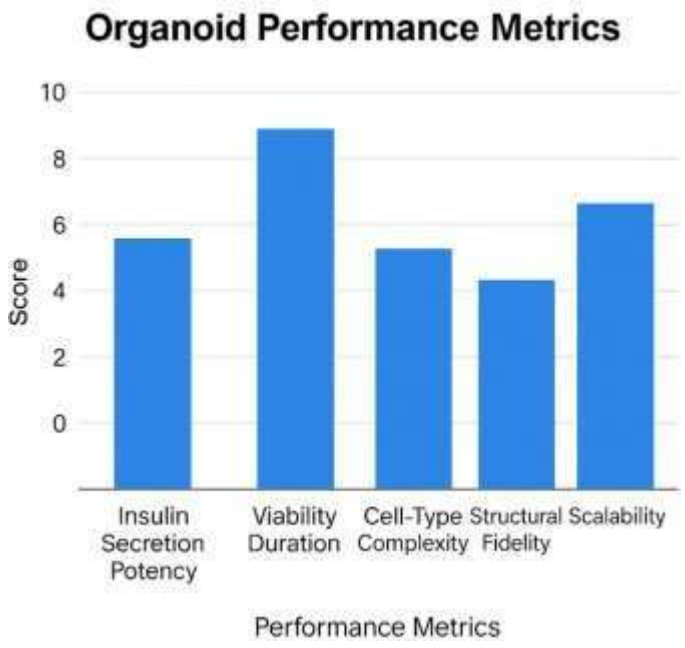
Model & Source	Spheroid Size	Maturity Markers	GSIS Response	In Vivo Functionality
hiPSC-ECCs (Kim 2016)	50–150 µm	Insulin, somatostatin, PP	↑ insulin secretion vs non-cluster cells	Diabetes normalization (~40 d)
hESC organoids (Wang 2017)	~100–150 µm	Pdx1, Nkx6.1, MafA, Glut2	Sharp spike at high glucose	Not yet evaluated in vivo

Recent breakthroughs have significantly advanced islet transplantation, particularly by overcoming immune rejection and donor shortages. In late 2024, the University of Chicago Medicines' experimental drug tegoprubart was used in human islet transplants [7]. In a small cohort of three T1D patients, two achieved insulin independence after 18 weeks and four weeks respectively, while the third reduced insulin requirements by 60%—all without serious side effects and with enhanced engraftment compared to standard drugs.

Meanwhile, Sana Biotechnology conducted a first-in-human trial (UP421) with CRISPR-engineered "hypoimmune" donor islets. At six months post-transplant (no immunosuppression), patients had consistent C-peptide production detected by mixed-meal tolerance tests, plus MRI evidence of graft survival—indicating functional, immune-evading transplanted cells [9].

The graph below shows how well current pancreatic or islet organoids perform across five critical dimensions.

The scores (roughly from 0–10) are relative, based on literature data and qualitative expert scoring — higher means better performance.



Metric	What it means	Why it matters	Typical score & explanation
Insulin Secretion Potency	Ability to release insulin appropriately in response to glucose	Reflects functional β-cell maturity	~5–6 (moderate): many organoids still underperform vs. native islets
Viability Duration	How long organoids remain alive & functional in vitro	Affects utility for therapy and testing	~9 (high): modern bioreactor and matrix systems keep them viable for weeks to months
Cell-Type Complexity	Inclusion of multiple islet cell types (α, β, δ, PP, etc.)	Needed for physiologic hormone interplay	~5 (moderate): most organoids are β-cell heavy; few have full complexity
Structural Fidelity	Whether organoids reproduce native islet 3D core–mantle structure	Needed for proper paracrine signaling	~4–5 (low–moderate): difficult to replicate precisely
Scalability	Capacity to produce large numbers uniformly	Critical for clinical or drug-screening use	~7 (fair–good): bioreactors can scale up, but variability remains

Advanced delivery technologies are also emerging:

1. A biovascular pancreas (BVP)—an acellular graft with hydrogel-coated islets—restored normal blood glucose in primates [14].
2. Immunomodulatory microgels (SA-FasL presenting) sustained islet survival and glycemic control in primates for over six months with minimal systemic immunosuppression [15].
3. Stem-cell-derived islet therapies are progressing fast.
4. Vascularized SC-islets (Max Delbrück Center/Sander lab) show enhanced β-cell maturity and insulin release due to integrated vasculature and nutrient flow [8], [18].

Multiple biotech firms—Vertex (VX-880), ViaCyte (PEC-Direct, VCTX210), Kyoto's OZTx-410—are running human trials using hPSC- or iPSC-derived islets [8], [18]. Initial data show safety, engraftment, and early insulin production without immunosuppression in some cases.

The regenerative medicine landscape for T1D now includes immune-evading donor islets [9], engineered vasculature [8],[18], advanced encapsulation methods [14], [15], and stem-cell-derived alternatives [5], [6]—all moving into or through early clinical trials. These promising developments indicate that scalable, durable cell therapies may soon transform T1D treatment beyond conventional insulin usage.

CONCLUSION

Regenerative medicine stands at the threshold of transforming the very fabric of therapeutic practice. Rather than merely managing disease, it aspires to restore, replace, and renew—drawing upon the remarkable potential of stem cells, bioengineered tissues, and three-dimensional organoids to reawaken the body's own regenerative capacities.

Early advances, from hematopoietic stem cell transplantation in autoimmune diabetes to the cultivation of vascularized islet organoids, have illuminated a path once thought unreachable. Yet this path is neither short nor simple. Challenges of immune compatibility, cellular maturation, ethical governance, and large-scale production remind us that scientific promise must always be tempered by rigour, patience, and care.

The narrative of regenerative medicine shows evidence steadily gathering strength: of damaged hearts beating

stronger, failing β-cells showing renewed insulin production, and what were considered impossible to possible

In time, through thoughtful innovation and sustained inquiry, regenerative medicine may fulfill its boldest vision: to move beyond palliation and towards true biological renewal — offering not just longer life, but restored function and renewed quality of life for millions worldwide.

REFERENCES

I. Mason, C., & Dunnill, P. (2008). A brief definition of regenerative medicine. Regenerative Medicine, 3(1), 1–5.

II. Takahashi, K., & Yamanaka, S. (2006). Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors. Cell, 126(4), 663–676.

III. Voltarelli, J. C., Couri, C. E. B., Stracieri, A. B. P. L., Oliveira, M. C., Moraes, D. A., Pieroni, F., Coutinho, M., Malmegrim, K. C. R., Foss-Freitas, M. C., Simões, B. P., & others. (2007). Autologous nonmyeloablative hematopoietic stem cell transplantation in newly diagnosed type 1 diabetes mellitus. JAMA, 297(14), 1568–1576.

IV. Couri, C. E. B., Oliveira, M. C., Stracieri, A. B. P. L., Moraes, D. A., Pieroni, F., Coutinho, M., & Voltarelli, J. C. (2009). C-peptide levels and insulin independence following autologous nonmyeloablative hematopoietic stem cell transplantation in type 1 diabetes. JAMA, 301(15), 1573–1574.

V. Kim, Y., Kim, H., Ko, S., & Park, S. (2016). Three-dimensional beta-cell spheroids derived from human pluripotent stem cells for transplantation therapy. Scientific Reports, 6, Article 35245.

VI. Wang, Y., Wang, L., Zhu, Y., Qin, J., & Zhang, C. (2017). Generation of functional islet organoids from human embryonic stem cells in biomimetic 3D scaffolds. Cell Proliferation, 50(6), e12388.

VII. Shapiro, A. M. J., Pokrywczynska, M., & Ricordi, C. (2017). Clinical pancreatic islet transplantation. Nature Reviews Endocrinology, 13(5), 268–277.

VIII. Sander, M., & Lickert, H. (2022). Engineering vascularized stem-cell derived islets for diabetes therapy. Nature Reviews Endocrinology, 18(9), 549–562.

IX. Zhao, T., Zhang, Z. N., Rong, Z., & Xu, Y. (2011). Immunogenicity of induced pluripotent stem cells. Nature, 474(7350), 212–215.

X. Zhang, Y., Wang, Q., Liu, M., & Yang, L. (2019). Hematopoietic stem cell transplantation for autoimmune diseases: Systematic review and meta-analysis. Autoimmunity Reviews, 18(2), 209–222.

XI. Zhang, L., Liu, Z., & Zhang, W. (2022). Clinical efficacy and safety of hematopoietic stem cell transplantation for type 1 diabetes: Systematic review and meta-analysis. Diabetes Therapy, 13(5), 1033–1047.

XII. Pagliuca, F. W., Millman, J. R., Gürtler, M., Segel, M., Van Dervort, A., Ryu, J. H., ... & Melton, D. A. (2014). Generation of functional human pancreatic β cells in vitro. Cell, 159(2), 428–439.

XIII. Rezania, A., Bruin, J. E., Arora, P., Rubin, A., Batushansky, I., Asadi, A., ... & Kieffer, T. J. (2014). Reversal of diabetes with insulin-producing cells derived in vitro from human pluripotent stem cells. Nature Biotechnology, 32(11), 1121–1133.

XIV. Vegas, A. J., Veiseh, O., Gürtler, M., Millman, J. R., Pagliuca, F. W., Bader, A. R., ... & Langer, R. (2016). Long-term glycemic control using polymer-encapsulated human stem-cell–derived beta cells in immune-competent mice. Nature Medicine, 22(3), 306–311.

XV. Pepper, A. R., Gala-Lopez, B., Ziff, O., & Shapiro, A. M. J. (2015). Revascularization of transplanted pancreatic islets and role of the transplantation site. Clinical Developmental Immunology, 2013, Article 352315.

XVI. Shapiro, A. M. J., & Lakey, J. R. T. (2001). Clinical islet transplantation. New England Journal of Medicine, 344(13), 889–892.

XVII. Atkinson, M. A., Eisenbarth, G. S., & Michels, A. W. (2014). Type 1 diabetes. Lancet, 383(9911), 69–82.

XVIII. Millman, J. R., Xie, C., Van Dervort, A., Gürtler, M., Pagliuca, F. W., & Melton, D. A. (2016). Generation of stem cell-derived β-cells from patients with type 1 diabetes. Nature Communications, 7, Article 11463.

XIX. Kulkarni, R. N., Stewart, A. F., & Klein, D. (2021). Regenerating pancreatic beta cells: Lessons from development, regeneration, and reprogramming. Diabetes, 70(1), 12–23.

XX. D'Amour, K. A., Bang, A. G., Eliazer, S., Kelly, O. G., Agulnick, A. D., Smart, N. G., ... & Baetge, E. E. (2006). Production of pancreatic hormone–expressing endocrine cells from human embryonic stem cells. Nature Biotechnology, 24(11), 1392–1401.