



USING STEM CELLS TO TREAT DIABETES: CONCEPTS AND ETHICS.

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ABSTRACT

The current paper utilizes academic literature in order to better understand the viability of using stem cells to cure diabetes. Not only does the current author attempt to present an objective point-of-view of the subject matter, but also present the ethical questions that such research can bring about as well as the possible future outcomes of utilizing such a method for treating a disease with such a long history as diabetes. The current study was conducted using a qualitative methodology, with a focus on academic literature obtained from various scholarly sources. This was done in order to not only save time, but also provide a broader view of the subject matter at hand, whilst analyzing previous studies regarding it. In conclusion, it was found that the use of stem cells, especially ones obtained from no embryonic sources, to cure diabetes mellitus has a prominent place for future studies and use. While the method itself has not been perfected as of yet, future research regarding the treatment may yield tremendous results, which may change the light that healthcare is viewed in. The current author recommends that future research utilize a quantitative and thematic approach to research so as to analyze how certain populations are affected by this treatment method.

INTRODUCTION

For years now, the primary cause or causes of diabetes have eluded scientists and academic scholars. However, in the case of Diabetes Type I, the immune system destroying the pancreas' beta islet cells is believed to be key. What has proven to be elusive, however, is that of a permanent cure for the disease. Conversely, research in the field of stem cells may prove to be a viable answer to such an elusive question.

Currently, more than four hundred million individuals, across Earth, are suffering from diabetes. This is expected to receive a two hundred million increase by 2035, making the overall population that suffers from diabetes nearly six hundred million (American Diabetes Association, 2017). While in the case of many, the illness can be managed through the use of insulin, exercise, or a healthy diet. For others, the complications that diabetes can cause can be quite severe, such as heart disease, kidney failure, loss of vision, nerve damage, and so on (Colberg, et al., 2016).

LITERATURE REVIEW

Stem cells are cells that have not developed any particular traits of their own. This allows these cells to develop to a variety of different types of cells, an ability that has piqued the interest of scientists since their discovery (Millman, et al., 2016). Research regarding these cells allows scientists to develop various human cells in a controlled environment, which thereby opens up a wide opportunity for cures for conditions such as diabetes. In one example, Atlas (2015) took human intestinal cells and disabled a gene that allowed the cells to create insulin. Stem cells come from various sources such as teeth, embryos, blood cells, the placenta, bone marrow, and the umbilical cord (Agulnick, et al., 2015).

In recent years, research regarding stem cells has become a significant aspect of the understanding of diabetes, especially type I. Research has displayed that these cells can be developed in controlled environments such as laboratories (Millman, et al., 2016). The Pittsburgh University, in 2004, had developed beta cells that produced insulin. This was performed by introducing the "cyclin d" and the "cdk" genes through the use of a virus. These researchers were able to stop the cells from continuing their growth and deactivate the virus (Georgia

& Bhushan, 2004). Such research can prove to better improve beta cell availability.

Individuals who have Type I diabetes are generally assisted in controlling their glucose levels through the use of insulin (Colberg, et al., 2016). On the other hand, these individuals do generally face difficulties in maintaining the level of sugar in their blood and have to measure their blood sugar levels at various points during the day (Colberg, et al., 2016). New developments, i.e. insulin pumps, have allowed for treatment improvements by allowing individualized dose delivery. Nonetheless, these technologies are unable to recreate processes similar to that of the human body.

While Type II diabetes can also be handled through the use of exercise and a healthy diet, many individuals suffering from this type need to inject insulin into themselves in order to maintain healthy blood sugar levels. Additionally, they need to take certain medications in order to avoid complications. Stem cell research is currently helping answer complex questions related to diabetes such as why the immune system does not attack pancreas tissue or other organs, in Type I diabetes, but rather attacks beta cells as well as what leads to insulin resistance in type II diabetes (Atlas, 2015). Furthermore, significant progress has been made in developing beta cells from induced pluripotent stem cells and embryonic stem cells (American Diabetes Association, 2017).

DM, or Diabetes Mellitus, is a significant health issue and is regarded as one of the leading causes of death across the Earth as, on an annual basis, four million people die due to diabetes mellitus (Paşca, et al., 2015). The incidence and prevalence of diabetes mellitus in most regions, particularly in nations that are developing, has been increasing at a rapid pace (Farooq, Rehman, Hameed, & Akash, 2018). Evidence revealed that, in 1985, there were more than thirty individuals, across the globe, suffering from diabetes mellitus; with more than two hundred and thirty million being affected in 2008; and, as mentioned previously, this number is expected to continue increasing till it reaches two hundred million by 2035 (American Diabetes Association, 2017).

Exogenous insulin administration via routine injections and other traditional techniques are the most prominent forms of treatment for diabetes mellitus. However, this administration is generally linked with glucose control failure in the metabolic system, which can lead to hyperglycaemic episodes. Therefore, research has constantly attempted to move away from traditional treatments and towards newer, innovative methods. One of these new methods that is gradually on the rise is stem cell therapy, which holds a potential strategy to evade the regular issues with insulin injections. This technique is expected to supply, produce, and store insulin in order to keep the homeostasis of glucose. These therapies are

focused on creating β -cells that secrete insulin in a functional manner (Drost, et al., 2015).

Through the years, academic scholars have closely studied the manner in which the cells that produce insulin, in the pancreas' β -cells, are destroyed and can be replaced with one's that are produced by the human immune system, particularly in people with diabetes mellitus (Drost, et al., 2015). Now the newest technique for replacing and transporting pancreas cells, known as islet, where are clusters of cells that produce insulin, is the transplantation of these cells from a donor to another (Cito, Pellegrini, Piemonti, & Sordi, 2018). This technique has proven to be excellent for treating patients with diabetes type I (Cito, Pellegrini, Piemonti, & Sordi, 2018).

Hypoglycaemia or the level of glucose in the blood is generally followed by insulin changes in the body. Both of the aforementioned changes can generally cause medical emergencies i.e. comatosis. Conversely, if an islet transplant works effectively and as planned, the outcomes have high potential as the body controls glycemia, homeostasis functions as planned, with the body glucose and insulin being normal. The use of stem cells for treating diabetes mellitus is a way to replace routine insulin injection, but can cause cancer and various infections (Merkle, et al., 2017).

The consequences of a treatment can occur at any given point, as is the case with the transplantation of stem cells. Consequences can occur months, days, during or right after the transplant. A hundred days after the transplant, acute (short-term) consequences take place, with chronic (long-term) consequences taking place after the hundred-day mark, following the transplant. Among the list of consequences of transplanting stem cells, infections are listed due to the immune system weakening and the overall number of white blood cells dropping. While fungal or viral infections can occur, bacterial infections are frequent.

In order to make sure that the new discipline of stem cell therapy is able to keep its potential and help individuals who suffer from diabetes, it is important to better understand the discipline's advantages and disadvantages. If the disadvantages rank fewer than the advantages, the development of this academic and practical discipline can lead to innovative and genius approaches toward solving numerous ailments. The remaining paper elaborates on this concept and, through a synthesis of literature, provides an adequate conclusion for the advantage or disadvantage of the use of stem cells for treating diabetes.

Induced Pluripotent Stem Cells vs. Human Embryonic Stem Cells

Apart from attaining stem cells from the embryo, while they are in the pluripotent phase, another technique for attaining cells that are pluripotent is by attaining

pluripotent induced stem cells. A pluripotent, induced stem cell is made by pluripotency induction into adult cells that have already differentiated themselves. This technique is different from the development of human embryonic stem cells as it is the reverse engineering of cells that have matured and become different, while human embryonic stem cells are ones that have not differentiated and can be changed to any tissue of choice.

A study by Drost, et al., (2015) offers protocols that are step-by-step, for creating pluripotent induced stem cells by using the pancreas cells from humans through the use of the CRISPR-Cas9 system. This technique is significant for the following reasons:

The first reason for this significance is that the therapy such as this can help create islet cells in the pancreas, which can be transplanted to patients who have type I diabetes mellitus or other diseases where the function or density of beta cells is reduced. If the objective is to develop islet cells that can be transplanted into another person, this can provide pluripotent induced stem cells that retain their heritage qualities, thereby making reprogramming effective and easy.

The second reason is that most techniques for creating pluripotent induced stem cell necessitates the use of viruses such as methods for delivering or reconstructing DNA. The technique highlighted by Drost, et al., (2015) shows the potential of reducing viral exogenous or transgenes factors incidences through the integration of pluripotent induced stem cells. Therefore, it is reasonable to state that when factors that are exogenous are less, transplant rejection and the production of antigen also reduces.

CRISPR-Cas9 is intuitive, inexpensive, and user-friendly. The system utilizes genetic engineering sciences and provides them to the many, from undergraduate assistants in laboratories to famous researchers of stem cells. In laymen's terms, the number of pluripotent induced stem cells that can be studied and made through this technique is high and thereby a desirable option which improves the reach and the potential of the research itself.

On the other hand, it begs to be questioned as to whether the accessibility that pluripotent induced stem cell technologies offer make their use justified over human embryonic stem cells. Dever, et al. (2016) looked to answer this by comparing a line of pluripotent induced stem cell to S7 embryonic cells from humans. In normal humans, the beta cells in the pancreas are able to regulate themselves; they are able to respond to glucose, create insulin, and turn off in order to prevent the risk of hypoglycaemia. Attempts have been made to have stem cells produce such behaviours, but these attempts have been met with various difficulties, particularly when the cells are *in vitro*.

Dever, et al. (2016) found that, by injecting the insulin secreting S7 cells into mice, there was a positive glucose sensitivity. While their responses to glucose were slower than in human beta cells, the cells demonstrated a reversal of diabetes. Moreover, this diabetes reversal was developed four times more rapidly than the progenitors in the pancreas were able to. According to Dever, et al. (2016), the human embryonic stem cells are much more efficient than pluripotent induced stem cells as pluripotent induced stem cells were not able to create as many insulin secreting cells as human embryonic stem cells were. Conversely, both types of cells were equal in their reversal of mice diabetes.

Other researchers had successfully made hundreds of millions of pancreas beta cells that were functional in the human body by using both human embryonic stem cells and pluripotent induced stem cells these cells demonstrated a sensitivity to glucose and were similar to the human beta cells and cadaveric islets. When injecting it into mice, these cells, attaining through the use of both human embryonic stem cells and pluripotent induced stem cells would secrete insulin into the bloodstream of the host and also displayed increased insulin secretion in the body after glucose issues arose (Guo, et al., 2016).

The capability to create vast amounts of pancreas beta cells *in vitro* overcomes one of the greatest of restrictions that is accompanied by replicating human beta cells. Conversely, the issue lies in preventing graft immunogenicity and transplanting or implanting these cells.

The Case for Adult Stem Cells in the Creation of Insulin-Producing Cells

From an ethics point-of-view, using human embryonic stem cells is quite debated and using them can place the patient at the risk of a tumour. Both of these issues limit human embryonic stem cells and their potential use as treatment for type I diabetes mellitus. Pluripotent induced stem cells can also place the patient at the risk of developing tumours and these cells can cause mutations in the genes due to the techniques used to induce them (Sugimura, et al., 2017). With that in mind, using stem cells taken from adult issue is a highly promising way to create beta cells.

Academic research shows that progenitor cells in humans, taken from the fetal pancreata can be utilized in order to develop cells that functionally produce insulin *in vitro*, and that after mice were implanted with these, the cells were able to maintain and resolve normoglycemia (Dever, et al., 2016). If the progenitor cells in the intestine can be brought *in vitro* in order to differentiate beta cells in order to sustain the cell's functionality in patients with type I diabetes mellitus, while avoiding autoimmune attacks (Sordi, et al., 2017). Reasonably, this technique can cure type I diabetes mellitus (Sordi, et al., 2017).

However, the primary issue with this technique is that of inducing beta cell to intestinal cell differentiation, which requires a considerable comprehension of the pathways of molecular signalling included in the development of beta cells. Various breakthrough studies have been published regarding how successfully pluripotent induced cells from the progenitor intestinal cells in mice by removing FOX-O1, which is a basis for the transcription of beta cells and is important for their development in the developing pancreas.

Kalra, Chandrabose, Ramasamy, & Kasim (2018) found various important pathways and factors that were impacted by the signaling downstream pathway by looking into the influence of the ablation of FOX-O1. Taking this element out, caused Wnt signaling to activate, which stopped Neurog3 from changing into different enteroendocrine cells. Activating the signaling of Wnt caused high Amino-terminal enhancer of split. This was important for creating progenitor intestinal cells by suppressing HES-1 and Notch expression and signaling (Agulnick, et al., 2015).

FOX-O1 ablation generating progenitor intestinal cells were able to secrete insulin by responding to the levels of glucose *in vivo*, which shows a potential technique for research into type I diabetes mellitus. Furthermore, the aforementioned mice was able to regenerate their progenitor intestinal cells upon being induced with STZ diabetes. Findings of authors such as Kalra, Chandrabose, Ramasamy, & Kasim (2018) demonstrate the potential for regenerating beta cells and taking steps toward curing type I diabetes mellitus.

Stem cells that are derived from adipose tissue have demonstrated potential for treating type I diabetes mellitus. Colberg, et al. (2016) had created a unique protocol for differentiating stem cells that are derived from adipose tissues into cell aggregates that are islet like and are considerably productive as they produce sixty-four per cent of the PX-1+ cells, which are important for differentiating beta cells and regulating the development of the pancreas, and forty-nine per cent cells that are positive for C peptides, which are important diabetes markers.

On the other hand, Sugimura, et al. (2017) treated mice that were induced with STZ diabetes with the intravenous transplantation of cell aggregates that are islet like that were transfected with PDX-1. These were largely inserted into the diabetic pancreata of mice, where beta cells develop functionally *in vivo* and support the concept that cell aggregates that are islet like taken from beta cells have properties that can be considered regenerative.

The Case for Non-Embryonic Stem Cell Therapy

So far, the current paper has elaborated on the several techniques and strategies that can be utilized in order to derive stem cells in regards to treating diabetes more

efficiently than traditional methods such as routine insulin injections. The advantages and disadvantages of these treatments have been deeply discussed in this synthesis of literature. On the other hand, there lies an argument regarding the use of these cells, particularly in the field of science, research, and ethics. While the mentioned sources have found success in their research, it is important to discuss and elaborate upon the risks that each method carries alongside it, particularly in a clinical environment.

As mentioned previously, cells that are pluripotent generally carry the risk of the patient developing a tumour upon the transplant from the host. Pluripotent induced stem cells are becoming increasingly popular relative to human embryonic stem cells, particularly in their clinical usage and research potential. On the other hand, the significant difference between pluripotent induced stem cells and human embryonic stem cells may restrict the usage of pluripotent induced stem cells in clinical settings. Human embryonic stem cells have demonstrated their ability to undergo and/or attain mutations in the genes during various points in their differentiation into somatic cells (American Diabetes Association, 2017).

Pluripotent induced stem cells, on the other hand, are vulnerable to incorporate mutations in the gene into their genome as they have to be reprogrammed first through a process of modification into pluripotency (American Diabetes Association, 2017). Upon being reprogrammed, these cells meet a similar fate to that of human embryonic stem cells, with more mutations being integrated later on into the genome at the time of the differentiation. The issue itself warrants the certainty for more protocols for pluripotent induced stem cells quality testing, relative to stem cells in adults or human embryonic stem cells.

Therefore, progenitor cells and stem cells that can be considered as adult cells need to be at the starting line of the regenerative therapy in clinical practice for individuals suffering type I diabetes mellitus. While the above section discussed techniques for attaining pancreatic beta cells through the use of adipocytes and progenitor cells from the intestine as a source of multipotent populations. Additionally, the human pancreatic and liver progenitor cells are effective in creating beta cells (Cito, Pellegrini, Piemonti, & Sordi, 2018).

Both *in vivo* and *in vitro*, these lines of cells have demonstrated their capability to developing the functions similar to that of human beta cells. These should be considered for future context in treating individuals suffering from type I diabetes mellitus. As neither oocytes or embryos are not used, pluripotent induced stem cells are not brought into heated arguments and discussions regarding the research on embryonic stem cells. Additionally, as a biopsy of the skin allows attaining somatic cells through methods that are not

invasive, there are very few concerns regarding the donor, relative to oocyte donations.

The Bioethics Council of the President stated that pluripotent induced stem cells are ethically acceptable and unproblematic in human use (Paşca, et al., 2015). Pluripotent induced stem cells, the materials they are derived from, and the act of deriving them does not bring about any particular ethical problems.

Downstream Research

Certain possible downstream uses of the derivatives of pluripotent induced stem cells can be sensitive enough to question if the donor of the somatic cell was agreed upon (Sordi, et al., 2017). Pluripotent induced stem cells are generally shared amongst academics who perform research using these cells and what is derived from them, through the use of accepted and common practices of science such as:

- Cell genetic modification;
- Injecting cell derivatives into animals in order to understand the function of the cell such as its effects on the animal brain;
- Sequencing the genome on a mass-scale;
- Distributing the lines of cells amongst other academics who properly protect confidentiality; and
- Developing commercial therapies and tests and patenting the academic findings without providing the donor with any royalties.

These standardized methods of research are used broadly in various forms of research, and even for the subject matter of the current paper. In general, those who donate biological materials are not told or educated as to the aforementioned research practices and procedures; however, the disclosure of this information is appropriate when sequencing an entire genome (Millman, et al., 2016). These types of studies are the basis of research in the discipline of stem cells such as the demonstration and characterization of cells being pluripotent.

The sequencing of genomes on a mass-scale provides knowledge regarding a disease's pathogenesis and helps in identifying targets for therapies. Injecting human stem cells into animal brains is needed before clinical testing of these therapies can take place i.e. therapies for stroke or Parkinson's and Alzheimer's disease. Downstream research has brought about various concerns in the field of ethics. Donors can regard it as being a privacy violation if a scientist knows the donor's vulnerability of various genetic ailments.

Therefore, it would be of tremendous restriction to the scientific community if donors refuse to have their pluripotent induced stem cells be used in research that is different from the one, they gave their consent to. Thus, it is important for researchers to obtain the entire consent of the donor prior to the donation being taken in order to not limit, but improve study. Another solution would be to carefully use the donation provided by the donor,

attain their consent regarding the use of their donation in other basic research, and contact them upon the need to perform further research on their donation so as to attain proper consent (American Diabetes Association, 2017).

Donors can be provided with the option to consent to their donation being used in additional research, but not downstream research such as reproductive research that involves creating totipotent bodies and allogenic transplants to other people. As these worries of consent regarding downstream research applies to stem cell research as well, it is important to place considerable consent standards for the materials being donated. On the other hand, these worries are not considerable in the research of pluripotent induced stem cells due to the broad perception of these cells being that they do not pose any ethical issues and that they only play a role in improving research regarding stem cells.

Ethical Concerns of Human Embryonic Stem Cells

Human embryonic stem cell research is politically and ethically controversial as it involves the destruction of human embryos. In the United States, the question of when human life begins has been highly controversial and closely linked to debates over abortion. It is not disputed that embryos have the potential to become human beings; if implanted into a woman's uterus at the appropriate hormonal phase, an embryo could implant, develop into a fetus, and become a live-born child. Some people, however, believe that an embryo is a person with the same moral status as an adult or a live-born child.

As a matter of religious faith and moral conviction, they believe that "human life begins at conception" and that an embryo is therefore a person. According to this view, an embryo has interests and rights that must be respected. From this perspective, taking a blastocyst and removing the inner cell mass to derive an embryonic stem cell line is tantamount to murder (Farooq, Rehman, Hameed, & Akash, 2018). Many other people have a different view of the moral status of the embryo, for example that the embryo becomes a person in a moral sense at a later stage of development than fertilization. Few people, however, believe that the embryo or blastocyst is just a clump of cells that can be used for research without restriction.

Many hold a middle ground that the early embryo deserves special respect as a potential human being but that it is acceptable to use it for certain types of research provided there is good scientific justification, careful oversight, and informed consent from the woman or couple for donating the embryo for research (Georgia & Bhushan, 2004). Opposition to human embryonic stem cells research is often associated with opposition to abortion and with the "pro-life" movement. However, such opposition to stem cell research is not monolithic. A number of pro-life leaders support stem cell research using frozen embryos that remain after a woman or

couple has completed infertility treatment and that they have decided not to give to another couple.

Ethical Concerns about Somatic Cell Nuclear Transfer

Some people who object to somatic cell nuclear transfer believe that creating embryos with the intention of using them for research and destroying them in that process violates respect for nascent human life. Even those who support deriving stem cell lines from frozen embryos that would otherwise be discarded sometimes reject the intentional creation of embryos for research. In rebuttal, however, some argue that pluripotent entities created through somatic cell nuclear transfer are biologically and ethically distinct from embryos (Millman, et al., 2016).

Use of animal oocytes to create somatic cell nuclear transfer lines using human DNA. Because of the shortage of human oocytes for somatic cell nuclear transfer research, some scientists wish to use nonhuman oocytes to derive lines using human nuclear DNA. These so-called “cytoplasmic hybrid embryos” raise a number of ethical concerns. Some opponents fear the creation of chimeras—mythical beasts that appear part human and part animal and have characteristics of both humans and animals (Cito, Pellegrini, Piemonti, & Sordi, 2018).

Opponents may feel deep moral unease or repugnance, without articulating their concerns in more specific terms. Some people view such hybrid embryos as contrary to a moral order embodied in the natural world and in natural law. In this view, each species has a particular moral purpose or goal, which mankind should not try to change. Others view such research as an inappropriate crossing of species barriers, which should be an immutable part of natural design. Finally, some are concerned that there may be attempts to implant these embryos for reproductive purposes. In rebuttal, supporters of such research point out that the biological definitions of species are not natural and immutable but empirical and pragmatic (Drost, et al., 2015).

Animal-animal hybrids of various sorts, such as the mule, exist and are not considered morally objectionable. Moreover, in medical research, human cells are commonly injected into nonhuman animals and incorporated into their functioning tissue. Indeed, this is widely done in research with all types of stem cells to demonstrate that cells are pluripotent or have differentiated into the desired type of cell. In addition, some concerns can be addressed through strict oversight (Agulnick, et al., 2015), for example prohibiting reproductive uses of these embryos and limiting in vitro development to 14 d or the development of the primitive streak, limits that are widely accepted for other human embryonic stem cell research.

Finally, some people regard repugnance per se an unconvincing guide to ethical judgments. People disagree over what is repugnant, and their views might

change over time. Blood transfusion and cadaveric organ transplantation were originally viewed as repugnant but are now widely accepted practices. Furthermore, after public discussion and education, many people overcome their initial concerns.

METHODOLOGY

The current research utilizes a qualitative methodology and focuses on secondary, academic research conducted by scholarly sources. This data has been gathered from various online databases and includes a variety of research. As any type of research can place a tremendous amount of time-related restrictions on the research, the best possible research method to be utilized to save not only time, but also money is that of the qualitative methodology.

This is due to the fact that this type of research aims less on measurements and much more on the information that can be found from observational research. This lets researchers provide an improved level of detail to previously conducted research by comparing it to modern research and also analyzing it in view of its contemporaries. While research generally follows a pattern of questioning, gathering data, and reporting information, qualitative research focused on adapting the quality of information collected and providing current and updated results. If the gathered data does not offer conclusive results, the researcher can move to different avenues of information in order to learn more about the subject matter.

Generally, qualitative research offers insight specific to the discipline in which it is focused on as it uses smaller sizes of samples in order to reduce overall monetary expenses. Qualitative research can be performed on a restricted budget and quickly as it uses smaller samples sizes than other types of research. This objective focus allows researchers to easily concentrate on the subject matter and offer quality results.

DISCUSSION AND CONCLUSION

There seems to be a prominent future for research in the field of stem cells and their use in treating those suffering from diabetes. However, the question lies in the ethics of such treatment as the source from which these stem cells are harvested needs to be thoroughly disclosed to patients prior to them receiving treatment, with the preferences of the patient and all those involved being treated with respect.

Studies on animals have demonstrated that the nature of beta cells to respond to glucose derived from human embryonic stem cells hidden in alginate and transplanted through diabetic mice who have been induced with STZ results in glycemia being effectively controlled (Farooq, Rehman, Hameed, & Akash, 2018). On the other hand, the ethical consequences included in the use of embryonic stem cells have restricted their application in the clinical setting. In light of this, pluripotent induced

stem cells have been suggested as a particular and appropriate solution sourced from cells that have similar pluripotent traits as embryonic stem cells.

Recommendations for Future Research

Future research regarding stem cells and their use in treating diabetes such should utilize a quantitative and thematic approach in order to better analyze how certain populations view such a treatment and their willingness to abide by this type of treatment. This type of research will help in building a customer base for the treatment and help understand the place of stem cell research in the general population. FOX-O1 ablation generating progenitor intestinal cells were able to secrete insulin by responding to the levels of glucose *in vivo*, which shows a potential technique for research into type I diabetes mellitus. Both *in vivo* and *in vitro*, these lines of cells have demonstrated their capability to developing the functions similar to that of human beta cells. These should be considered for future context in treating individuals suffering from type I diabetes mellitus.

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