Stem cell therapy for diabetes: Where are we?

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Diabetes is a life-long condition that occurs as a result of a defect in pancreatic beta cells to secrete enough insulin and/or the inability of insulin target tissues to use this hormone efficiently (insulin resistance). There are two major types of diabetes: Type 1 diabetes (T1D) is characterized by a pancreatic beta cell loss due to an autoimmune defect, while type 2 diabetes (T2D) is a metabolic disorder resulting from a reduction in beta cell function associated with insulin resistance.

TREATING DIABETES: HOW MAY STEM CELLS HELP?

There are a myriad of treatments and care available for patients of diabetes. For instance, patients with T2D can control their increased blood glucose levels indifferent ways, including exercise, diet, and oral blood glucose-lowering drugs. However, many other patients, who have lived with T2D for long period of time,may ultimately require insulin injections. Therefore, beta cell replacement therapy is consideredas a highly viable potential strategy to treat T1D and advanced cases of T2D, because in both cases most of the beta cells have been lost.

To date, transplantation of pancreatic islets from cadavers is the most effective approach for treating diabetic patients, but this approach has limitations in terms of the necessity of strong immunosuppressive drugs and the shortage of matching donors.

Alternatively, human pluripotent stem cells (hPSCs), including human embryonic stem cells (hESCs) and human induced pluripotent stem cells (hiPSCs), can be differentiated into insulin-secreting beta cells andhave a great potential for treating diabetes. This makes them a powerful tool in medicine with great promises to have a significant future impact on millions of diabetic patients in the coming years. However, generation of functional insulin-secreting cells similar to those found naturally in the pancreas is, so far, a work in progress.

STATUS OF STEM CELL THERAPY TODAY

Indeed, few studies claimed that they have generated functional beta cells from hPSCs, but those cells werelow in efficiency, creating a major obstacle to the use of these cells for cellular therapy. Therefore, efforts are currently being made by researchers to successfully produce insulin-secreting cells in large enough numbers and efficient in responding to a rise in blood glucose levels.

Recent progress showed that patients with diabetes could be transplanted with hPSC-derived pancreatic progenitors, which are precursors for insulin-secreting beta cells. The main advantage of using such progenitors is that they can be efficiently generated in large number in the laboratories.

After their transplantation under the skin, these progenitors are differentiated inside the patient's body into fully functional pancreatic insulin-secreting cells.

San Diego-based ViaCyte company is currently conducting the first human clinical trial using hPSC-derived pancreatic progenitors for assessing the safety and efficacy of their therapeutic potential in treating T1D patients (http://viacyte.com/clinical/clinical-trials/) (the only FDA-approved clinical trial in this field). In case of T1D, the pancreatic cells are encapsulated in a permeable device to protect the transplanted cells from the patient's immune cells and to allow the release of insulin into blood capillaries in response to high blood glucose level.

ACHIEVING NEW INSIGHTS INTO DIABETES THROUGH STEM CELLS

Stem cells can also be used to understand specific forms of diabetes. The recently establishment of stem cell technology called induced pluripotent stem cells (iPSCs) has allowed for generation of hPSCs from any cells in the body to understand human genetic diseases. The fact that iPSCs can be produced without the need of a human embryo enables us to avoid ethical concerns, which restricted researchers for decades to use hESCs in stem cell research studies.

iPSCs generated from specific patients are genetically identical to these patients; thus, they can be used to generate cells that are not rejected by the immune system if they are transplanted to the same patient. These iPSCs may be generated by taking blood sample or skin biopsy from diabetic patients and convert them in the laboratory into iPSCs, which have the ability to differentiate into all cell types of the body. These patient-specific iPSCs, harboring the disease genotype, are then differentiated into cells that are relevant to the disease, such as pancreatic beta cells or insulin-target cells (liver, fat, and skeletal muscle). For example, insulin resistance is a precursor and accelerating factor for T2D and occurs several years before patients develop diabetes.

The human genetic characteristics of insulin resistance are difficult to be studied in animal models. However, iPSC technology is a good model to study human insulin resistance by generating insulin-target cells genetically identical to the patient and then study the pathogenesis of insulin resistance in a dish to investigate genetic factors underlying the development of insulin resistance in those cells.

Also, some types of diabetes occur due to mutations in specific genes that are known for their function in pancreatic beta cells and/or insulin target cells. Generating iPSCs from those patients offersexaminers cells (beta, liver, fat, and muscle cells) that can give key information about the disease pathogenesis and provide cells for personalized therapies. Furthermore, these models can also be used for large-scale screens to examine candidate drugs on insulin-responsive targets. This method provides an essential platform for understanding the genetic factors of diabetes that can eventually be translated into effective treatment.

STEM CELLS MARKET REGULATIONS AND HOAXES

Currently, there is no internationally approved treatment available using insulin-secreting cells generated from stem cells to cure diabetes.

Governments, especially in Western Europe, United States, and Canada, heavily regulate stem cell research and use due to its far-reaching implications on ethics, economics, and on the human health. Thus, few exceptions are made, for a highly structured and controlled clinical trial for the testing of thoroughly vetted new treatments.

In Qatar, Qatar's Ministry of Public Health (MoPH) has clear guidelines and regulations for research involving different types of stem cells.

On the other hand, some healthcare facilities in Eastern Europe and Asia have reportedlyplayed on the vulnerabilities of patients and claimed to have the capacity to treat diabetic patients with several types of stem cells. These are false claims and scams, which at best, may not cause serious side-effects but do nothing to treat diabetes.

At worst, these interventionscan be dangerous for the patient, as those administering the "treatments" rely upon lax government regulations and poor oversight to inject patients with stem cells or other substances, which can cause serious side-effects and do lasting damage. Patients must therefore be cautious when seeking treatment abroad from any healthcare facility claiming to cure diabetes with stem cells.

QATAR AND ITS FIGHT AGAINST DIABETES

Diabetes is one of the greatest health challenges facing Qatar and the world today; therefore, it is one of the top priorities for Qatar National Research Strategy (QNRS). Given the significant impact this disease has, both directly and indirectly, on society, family, and economy through associated healthcare costs, diabetes research is given a top priority at Hamad Bin Khalifa University's (HBKU), Qatar Biomedical Research Institute (QBRI).

QBRI's cutting-edge research strategy supports innovative and multidisciplinary research in diabetes and related disorders. Stem cell research is one of the mainresearch areas at QBRI. The ultimate goal of our stem cell program at QBRI is to pave the way for developing novel therapeutic strategies for diabetes treatment.

The Institute's current stem cell projects aim to achieve two main goals: (1) Understanding genetic factors underlying the development of diabetes using iPSC technology; (2) Generation of functional insulin-secreting beta cells from hPSCs for cell therapy.

Given the groundbreaking nature of scientific research taking place at QBRI, the Qatar National Research Fund (QNRF) has actively stepped in to provide funding to several projects at the Institute to help overcome these challenges often faced by laboratories in other parts of the world.

All you wanted to know about hemoglobin A1c test (HbA1c)

Hemoglobin A1c is a protein on the surface of red blood cells that sugar molecules stick to, usually for the life of the red blood cell (about three months). The higher the level of glucose in the blood, the higher the level of hemoglobin A1c is detectable on red blood cells.

Hemoglobin A1c levels correlate with average levels of glucose in the blood over an approximately three-month time period. Normal ranges for hemoglobin A1c in people without diabetes is about 4% to 5.9%. People with diabetes with poor glucose control have hemoglobin A1c levels above 7%.

Hemoglobin A1c levels are routinely used to determine blood sugar control over time in people with diabetes.

Decreasing hemoglobin A1c levels by 1% may decrease the risk of microvascular complications (for example, diabetic eye, nerve, or kidney disease) by 10%.

Hemoglobin A1c levels should be checked every six months in individuals with stable blood sugar control, and every three months if the person is trying to establish stable blood sugar control. Hemoglobin A1c has many other names such as glycohemoglobin, glycated hemoglobin, glycosylated hemoglobin, and HbA1c.

To explain what hemoglobin A1c is, think in simple terms. Sugar sticks to things, and when it has been stuck to something for a long time it's harder to the get sugar (glucose) off. In the body, sugar sticks too, particularly to proteins. The red blood cells that circulate in the body live for about three months before they die.

When sugar (glucose) sticks to these red blood cells by binding to hemoglobin A1c, it gives us an idea of how much glucose has been around in the blood for the preceding three months.

Hemoglobin A1c is a minor component of hemoglobin to which glucose binds. Hemoglobin A1c levels depend on blood glucose concentrations. The higher the sugar concentration in the blood, the higher the detectable hemoglobin A1c levels. At any point in time, hemoglobin A1c levels represent the average blood sugar concentrations in the person with diabetes for approximately the preceding 3 months.

WHAT MAKES A PERSON'S HEMOGLOBIN A1C LEVELS HIGH OR LOW?

Hemoglobin A1c levels can be altered by

- Oral or IV glucose intake,
- fasting,
- use of insulin, and
- by combinations of these and other factors.

The goal for people with diabetes, with their doctor's help, is to establish stable blood glucose levels resulting in hemoglobin A1c levels that are at least below 7% to reduce or stop complications of diabetes (for example, diabetic nerve, eye, and kidney disease).

WHAT ARE NORMAL AND ELEVATED RANGES FOR HEMOGLOBIN A1C?

In most labs, the normal range for hemoglobin A1c is 4% to 5.9%. In well-controlled diabetic patients, hemoglobin A1c levels are less than 7.0%. In poorly controlled diabetes, its level is 8.0% or above.

The benefits of measuring hemoglobin A1c is that is gives a more reasonable view of what's happening over the course of time (about 3 months) to the average glucose level in the blood. Hemoglobin A1c value does not bounce up or down as much as daily finger stick blood sugar measurements.

While there are no guidelines to use hemoglobin A1c test levels as a screening tool, it gives a healthcare professional a good idea that someone may be have diabetes if the value is elevated; however, it is used as a standard tool to determine blood sugar control in patients known to have diabetes.

Studies have shown there is a 10% decrease in relative risk for microvascular complications for every 1% reduction in hemoglobin A1c.

So, if a person with diabetes has an initial hemoglobin A1c level of 10.7 and drops to 8.2, though they are not yet at goal (about 6.5%), they have managed to decrease their risk of microvascular complications by about 20%. The closer to normal the hemoglobin A1c, the lower the absolute risk for microvascular complications.

HOW OFTEN DOES A PERSON WITH DIABETES NEED TO HAVE THEIR HEMOGLOBIN A1C LEVELS CHECKED?

If people with diabetes want to reduce their hemoglobin A1c levels quickly, they should get their hemoglobin A1c levels checked every three months until they reach their treatment goals. People with diabetes who are meeting treatment goals and have stable blood control are recommended to check their hemoglobin A1c every six months. Tracking hemoglobin A1c levels allows an individual and their health-care professional to determine how well the person is controlling their blood sugar (glucose) levels over time. However, they are not a substitute for daily glucose monitoring.

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