Insight view of stem cells in treating Diabetes




Akhila Akkihebbal Ravikumar*[1], Bhavya K B[2], Likhitha T G[1] & Teja V V[3]

1 Department of Pharmaceutics, Cauvery College of Pharmacy, Mysore 570028, Karnataka, India.
2 Department of Analysis, Cauvery College of Pharmacy, Mysore 570028, Karnataka, India.
3 Department of Pharmacology, Cauvery College of Pharmacy, Mysore 570028, Karnataka, India.

akhilaravikumar19@gmail.com

Cellular therapy (CT) is an advanced therapy of transplantation of human cells to replace or repair damaged tissue or cells. In order to initiate an action, 'stem cells' should possess two essential characteristics. Firstly, stem cells should pertain an ability to unlimited self-renewal and to produce same photo copy as the originating cells. Secondly, capability of giving rise to specialized cell type which is part of the human body. CT is also termed as cell transplantation or cryotherapy. Stem cells are the master cells that act as fundamental building blocks to the human body. With the new technologies, cell therapies have advanced in innovation products and limitless imagination and many different types of cells that are injected, grated or implanted into a patient as part of therapy in a variety of diseases and conditions to regenerate diseased tissues [1].

During 19th century cell therapy was originated when scientists experimented by injecting animal material in an attempt to prevent and treat illness. Further, in mid of twentieth century positive benefit of human cell therapy led to a successful bone marrow transplantation. Now, it has become a regular practice for treatment of patients who have compromised bone marrow after disease, infection, chemotherapy and radiation. Stem cells and cell transplantation have gained interest for treating wide range of diseases, in particular to degenerative, regenerative medicine, drug discovery, toxicology and immunogenic pathologies.

The stem cells based therapy is classified based on the therapeutic indication as cardiovascular, neurological, ophthalmic; wherein the cells are taken from the donor person and administered to the same individual (autologous) or transferred to another (allogeneic) and obtained from animal source to human (Xenogeneic). The different types of cells are human embryonic cells, neural stem cells, mesenchymal stem cells, hematopoietic stem cell transplantation and differentiated or matured cell transplantation. The stem cell comprises of many distinct cell types, among animal form are embryonic and adult are two main modifiers for the development of new stem cells.

These stem cells are coined ‘somatic’ as they are basic building blocks of research but still lack due to differences in embryonic stem cells and adult stem cells. Based on the biological properties, stem cells are divided into two categories pluripotent stem cells and multipotent stem cells. These stem cells have definite sources, characteristics, cell differentiation and therapeutic applications. The other classification is based on the translational channels that need to overcome the therapy available to the patients. Further, to facilitate analysis the stem cell therapy is classified based on various technologies such as somatic cell, cell immortalization, ex vivo gene modification of cells using viral vector, in vivo gene modification of cells using viral vector, genome editing, cell plasticity, three-dimensional and lastly combinations of the above technologies [2].

Diabetes Mellitus (DM) is a metabolic disorder wherein body cannot take up sugar (glucose) resulting in inappropriate blood glucose levels. Glucose is required by the cells for energy production and normal functioning. This glucose enters to blood stream from the food we eat and it is further carried to cellular level by Insulin. The diabetes is developed when the body cannot prepare insulin or can’t respond to the insulin. Insulin is exogenously used to control of blood glucose in diabetic patients. DM is mainly classified into two categories – Diabetes Type 1(TIDM) and Diabetes Type 2 (T2DM). The number of DM patients in the world is increasing in recent years. If untreated, diabetes is one of the direct causes for death and 49% of deaths are due to diabetes occurred before the age of 70 years [3].

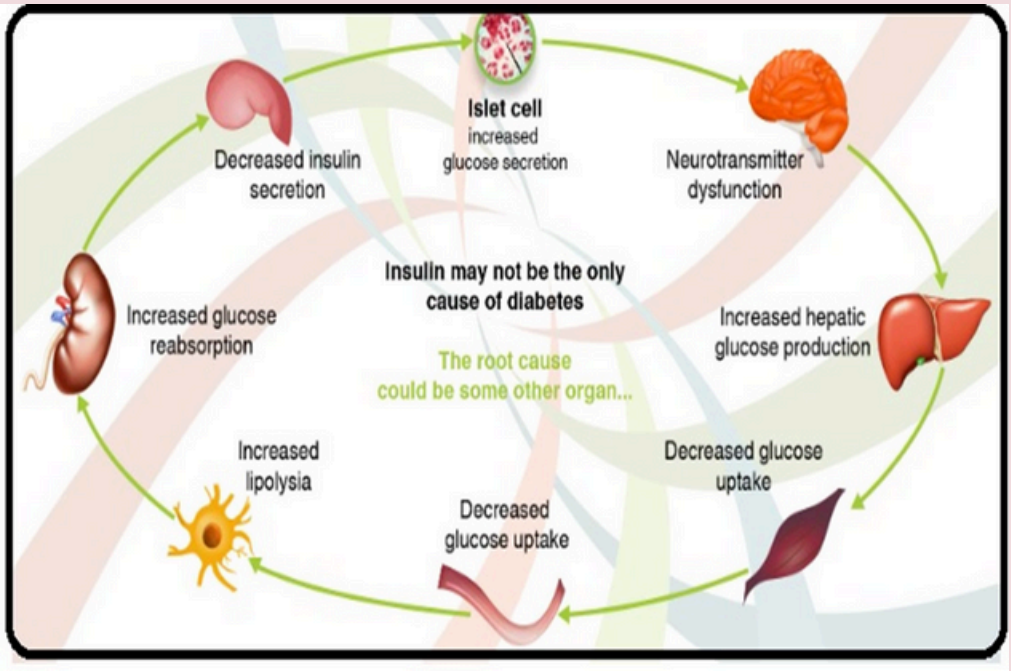

Figure 1: Causes for DM.
[*Figure obtained from https://www.giostar.com/about-us/publications-information-giostar-usa/*]

Stem cell therapy for DM

Stem cells therapy holds immense promise in treatment of patients with DM. The discovery of Insulin has enhanced the life span of T1DM in patients. The isolated islet/pancreas removed from a cadaveric pancreas transplantation have provided in vivo evidence in reestablishing β cells. However, the drawbacks of pancreas shortage have driven scientists to generate induced pluripotent stem cells (iPSCs).

The development of pluripotent adult stem cells into induced pluripotent adult stem cells, is more accessible method for new approaches. Much more positive results were derived from hematopoietic stem cells (hECs), embryonic stem cell (ESC) and adult stem cells. With upgrade of the research over time, scientists are now aware to persuade a cell and produce insulin with one step. The blood glucose concentration is controlled with specialized islets cells which controls the process and regulation of insulin secretion. The approaches to initiate stem cell production differ with different starting points. Differentiation is process in which stem cell reproduces itself and can then also divide asymmetrically. Stem cells were initially available only from embryos. Non-embryonic stem cells are now obtained without too much difficulty from umbilical cord, neonatal tissue and also from adult bone marrow, skin and fat. These cells are further expanded and made to different types of cells [4,5].

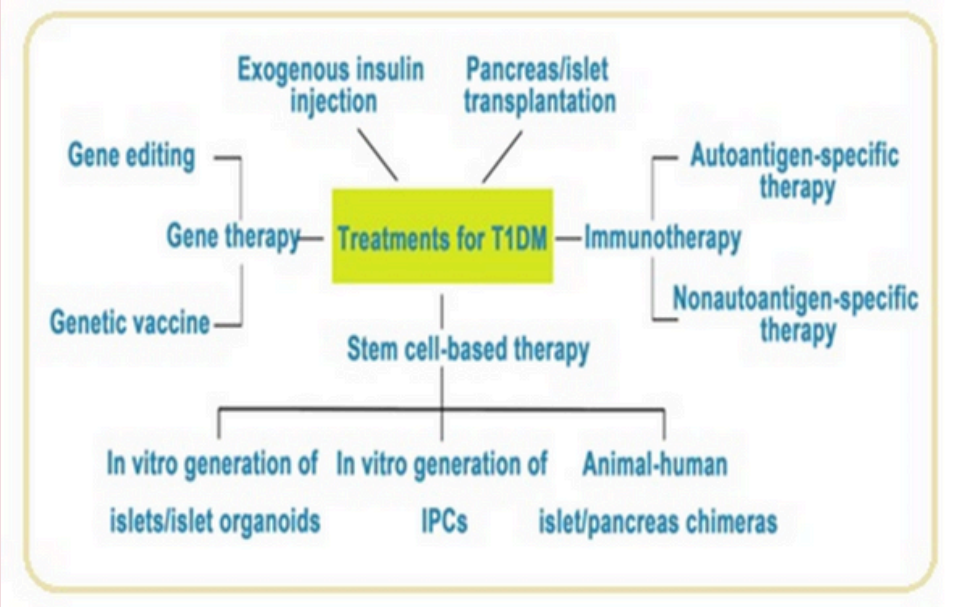

Figure 2: Treatment of T1DM.
[Figure obtained Gruessner RW, Gruessner AC. The current state of pancreas transplantation. Nat Rev Endocrinol. 2013;9(9):555–62.]

In 2006, Yamanaka was able to produce pluripotent stem cells from mouse neonatal and adult fibroblast cultures by adding a cocktail of four defined factors. This innovation led to a series for further innovations and development process which is repeatable with human tissue. Despite this, there has been very little success in directing differentiation of iPSCs to form islet beta-cells in sufficient quantity that will secrete and stop secretion in response to changes in blood glucose levels. Another approach that has been tried is combinational gene therapy with stem cells. With the use of human insulin gene construct and introduced ex vivo or in vivo into cells by direct electroporation (in ex vivo cells obviously) or by viral vectors. The adenovirus, adeno-associated virus and various retro viruses have been studied [6].

Type 2 Diabetes mellitus is characterized by insulin resistance, which may be combined with relatively reduced insulin secretion. T2DM patients who receive stem cell therapy receives various system targeted administration method like intravenously which delivers via a vein and distributed evenly and direct injection site, this delivers to the site that need repair like nerve damage or neuropathy, ischemic limbs in various areas to the body [7]. T2DM provides access to treatment that utilizes patients stem cell isolated from their own bone marrow [8].

There are multiple of inherent benefits afforded for the utilization of bone marrow component function in various diverse to innate therapeutic capacities. Hematopoietic stem cells are evident in treating chronic inflammatory and auto-immune conditions in red and white blood cells. In addition to HSCs, the mesenchymal stem cells (MSCs) are used to treat tissue damage and also exert protective cellular immunomodulatory effect [9].

Gestational diabetes resembles T2DM in several aspects wherein inadequate insulin secretion and responsiveness is seen. T2DM occurs in 2-10% in pregnancies and this may be improved or disappeared after delivery. Umbilical cord blood and hematopoietic stem cell (HSC) are used to treat total nucleated count during pregnancy abnormalities. Finally, there should be caution in selection of treatment using cell therapy. The cure of hyperglycemia, response to glucose tolerance test, evidence of appropriate insulin secretion, weight gain, prompt return of diabetes transfecting gene or insulin producing cells are removed, streptozotocin treated animals are not recommended (it may be pancreas or islet) and insulin stored stem cells. These mentioned 'Seven Pillars of Credibility' should be considered as essential criteria in evaluation and assert success in the use of stem cells or gene therapy [10].

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