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Mini Review

Investigating the Highlights of Pluripotent Stem Cells in Diabetes Type 2

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Abstract

Type 2 Diabetes Mellitus (T2DM) is a serious global pandemic and has a leading position among the causes of mortality. Diabetes mellitus is a heterogeneous disorder that both genetic background and environment can affect it. It is characterized by hyperglycemia due to a reduction in insulin secretion and action. In recent years, studies have proved that Human Pluripotent Stem Cells (hPSCs) have a remarkable role in showing genetic signs of this disease and using in clinical studies and treatment to show promising preliminary results.

Results

The published studies in 2022 examine the role of pluripotent stem cells in diabetes type 2 treatments.

Conclusion

The results of most studies show that studying and examining pluripotent stem cells can be practical and pave the way for drug treatment effects on different variants of diabetes type 2. The aim of this mini-review essay is to highlight the strength and shortcomings of pluripotent stem cells' role in the molecular mechanism of this disease.

Keywords: T2DM; hPSC; Diabetes type 2; Treatment.

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Introduction

Diabetes mellitus is an exploding health problem whole through the world and is categorized into several types, but the two major types are type 1 and type 2 [1]. Type 1 diabetes is an autoimmune disorder developed due to the autoimmune destruction of pancreatic beta cells. Type 1 diabetes also is the most communal metabolic and endocrine disorder in children and adolescents; its incidence is mostly due to genetic disorders [2]. Monogenic diabetes is

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another type of diabetes and defection or mutation in pancreatic beta cells can cause this type of disease. Another rare type of diabetes is MODY which most have identified in youths especially in early adulthood [3]. Type 2 diabetes mellitus (T2DM) is one of the most common forms of diabetes disease among patients. It is estimated that T2DM has rapid growth, and its prevalence will rise to 642 million by 2040 [4]. Individuals with T2DM are at high risk for both microvascular and macrovascular complications, owing to hyperglycemia and insulin resistance which occurred gradually [5]. Environmental factors and genetic background contribute to the various pathophysiological disturbances which are responsible for impaired glucose homeostasis in T2DM [5].

Genetic background plays a vital role in the pathogenesis of various kinds of diabetes. Genome-wide association studies have achievements showed distanced some Genes, Single Nucleotide Polymorphisms (SNPs), molecular mechanisms, and transcription factors in relation to T2DM [6]. In recent decades, using hPSCs for Beta cell replacement had a positive effect on personalized diabetes treatment. Stem cells derived from pancreatic and endocrine progenitors should pass the initial stages of differentiation and turn to Beta stem cells and their Reprogramming can be accomplished by recent technology [7].

Researchers could find reasonable role models of human stem cells in order to examine different conditions and drug treatment activity. Mutations in genes and transcription factors can promote the risk of diabetes type 2 [8]. Many types of research about related genes and transcription factors such as GIPR, HHEX, MNX1, GLIS3, GATA4, GCK, KCNJ11, and HNF4A took place in Pancreatic cells release insulin which controls glucose metabolism [8].

Human Pluripotent stem cells can differentiate into pancreatic B cells and examine two transcription factors PDX1 and NKX6 in insulin secretion. The pancreatic beta cells derived from hPSCs are faster in controlling glycemic levels in comparison with beta cells [9]. Their co-expression can have a vital role in mono hormonal and functional beta cells [9]. Using hPSCs can be helpful in personalized treatment and specifying drug targeting.

The present mini review aimed to examine pluripotent stem cells highlights as a role model in diabetes type 2 and their useful function in personalized medicine.

Discussion

It is investigated different novel studies which are helpful in bolding the role of pluripotent stem cells in observing the role of mutations in genes, molecular mechanisms, and even in transplantation of hPSCs which shows in a study by Yuanyuan Du, et al. their results of studies on hPSCs-islet for diabetic treatment in a preclinical treatment [10]. Human pluripotent stem cells which are derived from islets are a vital resource for diabetes remedies. Edwin A, Rosado-Olivieri's study on islet pluripotent stem cells showed that YAP as a transcription factor plays an inhibitor role in pluripotent stem cells' differentiation and proliferation to islet cells [11]. Anant Mamidi, et al. have done another research on human pluripotent islet stem

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cells (hPISCs) and identified factors that act as differentiation promoters or gatekeepers in cell fate. Their results showed that F-actin-YAP1 controls the fate of hPISC and ECM-integrin 5 promotes the differentiation of these cells to islet cells [12]. Sussel et al found that GATA6 inhibits the expression of Hedgehog ligands in hPSCs [13].

Diego Balboa, et al. examined the INS mutations in hiPSCs and their results showed that INS mutation can cause defective beta cells mass expansion and diabetes development [14]. Zengrong Zhu, et al. studied hESC and proved that RFX6 regulates the formation of early pancreatic progenitor cells [15]. Another study which has done by Qicheng Ni, et al. showed that mTORC1 regulates beta cells' survival, proliferation, and function [16].

Bruin, et al. investigated the ratio of SUR1:KIR6.2 may contribute to the KATP channel defects in human Embryonic Stems Cells-derived from islet endocrine cells [17].

In the following, Liping Su and colleagues examined the Thymosine beta-4 transcription factor in pluripotent stem cells and their results showed that this factor can improve angiogenic potency in diabetes [18]. In a study, Elisa De Franco, et al. examined GATA6 mutations and found that it can cause diabetes manifestation [19]. Totally, by combining all the results of previous studies we can obtain faster and better cure processes and have a better imagination of their molecular mechanism.

Conclusion

Human pluripotent stem cells suggest an opportunity for studying disease phenotypes that are observed in human or non-human model organisms. They could play an important role in investigating the underlying mechanisms of T2DM. Researching stem cells brings some opportunities and challenges. As diabetes has known as a polygenic disease, further studies and looking forward to making up some role models beyond hPISCs can be suitable strategies for discovering more rare variants in diabetes type 2. There are some phenotypes that cannot be predicted easily, and we need more practical techniques to find out them. Moreover, carefully well-designed experiments can be practical in understanding small differences in genetic heterogeneity. In conclusion, maintaining several mechanisms and pathways in hPISCs and other role models can be practical in the remedy process. The results of hPISCs studies can pave our way toward precision medicine and personalized treatment in near future.

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