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Type 1 Diabetes and Its Potential Treatments (GDF 15)

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Abstract. Type 1 diabetes is characterized by immune-mediated destruction of pancreatic beta cells, resulting in insulin deficiency. This autoimmune process is primarily mediated by autoreactive T lymphocytes, with genetic predisposition and environmental triggers, such as viral infections, contributing to disease onset. This disease usually results in hyperglycaemia and ketoacidosis, which is a severe disease that causes vomiting, nausea, fatigue, and headache. If untreated, diabetic ketoacidosis can progress rapidly to dehydration, electrolyte imbalance, and even coma, making early diagnosis and intervention critical. The clinical presentation varies depending on the beta cells' failure. Right now, recognition of diabetes increases in adulthood, and a blurring of the margins between type 1 and type 2 diabetes. This overlap complicates clinical classification and may delay the initiation of optimal therapy, underscoring the importance of precise diagnostic criteria. GDF15 is a possible therapeutic protein that could be used to treat disease. Preclinical studies suggest that GDF15 may exert anti-inflammatory and metabolic regulatory effects, offering potential benefits in preserving residual beta-cell function and improving glycaemic control.

Keywords: Type 1 diabetes, treatment, mechanism

1. Introduction

Recently, the treatments for type 1 diabetes have focused on insulin supplementation to manage the effects of pancreatic beta-cell loss. Followed by the mechanism of type 1 diabetes, a discussion of the advantages and disadvantages of current treatment and new treatments will be included in the essay. The use of GDF 15, which targets the failed beta cell, results in to decrease in the disease incidence. Polymerase chain reaction (PCR), a biological technique that is used to produce many copies of a specific DNA region in vitro. The process of PCR to produce type 1 diabetes is separated into four parts. First is to choose the restriction enzyme; BamHI(5') and NotI(3') are two of the restriction enzymes used. Then, digest the vector and insert, digest pcDNA 3.1, and insert GDF 15. Ligation is where we use ligase enzymes to produce pcDNA 3.1 + GDF 15 plasmid. Step 4 transformation uses E. coli as a host to produce this plasmid. In the last step, transfection, we transfer the plasmid into mammalian cells to produce the GDF-15 protein. This process helps to produce lots of GDF 15 out in the lab, which lowers the cost of the protein and ensures all patients will be able to afford it. Discussion parts include social and economic impacts of how this protein will affect patients and the biotechnology Market [1].

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2. Mechanism of type 1 diabetes

Type 1 diabetes is a polygenic autoimmune disease, which is mainly caused by a genetic disorder in a person. The gene that is commonly caused by the HLA class II genes, some of the examples, such as HLA-DR3-DQ2 and HLA-DR4-DQ8, account for 30 to 50 percent of the genetic susceptibility. Other genes, such as the INS genes, which are responsible for insulin production, PTPN22, CTLA-4, and IFIH1, all the genes link viral response pathways to Type 1 Diabetes. There are also some environmental triggers, viral infections: enteroviruses or rubella, early dietary exposures like milk or gluten, and alterations in the gut microbiota. Loss of immune tolerance [2]. Normally, T cells prevent autoimmunity; however, in type 1 diabetes, this mechanism fails due to genetic variants, such as CTLA-4, which allow self-reactive immune cells to survive and persist. Over time, immune cells infiltrate pancreatic islets, which is well known as insulitis. This is caused by a variety of genes, such as CD4 helper T cells, which produce cytokines in the human body. B cells, also known as antigen-presenters and autoantibody producers, and macrophages. What is the role of beta cells in the immune response? Beta cells release neoantigens also act as antigen-presenting cells, enabling the autoimmune attack. Beta cell destruction, which is mainly caused by CD8 T cells, recognises islet cells through their MHC I presentation and directly kills them. CD4T cells produce inflammatory cytokines, which are toxins that permit macrophage activation and help B cells produce autoantibodies. Other mechanisms include Fas-mediated apoptosis pathways and cytokine-induced caspase activation [2] [3]. By the time all the processes, more than 80 to 85 percent of the beta cells are destroyed, and this causes insulin deficiency and consequent hyperglycaemia, which is a disease caused by high blood glucose levels. A small proportion of people's beta cells are destroyed without detectable autoimmunity.

3. Production of GDF-15

3.1. The mechanism of GDF-15 acts as a potential treatment

GDF 15 stands for growth differentiation factor 15. It helps to treat type 1 diabetes in several ways: weight regulation and cellular stress modulation. Weight regulation GDF 15 helps to reduce food intake and promote weight loss by binding to the receptors GFRAL in the brain. This energy balance. Cellular stress modulation, GDF 15 plays an important role in supporting cellular repair processes; these functions are beneficial in numerous diseases, such as metabolic disorders. Metabolic stress regulation GDF 15 can act as a mitokine, which works by responding to mitochondrial and metabolic stress, which is significant in type 1 diabetes, as the disease will induce systemic stress. GDF 15 can balance these effects, and it also helps in inflammation control. GDF 15 can theoretically mitigate immune-related damage to pancreatic beta cells, which potentially slows disease progression [3].

3.2. Extraction

Extraction of the GDF 15 gene begins with isolating the gene from a source such as animals or bacteria. If the gene is highly expressed in specific tissues, reverse transcription can be applied to convert mRNA to complementary DNA cDNA [4]. During transcription, the DNA double helix unwinds. Free nucleotides pair with the complementary DNA base according to base-pairing rules. RNA polymerase then catalyzes the formation of phosphodiester bonds, generating an RNA strand. Once synthesized, the RNA dissociates from the DNA template, and the DNA double helix reforms.

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3.3. Designing PCR primers for GDF 15

Now design specific PCR primers that are complementary to the flanking regions of the GDF 15 gene sequence; these primers will help amplify the gene region of interest. The forward primer: designed to bind to the 5' end of the gene. The reverse primer's job is to bind to the third end of the gene. Reverse transcription is taking place first, as we use the process with RNA. GDF 15 is expressed as mRNA in certain cells, and mRNA is the template for protein synthesis. During the synthesis, reverse transcriptase is used to synthesise cDNA from mRNA. What are some factors that we need to consider for primer design: melting temperature, both primers should have similar melting temperature(around 50 to 60 degrees). You can use tools such as primer3 to help calculate the temperature. The length of the primers, primer length should be controlled between 18 to 25 nucleotides long. Specifically, the primers should be used only to synthesise GDF 15 cDNA without binding to other similar sequences, which will lead to the production of other chemicals [5]. What are some examples of primers that can be used to design the cDNA of GDF 15: Forward Primer, Sequence: 5'-ATGAGCGACACAGCCAGGGA-3'. This primer binds to the 5' untranslated region (UTR) or the beginning of the coding sequence of GDF-15. Reverse Primer, Sequence: 5'-CTAAAGAGCAGGCCATCCAC-3. This primer binds to the 3' UTR or the sequence just before the stop codon [5].

3.4. Amplification of the GDF 15 cDNA

Denaturation: heat the mixture to a temperature around 94 to 98 degrees to denature the cDNA, separating the double-stranded DNA, then annealing, lower the temperature to 50 to 65 degrees to allow the forward and reverse primers to bind to their complementary sequences on the cDNA template. Extension, raise the temperature to around 72 degrees (this is the optimum temperature for DNA polymerase to extend the primers, synthesizing the new complementary strand of DNA. Optimum temperature means that the enzyme and substrate both have the highest activation energy. During this time, the number of collisions is at its peak, and the number of induced fit models is at its peak as well. The last step is amplification, repeat the step, denaturation, annealing, and extension for 25 to 40 times. This process will enable millions of copies of the specific GDF 15 gene region.

3.5. Cloning of the GDF-15 into an expression vector

After the process of amplification of the GDF 15 to obtain a high-quality GDF 15 gene, the gene is then inserted into a cloning vector, for example, a plasmid. This vector will allow you to clone the gene into a host organism, for example, into E. coli or mammalian cells for expression. The step for the cloning process, digestion, uses of restriction enzyme to cut both the vector and the amplified GDF 15 gene at specific sites [4]. Ligation: Use of the DNA ligase to insert the GDF 15 gene into the vector. A promoter could also be used, such as the T7 promoter for bacterial expression, to drive the gene expression in the host cells [6].

3.6. Transformation of the host cells

The recombinant vector contains the GDF 15 gene, which is then introduced into a host cell, which as bacteria, such as E. coli, or a mammalian cell, using methods such as electroporation or chemical transformation. This method is only used for bacteria. Lipofection and viral transfection could also be used to perform transformation. Lipofection is a non-viral method that uses lipid-based molecules to deliver nucleic acids like DNA into cells [7]. Viral transfection is a method in which viruses are

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used to introduce genetic materials into cells. In this process, viruses act as a delivery medium, carrying the desired gene into the target cell.

3.7. Expression of the GDF 15

Once the vector has been introduced into the host cells, continue to grow the cells in suitable culture media. The promoter in the vector drives the transcription of the GDF 15 gene into mRNA, and the cell's machinery will translate the mRNA into the GDF 15 protein. In bacteria, the GDF 15 protein can be expressed in inclusion bodies and purified from the cells. And in human cells, the GDF 15 can be created into the culture medium and purified via various techniques for eco-apple chromatography and affinity [8].

However, if the protein is expressed using E. coli, the protein might be produced as a soluble or insoluble protein, which often requires extra steps, such as redoing for soluble expression. For mammalian expression, the protein might be properly folded and post-translationally modified, glycosylated.

3.8. Purification of the GDF 15 protein

The last step of the procedure is to purify the GDF 15 protein. After the expression, the GDF 15 protein is purified from the culture media or cell lysates. The protein is then tested for purity and functional activity to ensure that it matches the characteristics of native GDF 15.

4. Discussion

Recently, taking insulin has been one of the most essential ways of treating type 1 diabetes [3]. First, insulin is a hormone produced by the beta cells of the pancreas. It can be used to facilitate glucose uptake into cells, especially in the muscle and fat cells. Secondly, it can lower the blood glucose levels by removing glucose from the bloodstream. Lastly, it can promote the storage of glucose or glycogen in the liver and muscles. Injection of insulin into subcutaneous tissues by using a syringe, pen, or pump. It enters the bloodstream and circulates to target tissues. Binding to insulin receptors on the surface of the cells activates a signaling pathway inside the cell. The insulin signal causes GLUT4 transporters to move to the cell surface. These transporters allow glucose to enter the cell from the bloodstream. The glucose inside the cells can be used for energy (ATP production). Excess glucose is stored as glycogen (in muscle and liver) or fat inside the adipose tissue. By promoting glucose uptake and storage, insulin lowers blood glucose to normal levels. What are some benefits of using GDF-15 as a potential treatment instead of using insulin treatments? This usually costs a lot of money to afford the treatments and takes up the patient's life until the patient’s death. However, the use of GDF 15 will reduce the cost and the duration of the medication. GDF 15 will treat the disease, while the recent treatments only use medicine to maintain the current conditions.

While the GDF 15 is in production, there are lots of benefits around this new medication. This will increase the number of biotechnology companies, increase in the number of biotechnology companies increase the number of job opportunities for the workers. The recent market value of the biotechnology companies is worth 520 billion dollars, and in 2030 it is expected to have a market value of 1,13 trillion dollars. There are also some health issues included in the treatment of using GDF 15. First, there might be rare cases in which the protein injected doesn’t fit into the patient's receptor, which doesn’t work for specific patients. Secondly, there might be side effects that have

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not been discovered yet. However, using the normal treatments with insulin, there are no major side effects that will lead to negative feedback.

5. Conclusion

Due to the fast development of technology, the use of new treatments such as GDF 15 has a significant change on the way people can treat type 1 diabetes, a significant change in the development of the new medicine. This leads to the possibility of people successfully treating this disease.

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