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NUCLEIC ACID-BASED THERAPEUTIC DELIVERY SYSTEMS

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ABSTRACT

A patient's clinical condition can be improved through gene therapy, which involves transferring genetic material to treat an illness. In order to carry the desired gene to the target cells in gene therapy, viruses are modified to act as genetic carriers. These carriers are categorized as RNA-based or DNA-based viral carriers depending on the type of genome they are carrying. The common retrovirus-based RNA carriers, including the murine leukemia virus, are basic retroviruses. These viruses' inability to infect non-dividing cells is a significant limitation (post-mitotic cells). This drawback can be resolved by using fresh retroviral carriers made from lentiviruses like the human immunodeficiency virus. DNA-based carriers are produced by adenoviruses and adeno-associated viruses (AAVs). Although existing vector systems can transfer genes to living cells, the ideal carrier for doing so has yet to be found. Consequently, extreme caution should be exercised while using the present viral vectors in human situations. Moreover, gene therapy offers the potential to treat illnesses that are resistant to treatment with traditional drugs.

Keywords-gene therapy, viral vectors, thalassemia, hemophilia, cancer therapy

INTRODUCTION

Numerous human geneticists have proposed gene transfer as a potential treatment for inherited diseases. Given the advancements in cell biology and the creation of recombinant DNA technologies, it is more likely than ever that this unrealistic dream will come true.Gene therapy will also be used in a variety of different medical specializations rather than just for the treatment of certain genetic illnesses.

The gene is the key architectural and functional element of inheritance. A gene is an organized sequence of nucleotides that is located on a certain chromosome and encodes a specific biological product like a protein or RNA molecule. A "**living unit of heredity**" is referred to as a gene. The distinctive qualities, including the color and texture of the hair and the color of the eyes, are inherited from the parents. They also concludes the child's gender, the quantity of oxygen the blood can carry, and the intelligence quotient of the child. [1,2]

GENE THERAPY

An experimental technique intended to replace, modify, or supplement healthy genes with non-functional or dysfunctional genes is referred to as Gene Therapy.Genes are particular nucleotide sequences that store instructions for building proteins. Despite the fact that genes receive a lot of attention, proteins actually carry out the majority of life's functions and even make up the majority of cellular structures. Genetic abnormalities can happen when genes are changed so that the encoded proteins can no more function normally.Long-term cures from gene therapy have recently been recorded, while the practice has not historically been effective. Many genetic abnormalities, including blood disorders, immunological deficiencies, vision issues, regeneration of nerve cells, metabolic disorders, and different types of cancer, haveshown promising results. Gene therapy has the potential to treat illnesses that are intractable by traditional medical methods. The creation of gene therapy vectors, improvement of the clinical experience, and optimization of gene delivery under in vivo and in vitro settings are the primary considerations for gene therapy for human diseases.[2,3,4]

Gene administration to non-dividing cells and tissues in vivo or gene delivery to autologous cells outside the body, in which the gene is given to the patient through adoptive transfer, are both effective methods of clinical gene therapy. Adeno-associated viruses (AAVs) have demonstrated the maximum clinical success in in-vivo gene transfer among viral vectors. Clinical gene therapy in vitro focuses on the gene transfer to autologous hematopoietic stem cells (HSCs) for the treatment of various diseases, particularly hematologic ones, and to other blood cells such as various types of T lymphocytes for immunotherapy.

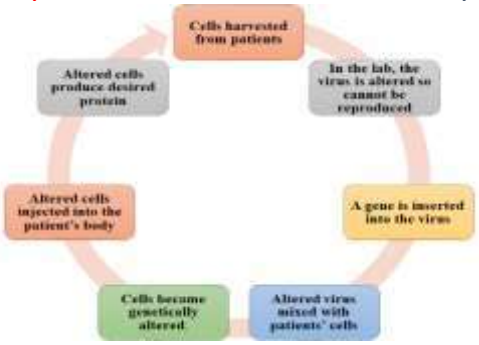

Figure 1 – The process of gene therapy

TYPES OF GENE THERAPY

- **Somatic gene therapy-** It is the process of putting a "good" gene into certain cells to cure the patient, but not their offspring because these genes are not passed on to their progeny. To put it another way, even if a patient's genes are modified to correct a sickness, it is still likely that the patient's children will develop the same illness. This kind of gene therapy is utilized in most genetic laboratories all over the world.
- **Germline gene therapy** includes inserting non-native genes into cells that make sperm or fertilized eggs. Any genetic alterations carried by these cells will then be passed on to the progeny. Despite the fact that this sort of gene therapy has the potential to prevent hereditary disease, it is regrettably highly contentious, and now very little research is being done in this field due to both technological and ethical considerations.[5]

VECTORS USED IN GENE THERAPY

1. **VIRAL VECTORS**
   - Retroviruses
   - Adenoviruses
   - Adeno-associated virus
   - Herpes simplex virus
2. **NON-VIRAL VECTORS**
   - Ormasil
   - Injection of naked DNA
   - Lipoplexes
   - Polyplexes

METHODS USED FOR GENE TRANSFER

1. **PHYSICAL METHODS**
   - Electroporation
   - Sonoporation
   - Gene gun
   - Magnetofaction
2. **CHEMICAL METHODS**
   - Oligonucleotides
   - Hybrid methods
   - Lipoplex and poyplex
   - Dendrimer

CONCLUSION-

To treat genetic disorders, researchers must first identify the gene or genes that are responsible for each disease. Nearly all 30,000 genes in a human cell have been sequenced and mapped as part of the Human Genome Project and other recent international initiatives. New methods for identifying, treating, curing, and perhaps even preventing human diseases will be made available by this research. It will be a while before diseases can truly be cured via gene therapy, despite the fact that this information will assist scientists in understanding the genetic basis of numerous diseases. Nicholson asserts that "The Human Genome Project is simply a start." It will help us find genes, but it won't explain what these genes do.

It's intriguing to think about how gene therapy can change medicine in the future because it holds out hope for both treating and preventing pediatric illnesses. One day, it might be feasible to treat a genetic condition in an unborn kid even before the child is born29). Scientists are hopeful that the mapping of the human genome will pave the way for the development of treatments for a wide range of illnesses, and that the positive results of recent clinical trials will open up new possibilities and difficulties. Yet for now, things must wait and be seen, necessitating cautious optimism. [6,7]

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