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Review Article

Gene Therapy- A New Hope in Future Medicine

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***ABSTRACT*:**
Gene therapy is an emerging field of biomedicine. As evolution is a continuous process with the advancement of the technology, the researchers are more focused to understand the cellular and molecular basis of every disease. As in some of the diseases conventional method is not giving satisfactory results, thus focus is on gene therapy located to treat not only inherited disease but also acquired ones. This review provides an update on gene therapy and its types with different gene transfer strategies and disadvantages of gene therapy.
Key words: Gene therapy, diseases, medicine.

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INTRODUCTION

Gene therapy is defined as the procedure used to treat or improve the health condition of the patient by modifying the patient's cells genetically.[1] The technique may be used to replace a faulty gene, or to introduce a new gene whose function is to cure or to favourably modify the clinical course of a condition.[2] The objective of gene therapy is to introduce new genetic material into target cells while causing no damage to the surrounding healthy cells and tissues, hence the treatment related morbidity is decreased.[2] Genes are the fundamental physical and functional unit of heredity. A gene is an ordered sequence of nucleotides located in a particular position on a particular chromosome that encodes a specific functional product (i.e., a protein or RNA molecule). Gene is termed as a "biological units of heredity.[3] When genes are altered so that encoded proteins are unable to carry out their normal functions, genetic disorders can result.

Gene therapy essentially consists of introducing specific genetic material into target cells to compensate for abnormal genes or to make a beneficial protein without producing toxic effects on surrounding tissue. Transferred genes can be used for either reparative or pharmacological purposes.[4]

GENE DELIVERY SYSTEMS: Vectors are vehicles that ferry the genetic material into a wide variety of cells, tissues and whole organs. The optimal vector and delivery system depends on the target cells and its characteristics, duration of expression and the size of the genetic material to be incorporated in the vector.[5,6] Functional proteins are created from the therapeutic gene causing the cell to return to a normal stage.

Gene delivery systems are categorized as:[7]

- Viral-based systems
- Non-viral-based systems

VIRAL-BASED SYSTEMS:

Viral-mediated gene delivery systems consist of viruses that are modified to be replication-deficient, but which can deliver DNA for expression. Adenoviruses, retroviruses, and lentiviruses are used as viral gene delivery vectors.[8]

NON-VIRAL-BASED SYSTEMS:

Non-viral gene delivery systems were introduced as an alternative to viral-based systems. One of the most important advantages of these systems is improved transfection. Non-viral systems are categorized according to preparation, as physical or chemical types. The most common physical methods are micro-injection, electroporation, ultrasound, gene gun, and hydrodynamic applications. In general terms, physical methods refer to delivery of the gene via the application of physical force to increase permeability of the cell membrane.[9]

TYPES OF GENE THERAPY:

There are 2 types of gene therapy:

1. Germ line gene therapy: where germ cells (sperm or egg) are modified by the introduction of functional genes, which are integrated into their genome. Therefore changes due to therapy would be heritable and would be passed on to later generation. Theoretically, this approach should be highly effective in counteracting genetic disease and hereditary disorders.[10] This form of gene therapy is extremely controversial and currently very little research is being done in this area, both for technical and ethical reasons.[3]
2. Somatic gene therapy: involves introducing a "good" gene into targeted cells with the end result of treating the patient - but not the patient's future children.[3] That means the therapeutic genes are transferred into the somatic cells of a patient. Any modifications and effects will be restricted to the individual patient only and will not be inherited by the patient's offspring or any later generation.[11]

GENE TRANSFER STRATEGIES:

Gene transfer protocols have been approved for human use in inherited diseases, cancers and acquired disorders. In 1990, the first successful clinical trial of gene therapy was initiated for adenosine deaminase deficiency. Since then, the number of clinical protocols initiated worldwide has increased exponentially. Although systemic intravenous route can be applied to deliver the genetic material to the cells, local delivery methods are more commonly used.

a. Percutaneous injection: If paracrine effect of the gene product is therapeutic, vector solution can be injected percutaneously into the tissue around the vessel. This simple and locally effective technique can be efficacious for increasing the number of capillaries within ischemic muscles.

b. Surgical method: This is the most common method used in the vascular gene therapy in animal models. In this procedure, the related vascular area is isolated by clamping from proximal and distal ends and it's all side branches are ligated. The blood inside is drained and vector solution is injected into this isolated segment. After a certain time of incubation the vector solution is aspirated and the involved segment is washed unclamped, and ligations are removed. This technique has high transfection efficiency and only the isolated corresponding area is transfected. Its disadvantage is that it is an invasive procedure and the vessel is exposed to the straining effects of clamping and ligation of side branches.

c. Catheter systems: New catheter systems are developed to increase the interaction between vectors and endothelial cells. Mechanical or electrically strengthened catheters are needle injection catheter, iontophoretic electric current-enhanced balloon, and stent based systems.[12]

DISADVANTAGES OF GENE THERAPY

1) Uncertainty: Germ-line gene therapy experiments would involve too much scientific uncertainty and clinical risks, and the long term effects of such therapy are unknown.[3]
2. Short-lived nature of gene therapy: Before gene therapy can become a permanent cure for any condition, the therapeutic DNA introduced into target cells must remain functional and cells containing the therapeutic DNA must be long-lived and stable. Problems with integrating therapeutic DNA into the genome and the rapidly dividing nature of many cells prevent gene therapy from achieving any long-term benefits. Patients will have to undergo multiple rounds of gene therapy.[12]
3. Expensive: Gene therapy is very expensive, and will never be cost effective enough to merit high social priority.[3]
4. Immune response: Anytime a foreign object is introduced into human tissues, the immune system has evolved to attack the invader. The risk of stimulating the immune system in a way that reduces gene therapy effectiveness is always a possibility.
5. Problem with viral vectors: Viruses, while the carrier of choice in most gene therapy studies present a variety of potential problems to the patients such as toxicity, immune and inflammatory response and gene control and targeting issues.
6. Multigenic disorders: Conditions or disorders that arise from mutation in a single gene are best candidates for gene therapy. Unfortunately, some of the most commonly occurring disorders, such as heart disease, high blood pressure, Alzheimer's disease, arthritis and diabetes, are caused by the combined effects of variations in many genes. Multigenic or multifactorial disorders would be especially difficult to treat effectively using gene therapy.[13,14]

CONCLUSION

Persistent efforts have been going on developing treatment methodologies to eliminate underlying factors rather than to treat the symptoms of a disease. Therefore, research is increasingly utilizing knowledge from the field of genetics. The current gene therapy is primarily experimental, with most human clinical trials only in the research stages. Over time and with proper oversight, human gene therapy might become an effective weapon in modern medicine's arsenal to help fight diseases such as cancer, HIV/AIDS, diabetes and many more over the years.

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