Gene Therapy hope of Future

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Abstract: The concept of gene therapy arose during the 1960s and 1970s and is still in its infancy, meaning there is a paucity of reliable, long-term data on the safety and efficacy of this therapy. In 1972, Theodore Friedman and Richard Roblin published a paper in Science called "Gene therapy for human genetic disease?" which cited Stanfield Roger's proposal in 1970 that "good DNA" could be used to replace defective DNA in people with genetic disorders. In 1985, Anderson and colleague Michael Blease started working together to demonstrate how cells from people with ADA deficiency could be modified in tissue culture.

Key words: gene therapy, prevent disease, human diseases

I.INTRODUCTION:

Gene therapy is when DNA (or) Gene is introduced into a patient to treat a genetic disease. The new DNA usually contains a functioning gene to correct the effects of a disease-causing mutation. Gene therapy uses sections of DNA (Usually genes) To treat or prevent disease. The DNA is carefully selected to correct the effect of a mutated gene that is causing disease. The technique was first developed in 1972 but has, so far, had limited success in treating human diseases. Gene therapy may be a promising treatment option for some genetic diseases, including muscular dystrophy and there are two different types of gene therapy depending on which types of cells are treated:

Somatic gene therapy: Transfer of a section of DNA to any cell of the body that doesn't produce sperm or eggs. Effects of gene therapy will not be passed onto the patient's children.

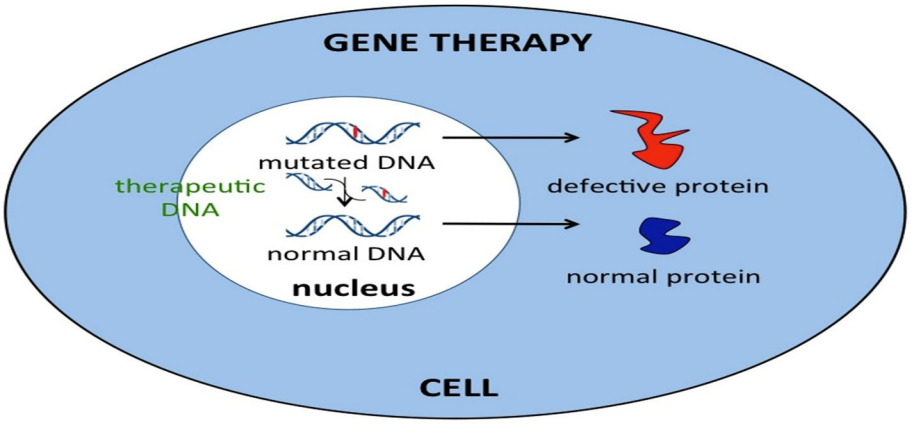
Germ line gene therapy: Transfer of a section of DNA to cells that produce eggs or sperm. Effects of gene therapy will be passed onto the patient's children and subsequent generations.

The concept of gene therapy arose during the 1960s and 1970s and is still in its infancy, meaning there is a paucity of reliable, long-term data on the safety and efficacy of this therapy. In 1972, Theodore Friedman and Richard Roblin published a paper in Science called "Gene therapy for human genetic disease?" which cited Stanfield Roger's proposal in 1970 that "good DNA" could be used to replace defective DNA in people with genetic disorders. In 1985, Anderson and colleague Michael Blease started working together to demonstrate

how cells from people with ADA deficiency could be modified in tissue culture. They used a retrovirus as a vector to carry the correct ADA gene into the cells. In 1986, they tried transferring the correct genes into the bone marrow of animals, but in 1988, found that transferring them to white blood cells was much more successful, with a dramatic increase in the amount of the correct genes being taken up by cells. In 1989, the researchers teamed up with Dr. Steven Rosenberg to test how safe and effective the gene therapy would be in cancer patients. The team cultured tumor infiltration lymphocytes cells (TIL cells) from people with malignant melanoma. In 1990, the four-year old girl and another nine-year old girl with ADA deficiency were infused with their own corrected cells over two years and in 1993; the team used the gene therapy to treat newborn infants with ADA deficiency. The corrected ADA genes were transferred to immature blood cells obtained from the babies' umbilical cords. In the 1970s, research into recombinant DNA was moving forward. Extreme foresight has to be credited to the National Institutes of Health (NIH) in 1974 when it took theleadinregulating recombinant DNA research. A regulatory oversight body was created, which was called “the Recombinant DNA Advisory Committee (RAC) to the NIH Director,” with RAC members initially being experts in mainly recombinant DNA technology. Over time membership was expanded to individuals coming from a wide range of scientific and medical disciplines, including ethicists and members of patient and other lay communities. The RAC was initially put in charge of approving research projects involving recombinant DNA in NIH-funded laboratories in the United States. The RAC then got involved in regulating gene marking research projects and finally started to review gene therapy protocols together with the United States Food and Drug Administration (FDA). While the RAC would reviewthesoundness and merit of the scientific aspect of the recombinantDNAtechnologyapplied, theFDAwouldfocusonthesafetyandefficacyofthegenetically modified products, including their manufacturing processes. Regulations that both the RAC and the FDA apply are based on the guidelines on human experimentation that stem from the work of the National

Gene therapy is the process of inserting genes into cells to treat diseases. The newly introduced genes will encode proteins and correct the deficiencies that occur in genetic diseases. Thus, gene therapy primarily involves genetic manipulations in animals or humans to correct disease, and keep the organism in good health. The initial experiments on gene therapy are carried out in animals, and then in humans. Obviously, the goal of the researchers is to benefit the mankind and improve their health. In gene augmentation therapy, a DNA is inserted into the genome to replace the missing gene product in case of gene product in case of gene inhibition therapy, the

antisense gene inhibits the expression of the dominant gene



Genes:

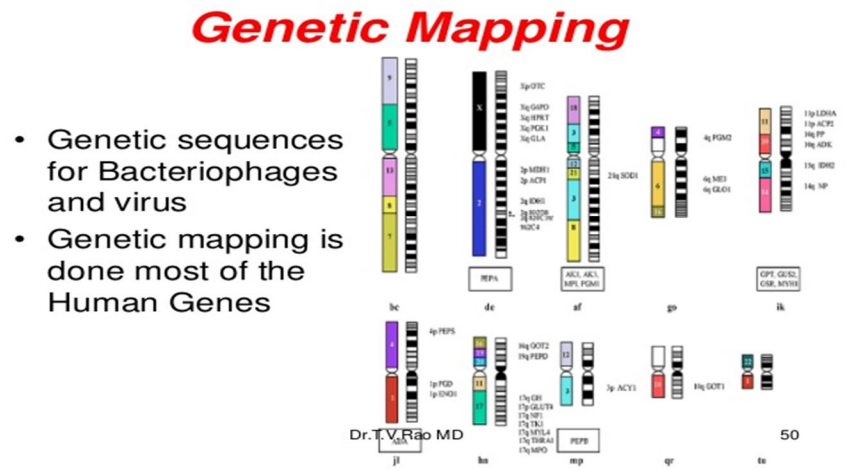
A gene is the molecular unit of heredity of a living organism. It is used extensively by the scientific community as a name given to some stretches of deoxyribonucleic acids (DNA) and ribonucleic acids (RNA) that code for a polypeptide or for an RNA chain that has a function in the organism. Living beings depend on genes, as they specify all proteins and functional RNA chains. Genes hold the information to build and maintain an organism's cells and pass genetic traits to offspring. All organisms have genes corresponding to various biological traits, some of which are instantly visible, such as eye color or number of limbs, and some of which are not, such as blood type, increased risk for specific diseases, or the thousands of basic biochemical processes that comprise life. The word gene is derived from the Greek word genesis meaning "birth", or genos meaning "origin".

Approaches for gene therapy

There are two approaches to achieve gene therapy

a. Somatic cell gene therapy

The non reproductive (non-sex) cells of an organism are referred to as Somatic cells. There are the cells of an organism other than sperm or egg cells .e.g. bone marrow cells blood cells, skin cells, intestinal cells At present all the research on gene therapy is directed to correct the genetic defects in somatic cells. In essence, somatic cell gene therapy involves the insertion of a fully functional and expressible gene into a target somatic cell to correct a genetic disease permanently.



b. Germ cell gene therapy

The reproductive (sex) cells of an organism constitute germ cell line. Gene therapy involving the introduction of DNA into germ cells is passed on to the successive generations. For safety, ethical and technical reasons, germ cell gene therapy is not being attempted at present The genetic alterations in somatic cells are not carried to the next generations Therefore, somatic cell gene therapy is preferred and extensively studied with an ultimate objective of correcting human diseases.

II.Types of gene therapy

There are two types of gene therapies.

1. Ex-vivo gene therapy

Ex-vivo gene therapy involves the transfer of genes in cultured cells (e.g., bone marrow cells) which are then reintroduced into the patient.

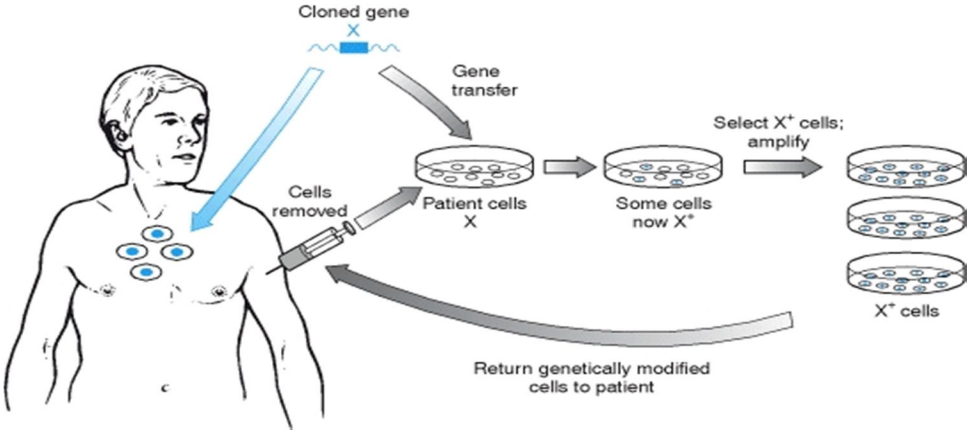
Ex vivo gene therapy can be applied to only selected tissues eg bone marrow whose cells can be cultured in the laboratory.

The technique of ex vivo gene therapy involves the following steps:-

1) Isolate cells with genetic defect from a patient
2) Grow the cells in culture
3) introduce the therapeutic gene to correct gene defect
4) Select the genetically corrected cells (stable transfer mats) and grow
5) Transplant the modified cells to the patient

The procedure basically involves the use of the patients own cells for culture and genetic correction and then their return back to the patient this technique is therefore, not associated with adverse immunological responses after transplanting the

cells, Ex vivo gene therapy is efficient only if the therapeutic gene (remedial gen e) is stably incorporated and continuously expressed, this can be achieved by use of vectors



2) In vivo gene therapy

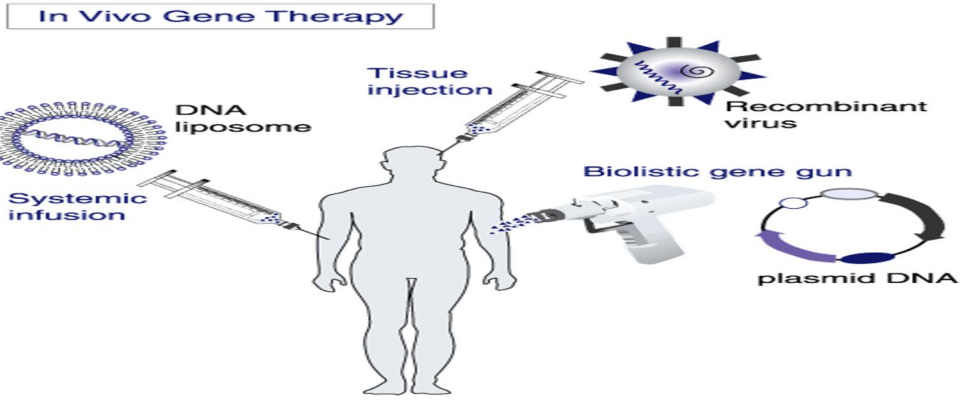
The direct delivery of the therapeutic gene (DNA) into the target cells of a particular tissue of a patient constitutes in vivo gene therapy many tissues are the potential candidates for this approach. These include liver, muscle skin spleen lung brain and blood cells

Gene delivery can be carried out by viral or non viral vector systems. The success of in vivo gene therapy mostly depends on the following parameters

The efficiency of the uptake of the remedial (therapeutic gene by the target cells)

Intracellular degradation of the gene and its uptake by nucleus

The expression capability of the gene.



CONCLUSION

Gene therapy technologies are described in detail including viral vectors, nonviral vectors and cell therapy with genetically modified vectors. Gene therapy is an excellent method of drug delivery and various routes of administration as well as targeted gene therapy are described. There is an introduction to technologies for gene suppression as well as molecular diagnostics to detect and monitor gene expression.

Clinical applications of gene therapy are extensive and cover most systems and their disorders. Full chapters are devoted to genetic syndromes, cancer, cardiovascular diseases, neurological disorders and viral infections with emphasis on AIDS. Applications of gene therapy in veterinary medicine, particularly for treating cats and dogs, are included.

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