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GENE THERAPY – A REVIEW

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ABSTRACT

The ability to transfect genes into cells and to cause their expression is leading to the practical emergence of human gene therapy, wherein, functionally active genes are putatively inserted into the (somatic) cells of a person requiring the expression of a given protein. A novel adaptation of gene therapy is the transfection of cells with non-resident genes in order to accomplish in situ expression of a pharmacologically beneficial protein or create a site for further therapeutic intervention. In other words, genes would act like drugs, generating a product with a specific pharmacological effect. In simple terms, gene therapy involves insertion of genetic material into a patient's cells to make them capable of producing therapeutic protein.

KEYWORDS: Gene, germ line, somatic, retrovirus, vectors.

INTRODUCTION

In gene therapy, a functional or healthy or useful gene is introduced into the cell or a tissue to cure heritable disorders and the defective or faulty gene is replaced by the new useful gene (Figure 1).

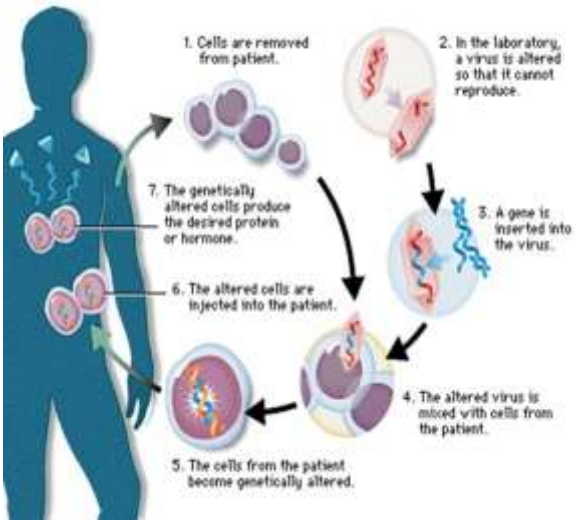

Figure 1: A flowchart representing gene therapy.

There are two kinds of gene therapy

1. Germ line gene therapy.
2. Somatic cell gene therapy.

Germ line gene therapy is a kind of gene therapy in which DNA is transferred to cells that produce eggs or sperm.

The main advantages of germ-line cell gene therapy are the following.

1. It offers the possibility for a true cure of several diseases and it is not only a temporary solution.
2. It might be the only way to treat some genetic diseases.
3. The benefits would be extended for several generations, because genetic defects are eliminated in the individual's genome and, consequently, the benefits would be passed to his or her offspring.

Some of the objections of germ-line cell gene therapy are as follows.

1. This involves many steps that are poorly understood, and the long-term results cannot be estimated.
2. It would open the door for genetic modifications in human traits with profound social and ethical implications.
3. It is very expensive and it would not benefit the common citizen.
4. The extension of the cure to a person's offspring would be possible only if the defective gene was directly modified, but probably not if a new gene was added to another part of the genome.[1]

Somatic cell gene therapy is a kind of gene therapy in which the therapeutic genes are transferred into the somatic cells of a patient (DNA transfer to our normal body tissue). The results of any somatic gene therapy are restricted to the actual patient and are not passed on to his or her children.

VECTORS FOR GENE THERAPY

There are basically three vectors for gene therapy.

1. Virus (Figure 2)
2. Non-virus method
3. Hybrid method (combination of virus + non-virus method)

Virus

Viruses used for gene therapy are.

a. Retro-virus.
b. Adenovirus.
c. Adeno-associated virus (non-pathogenic).
d. Enveloped protein pseudo typing of virus vector.[2, 3]

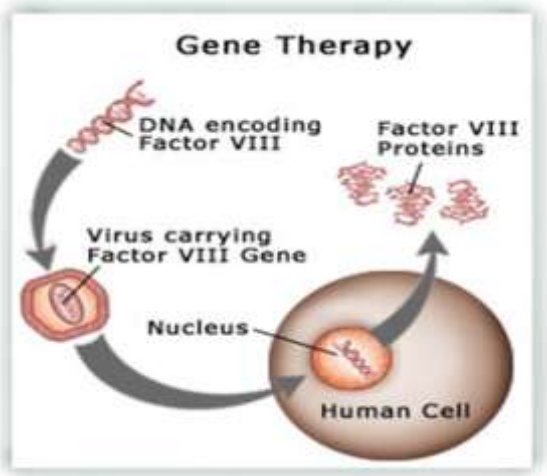

Figure 2: Viral method of gene therapy

a. Retro-virus

In retrovirus the genetic material is in the form of RNA molecules, while that in the host is in the form of DNA. A class of viruses that can create double-stranded DNA copies of their RNA genomes. These copies of its genome can be integrated into the chromosomes of host cells. Human immunodeficiency virus (HIV) is a retrovirus.

b. Adenovirus

A class of viruses with double-stranded DNA genomes that cause respiratory, intestinal, and eye infections in humans. The virus that causes the common cold is an adenovirus.

c. Adeno-associated Virus

It is a class of small, single-stranded DNA viruses that can insert their genetic material at a specific site on chromosome 19.[4]

d. Enveloped Protein Pseudo typing of Virus Vector

A classical example of such a vector is VSV-G pseudo typed lenti-virus (G-protein and Vesicular Somatis Virus coat added to lenti-virus).

e. Herpes simplex viruses

These are a class of double-stranded DNA viruses that infect a particular cell type, neurons. Herpes simplex virus type 1 is a common human pathogen that causes cold sores.[5]

Non- Virus Method

These include.

1. Naked DNA injected intra-muscularly, by gene gun, sonoporation and electroporation
2. Oligonucleotides: Synthetic oligonucleotides inactivate genes involved in a disease process
3. Lipoplexes and polyplexes: DNA is coated with lipids and is called liposome (Figure 3). Polyplexes are complex polymers with DNA and consist of cationic polymers.[6]

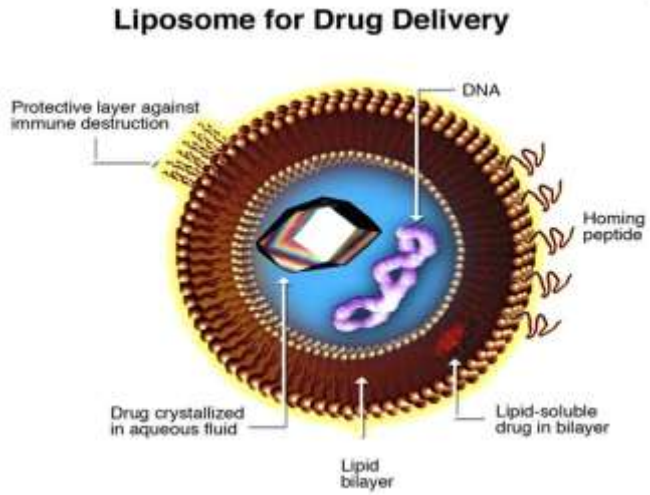

Figure 3: Liposome for drug delivery.

Hybrid Method

These include

1. Virosomes (Virus + Liposomes)
2. Dendrimers (Macromolecules with cationic structure)[7]

DISEASES AND GENE THERAPY

Diseases wherein gene therapy has been focused upon include

1. Cystic fibrosis.
2. Thalassaemia.
3. Malignant melanoma.
4. Pediatric AML.
5. Neuroblastoma.
6. Adenosine deaminase deficiency SCID.
7. Hemophilia B.
8. Chronic myleogenous leukemia.
9. Hepatitis B.
10. Hypercholesterolemia.
11. Diabetes.
12. Cardiovascular diseases.
13. Phenylketonuria.
14. Acquired immunodeficiency syndrome (AIDS).[8]

PROBLEMS OF GENE THERAPY

1. The short-lived nature of gene therapy: Before gene therapy can become a permanent cure for any condition, the therapeutic DNA introduced into the target cells must remain functional and the cells containing therapeutic DNA must be long-lived and stable.

2. Immune system produces a response against invaders and it is difficult for gene therapy to be repeated.
3. Virus vector used in gene therapy presents many problems.
4. Multi-genic disorders (Gene therapy is used for disorders that arise from mutation of single gene. But diseases such as heart failure, blood pressure, arthritis, diabetes, Alzheimer's disease, etc., which are due to multiple genes, cannot be treated.
5. Chances of inducing tumor (if DNA is interplaced at wrong place).[9, 10]

SUMMARY AND CONCLUSION

Gene therapy's potential to revolutionize medicine in the future is exciting, and their expectation for curing and preventing childhood diseases is encouraging. One day it may be possible to treat an unborn child for a genetic disease even before symptoms appear. Scientists are hoping the mapping of the human genome will lead the way toward cures for many diseases and that the successes of current clinical trials will create new opportunities and challenges. With the explosive increase in the availability of information on human genome, several genetic disorders would become candidates for gene therapy. The field is still at its infancy and relevant. Inspite of the various drawbacks, gene therapy has witnessed a rapid growth towards the end of this century and hopefully the progress would continue.

REFERENCES

1. Akhtar, S., James, H. and Gibson, I. Nature Medicine, 1995; 1: 300-302.
2. Cohen, J.S. Pharmacol. Ther, 1991; 52: 211-225.
3. Crstal, R.G. Nature Genet, 1994; 8: 42-51.
4. Patil P.M., Chaudhari P.D., Megha Sahu, Duragkar N.J. Review Article on Gene Therapy. International Journal of Genetics, 2012; 4(1): 74-79.
5. Inouye, M. Gene, 1988; 72: 25-34.
6. Gao, X.A. and Huang, L. Biochim. Biophys. Res. Commun, 1991; 179: 280-285.
7. Strauss, J.H. and Strauss, E.G. Microbiol. Rev, 1994; 58: 491-562.
8. Palmer, T.D., Thompson, A.R. and Miller, A.D. Blood, 1989; 73: 438-445.
9. Zhao, X., Zhange, P.J. and Wong, T.K. Mol. Marine Biol. Biotech, 1993; 2: 63-69.
10. Ramawat, K.G. and Tanwar, Y.S., Pharmaceutical Biotechnology, Yash Publishing House, Bikaner, 1st Edn, 2007; 196-206.