

## Advances in Gene therapy

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### 1. Introduction

Despite advances in clinical treatment many diseases are incurable and patients need expensive and long treatment to prolong life and the idea of gene transfer for the treatment was considered.[1] Genes are inherited factors and recently the genetic knowledge aware us from abnormalities of defects in the genetic map. Gene therapy is the application of genetic principles in the treatment of human disease. The introduction of genetic material into normal cells in order to dispelling the effects of a disease gene or inducing a new function is the aim of gene therapy. Gene therapy is used to correct a deficient phenotype so that sufficient amounts of a normal gene product to be synthesized to improve a genetic disorder. It can also be applied as therapy for cancers, inherited disorders, infectious diseases, immune system disorders and... [2][3] The history of gene therapy starts from late 1960 and early 1970. The first ideas of using genes therapeutically appeared in 1972. Gene transferring by retroviral vectors for treatment goals started at 1980s when recombinant DNA technology was developed. In 1990 for the first time gene therapy was applied for a four-year old girl who became the first gene therapy patient on September 14, 1990 at the NIH Clinical Center. She has adenosine deaminase (ADA) deficiency, a genetic disease which leaves her defenseless against infections. [White blood cells](#) were taken from her, and the normal genes for making adenosine deaminase were inserted into them. The corrected cells were reinjected into her. Dr. W. French Anderson helped develop this landmark clinical trial when he worked at the National Heart, Lung, and Blood Institute. Gene therapy can be targeted to somatic (body) or **germ** (egg and sperm) cells. [4]-[6] Other types of gene therapy include monogenic gene therapy , suicide gene therapy and antisense gene therapy. [7],[8].

#### *Gene therapy in somatic cells*

In [somatic cell](#) gene therapy (SCGT), the therapeutic genes are transferred into any cell other than a [gamete](#), [germ cell](#), [gametocyte](#) or undifferentiated [stem cell](#). Any such modifications affect the individual patient only, and are not inherited by [offspring](#). Somatic gene therapy represents mainstream basic and clinical research, in which therapeutic DNA (either integrated in the [genome](#) or as an external [episome](#) or [plasmid](#)) is used to treat disease.

Over 600 [clinical trials](#) utilizing SCGT are underway in the US. Most focus on severe genetic disorders, including [immunodeficiencies](#), [haemophilia](#), [thalassaemia](#) and [cystic fibrosis](#). Such single gene disorders are good candidates for somatic cell therapy. The complete correction of a genetic disorder or the replacement of multiple genes is not yet possible. Only a few of the trials are in the advanced stages. Despite all the benefits somatic cell gene therapy it has also risks including causing cancer. [9]-[11]

#### *Sexual gene therapy*

In this method changes or replacement of abnormal gene must be effective on gamete producing cells. By inserting genes into germ cells genetic information can be transferred to future generations.[12] In this method, regulations and laws and safety should be focused. Like having previous experience of somatic gene therapy and offering safe results and have experience of animal patterns for proofing safety. Society and people should have enough understanding of this treatment.

### ***Disease that can be treated by gene therapy***

More than 40,000 different kind of disease are caused by genetic disorders. Many of them are occurred because of acid nucleotide mutations resulting in complete protein synthesis that are not able to do their own responsibilities in some cases. If the protein be quietly abnormal it leads to the activation of immune response. Proteins that are coded by repressive protein gene mutation in p53 have been observed in 50% of total cancers . [13] p53 has important role in inhibition of cell growth and DNA damage . After cell damage, the DNA decides to repair or go for apoptosis pathway.[14] Nowadays the usage of this method should be just in serious disease .[15]

### ***Various methods for gene therapy***

- 1-Gene silencing:** Gene silencing is often considered the same as [gene knockout](#).<sup>[3][4]</sup> When genes are silenced, their expression is reduced. In contrast, when genes are knocked out, they are completely erased from the organism's [genome](#) and, thus, have no expression.<sup>[3][4]</sup> Gene silencing is considered a gene knockdown mechanism since the methods used to silence genes. Methods using gene silencing are often considered better than gene knockouts since they allow researchers to study essential genes that are required for the [animal models](#) to survive and cannot be removed. In addition, they provide a more complete view on the development of diseases since diseases are generally associated with genes that have a reduced expression. [16]
- 2- Exvivo delivery:** In this technique first the genetic material is extracted then the cells are cultured in the laboratory, manipulated and finally the cells are returned to the body [17]
- 3- In situ Delivery:** In this technique DNA is transferred to a tissue [18]
- 4- In vivo Delivery:** In this method has been slowly progressed but it has lots of benefits. [19][20]

## **2. Conclusion**

Despite numerous advances in gene therapy, it has not fully achieved its aims. Gene therapy is the treatment of disease by replacing, altering, or supplementing a gene that is absent or abnormal and whose absence or abnormality is responsible for the disease. Most, if not all, diseases have a genetic factor. The genetic factor can be wholly or partially responsible for the disease. For example, in disorders such as cystic fibrosis, hemophilia, and muscular dystrophy, changes in a gene directly result in the condition. In other conditions such as high cholesterol and high blood pressure, genetic and environmental factors interact to cause disease. Disorders associated with aging often involve the loss of gene activity in specific types of cells. Even infections can be related to genes. In future, it is not impossible to say that human being will prescribe gene therapy for many diseases!

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