



Genetics Home Reference

Your Guide to Understanding Genetic Conditions

Handbook

Help Me Understand Genetics

Gene Therapy

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Lister Hill National Center for Biomedical Communications
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Chapter 6

Gene Therapy

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What is gene therapy?

Gene therapy is an experimental technique that uses genes to treat or prevent disease. In the future, this technique may allow doctors to treat a disorder by inserting a gene into a patient's cells instead of using drugs or surgery. Researchers are testing several approaches to gene therapy, including:

- Replacing a mutated gene that causes disease with a healthy copy of the gene.
- Inactivating, or “knocking out,” a mutated gene that is functioning improperly.
- Introducing a new gene into the body to help fight a disease.

Although gene therapy is a promising treatment option for a number of diseases (including inherited disorders, some types of cancer, and certain viral infections), the technique remains risky and is still under study to make sure that it will be safe and effective. Gene therapy is currently only being tested for the treatment of diseases that have no other cures.

For general information about gene therapy:

MedlinePlus (from the National Library of Medicine) offers a list of links to information about [genes and gene therapy \(http://www.nlm.nih.gov/medlineplus/genesandgenetherapy.html\)](http://www.nlm.nih.gov/medlineplus/genesandgenetherapy.html).

The fact sheet [Gene Therapy \(http://www.ornl.gov/TechResources/Human_Genome/medicine/genetherapy.html\)](http://www.ornl.gov/TechResources/Human_Genome/medicine/genetherapy.html) from the U.S. Department of Energy Office of Science offers an overview of this topic.

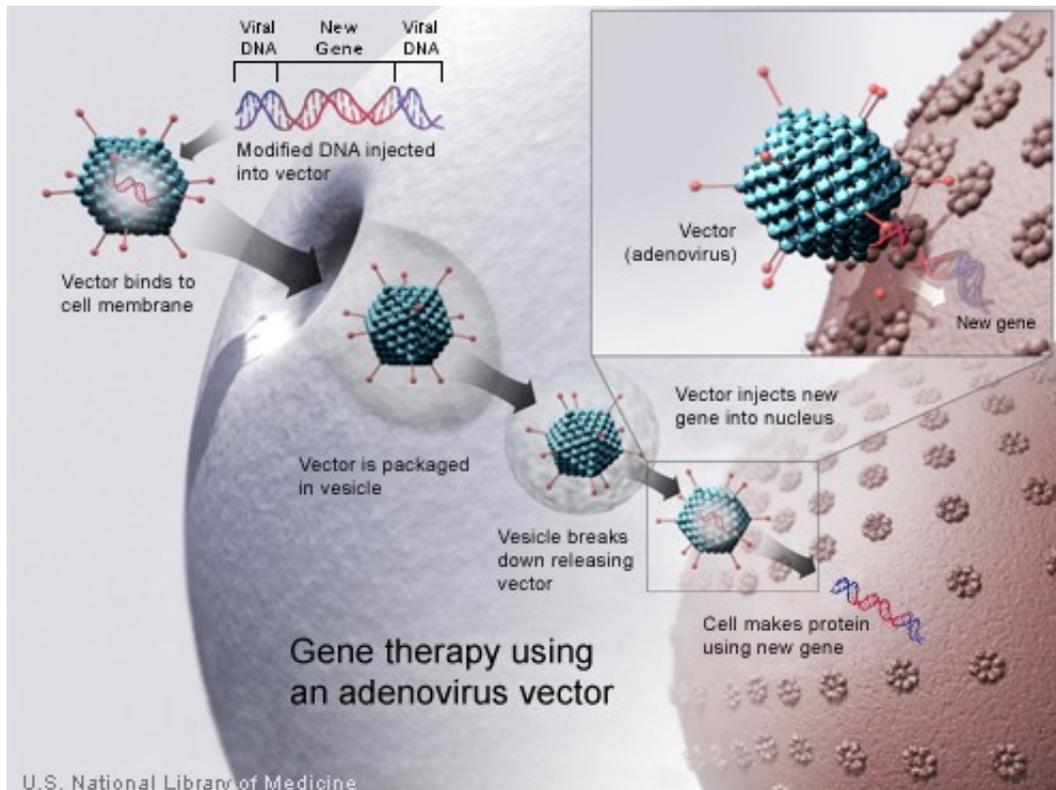
How does gene therapy work?

Gene therapy is designed to introduce genetic material into cells to compensate for abnormal genes or to make a beneficial protein. If a mutated gene causes a necessary protein to be faulty or missing, gene therapy may be able to introduce a normal copy of the gene to restore the function of the protein.

A gene that is inserted directly into a cell usually does not function. Instead, a carrier called a vector is genetically engineered to deliver the gene. Certain viruses are often used as vectors because they can deliver the new gene by infecting the cell. The viruses are modified so they can't cause disease when used in people. Some types of virus, such as retroviruses, integrate their genetic material (including the new gene) into a chromosome in the human cell. Other viruses, such as adenoviruses, introduce their DNA into the nucleus of the cell, but the DNA is not integrated into a chromosome.

The vector can be injected or given intravenously (by IV) directly into a specific tissue in the body, where it is taken up by individual cells. Alternately, a sample of the patient's cells can be removed and exposed to the vector in a laboratory setting. The cells containing the vector are then returned to the patient. If the treatment is successful, the new gene delivered by the vector will make a functioning protein.

Researchers must overcome many technical challenges before gene therapy will be a practical approach to treating disease. For example, scientists must find better ways to deliver genes and target them to particular cells. They must also ensure that new genes are precisely controlled by the body.



A new gene is injected into an adenovirus vector, which is used to introduce the modified DNA into a human cell. If the treatment is successful, the new gene will make a functional protein.

For more information about how gene therapy works:

The National Cancer Institute fact sheet [Questions and Answers About Gene Therapy](http://cis.nci.nih.gov/fact/7_18.htm) (http://cis.nci.nih.gov/fact/7_18.htm) includes a discussion of the technical aspects of gene therapy. In particular, refer to question 3, “How are genes transferred into cells so that gene therapy can take place?” and question 5, “What are the basic steps involved in gene therapy?”

A short description and diagram of gene therapy is available in the article [Fundamentals of Gene Therapy](http://www.fda.gov/fdac/features/2000/gene.html) (<http://www.fda.gov/fdac/features/2000/gene.html>) from the September-October 2000 issue of FDA Consumer magazine.

Is gene therapy safe?

Gene therapy is under study to determine whether it could be used to treat disease. Current research is evaluating the safety of gene therapy; future studies will test whether it is an effective treatment option. Several studies have already shown that this approach can have very serious health risks, such as toxicity, inflammation, and cancer. Because the techniques are relatively new, some of the risks may be unpredictable; however, medical researchers, institutions, and regulatory agencies are working to ensure that gene therapy research is as safe as possible.

Comprehensive federal laws, regulations, and guidelines help protect people who participate in research studies (called clinical trials). The U.S. Food and Drug Administration (FDA) regulates all gene therapy products in the United States and oversees research in this area. Researchers who wish to test an approach in a clinical trial must first obtain permission from the FDA. The FDA has the authority to reject or suspend clinical trials that are suspected of being unsafe for participants.

The National Institutes of Health (NIH) also plays an important role in ensuring the safety of gene therapy research. NIH provides guidelines for investigators and institutions (such as universities and hospitals) to follow when conducting clinical trials with gene therapy. These guidelines state that clinical trials at institutions receiving NIH funding for this type of research must be registered with the NIH Office of Biotechnology Activities. The protocol, or plan, for each clinical trial is then reviewed by the NIH Recombinant DNA Advisory Committee (RAC) to determine whether it raises medical, ethical, or safety issues that warrant further discussion at one of the RAC's public meetings.

An Institutional Review Board (IRB) and an Institutional Biosafety Committee (IBC) must approve each gene therapy clinical trial before it can be carried out. An IRB is a committee of scientific and medical advisors and consumers that reviews all research within an institution. An IBC is a group that reviews and approves an institution's potentially hazardous research studies. Multiple levels of evaluation and oversight ensure that safety concerns are a top priority in the planning and carrying out of gene therapy research.

For more information about the safety and oversight of gene therapy:

A discussion of the safety concerns surrounding gene therapy research is available in the article [Human Gene Therapy: Harsh Lessons, High Hopes \(http://www.fda.gov/fdac/features/2000/500_gene.html\)](http://www.fda.gov/fdac/features/2000/500_gene.html) from the September-October 2000 issue of FDA Consumer magazine.

Additional information about the FDA's role in overseeing the safety of gene therapy research can be found in the fact sheet [Human Gene Therapy and The Role of the Food and Drug Administration](http://www.fda.gov/cber/infosheets/genezn.htm). (<http://www.fda.gov/cber/infosheets/genezn.htm>)

The NIH provides several resources about its role in the safety of gene therapy research:

[Office of Biotechnology Activities](http://www4.od.nih.gov/oba/) (<http://www4.od.nih.gov/oba/>)

[Frequently Asked Questions: Recombinant DNA and Gene Transfer](http://www4.od.nih.gov/oba/RAC/RAC_FAQs.htm)
(http://www4.od.nih.gov/oba/RAC/RAC_FAQs.htm)

What are the ethical issues surrounding gene therapy?

Because gene therapy involves making changes to the body's set of basic instructions, it raises many unique ethical concerns. The ethical questions surrounding gene therapy include:

- How can “good” and “bad” uses of gene therapy be distinguished?
- Who decides which traits are normal and which constitute a disability or disorder?
- Will the high costs of gene therapy make it available only to the wealthy?
- Could the widespread use of gene therapy make society less accepting of people who are different?
- Should people be allowed to use gene therapy to enhance basic human traits such as height, intelligence, or athletic ability?

Current gene therapy research has focused on treating individuals by targeting the therapy to body cells such as bone marrow or blood cells. This type of gene therapy cannot be passed on to a person's children. Gene therapy could be targeted to egg and sperm cells (germ cells), however, which would allow the inserted gene to be passed on to future generations. This approach is known as germline gene therapy.

The idea of germline gene therapy is controversial. While it could spare future generations in a family from having a particular genetic disorder, it might affect the development of a fetus in unexpected ways or have long-term side effects that are not yet known. Because people who would be affected by germline gene therapy are not yet born, they can't choose whether to have the treatment. Because of these ethical concerns, the U.S. Government does not allow federal funds to be used for research on germline gene therapy in people.

For more information about the ethical issues raised by gene therapy:

The National Cancer Institute fact sheet [Questions and Answers About Gene Therapy \(http://cis.nci.nih.gov/fact/7_18.htm\)](http://cis.nci.nih.gov/fact/7_18.htm) offers information on this topic. Refer to Question 12, “What are some of the social and ethical issues surrounding human gene therapy?” and Question 13, “What is being done to address these social and ethical issues?”

Information about the ethics of germline gene therapy is provided in chapter 7 of the publication [Your Genes, Your Choices \(http://www.ornl.gov/TechResources/Human_Genome/publicat/genechoice/7_dr.html\)](http://www.ornl.gov/TechResources/Human_Genome/publicat/genechoice/7_dr.html). Scroll down to the section “Germ-Line Therapy.”

The Genetics and Public Policy Center also outlines [scientific issues and ethical concerns regarding gene therapy](http://www.dnapolicy.org/genetics/transfer.jhtml) (<http://www.dnapolicy.org/genetics/transfer.jhtml>).

Is gene therapy available to treat my disorder?

Gene therapy is currently available only in a research setting. The U.S. Food and Drug Administration (FDA) has not yet approved any gene therapy products for sale in the United States.

Hundreds of research studies (clinical trials) are under way to test gene therapy as a treatment for genetic conditions, cancer, and HIV/AIDS. If you are interested in participating in a clinical trial, talk with your doctor or a genetics professional about how to participate.

You can also search for clinical trials online. [ClinicalTrials.gov](http://clinicaltrials.gov) (<http://clinicaltrials.gov/>), a service of the National Institutes of Health, provides easy access to information on clinical trials. You can search for specific trials or browse by condition or trial sponsor. You may wish to refer to a list of [gene therapy trials](http://clinicaltrials.gov/search/?term=gene+therapy) (<http://clinicaltrials.gov/search/?term=gene+therapy>) that are accepting (or will accept) patients.



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