# Gene Therapy in Rare Diseases

**Over the last three decades, gene therapy has evolved as an approach to treating many serious diseases, including rare and hereditary diseases passed down from parent to child.[1] Gene therapy has also enabled doctors to make extraordinary progress in the treatment of rare hereditary and genetic diseases.[1,2]**

For most rare diseases, there have been limited or no treatment options available. When a gene therapy is shown to be effective for a rare disease, it may provide an alternative treatment option or, in some cases, be the only treatment option ever developed.[2] As such, gene therapy may represent a true breakthrough for the individuals and families affected by rare diseases.

Gene therapies continue to gain government approval around the world.[1] More than half a dozen gene therapies have already been approved in one or more countries as of 2019, including some therapies for rare, genetic diseases approved by the European Commission (EC) in Europe and by the Food and Drug Administration (FDA) in the United States.[1-4] Other promising gene therapies are currently in development, and experts predict that dozens more are likely to be approved in the coming decade.[2,5]

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## What is gene therapy?

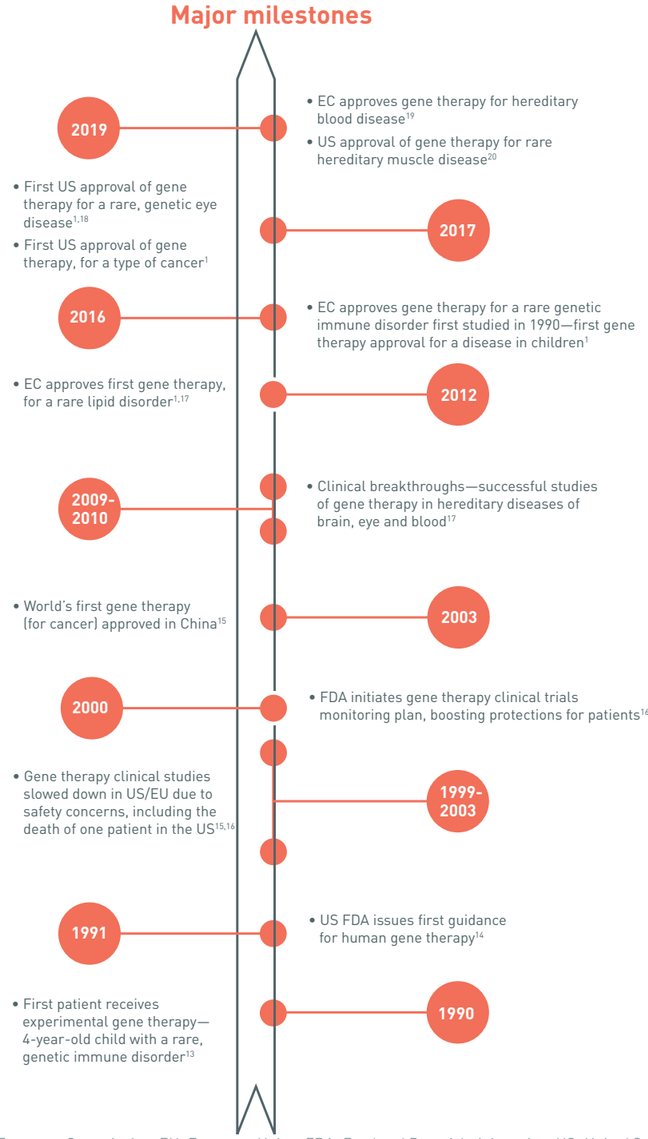
Gene therapy is defined as the introduction, removal, or change in genetic material to a person to treat a disease.[1,6] In some cases, the transfer of genetic material compensates for or alters gene variants (also known as mutations) in a person's own cells, to control disease caused by those gene variants.[7]

**Depending on the type of gene therapy, the transfer of genetic material may:**

- **Add a healthy gene** that functions normally, when a person's own gene works incorrectly.[7] Doctors sometimes use the term "augmentation" to describe this kind of therapy.[1] For example, a rare eye disease has been linked to the deficient function of an enzyme linked to a specific gene. When doctors transfer a working copy of the gene into their eyes, people with this disease can see better[1,8]
- **Fix the effects of genes** that cause disease. Gene variants could be reduced or turned off so that they no longer cause disease. Doctors sometimes use the terms "silencing" or "suppression" to describe this therapy.[1,9] In a rare disease caused by abnormal protein deposits, researchers have studied gene therapy that turns off gene variants that drive these deposits.[9] Conversely, healthy genes that prevent disease can be turned on to control disease—an approach that has been suggested for a form of dementia[6,10,11]
- **Make diseased cells more "visible"** to the immune system.[7] In some diseases, the immune system doesn't attack diseased cells because it doesn't see them as invaders. Gene therapy might help the immune system recognise and suppress the cells that threaten health.[7] This approach has been used in gene therapy treatment for some cancers, and is being considered for rare immune system diseases[1,12]



## Brief history of gene therapy




**Abbreviations:** EC=European Commission; EU=European Union; FDA=Food and Drug Administration; US=United States.

## How gene therapy works

**With gene therapies, material—usually DNA, the "building block" of genes—is transferred to a person in one of two ways.[2]**

- **In vivo transfer:** Transfer of genetic material occurs inside a person's body. The gene therapy is injected into the body to target the cells affected by a disease, either directly or indirectly
- **Ex vivo transfer:** Transfer of genetic material occurs outside a person's body. Cells are taken from a person and corrective genetic material is placed into the cells. Technicians then culture the genetically modified cells—a term that means to grow the cells in a lab. The cultured cells are injected back into the person

### Vectors for gene therapy

The gene therapy always has to be carried into cells by a vector. A vector transports DNA or other genetic materials, and allows these to enter a cell.[2] Examples of vectors include:

- Modified viruses that do not cause infection[21-23]
- Small particles, such as tiny fat particles called liposomes or complex molecules called polymers[22,24]

Sometimes, additional biological materials help a vector function better. An example is the use of a special protein molecule, called a chaperone, which may improve the effectiveness of gene therapy carried by a viral vector.[25,26]

### Questions About Gene Therapy

**Does gene therapy have side effects?**

All therapies have potential side effects. Discuss any possible side effects with your health-care team.

**What is informed consent?**

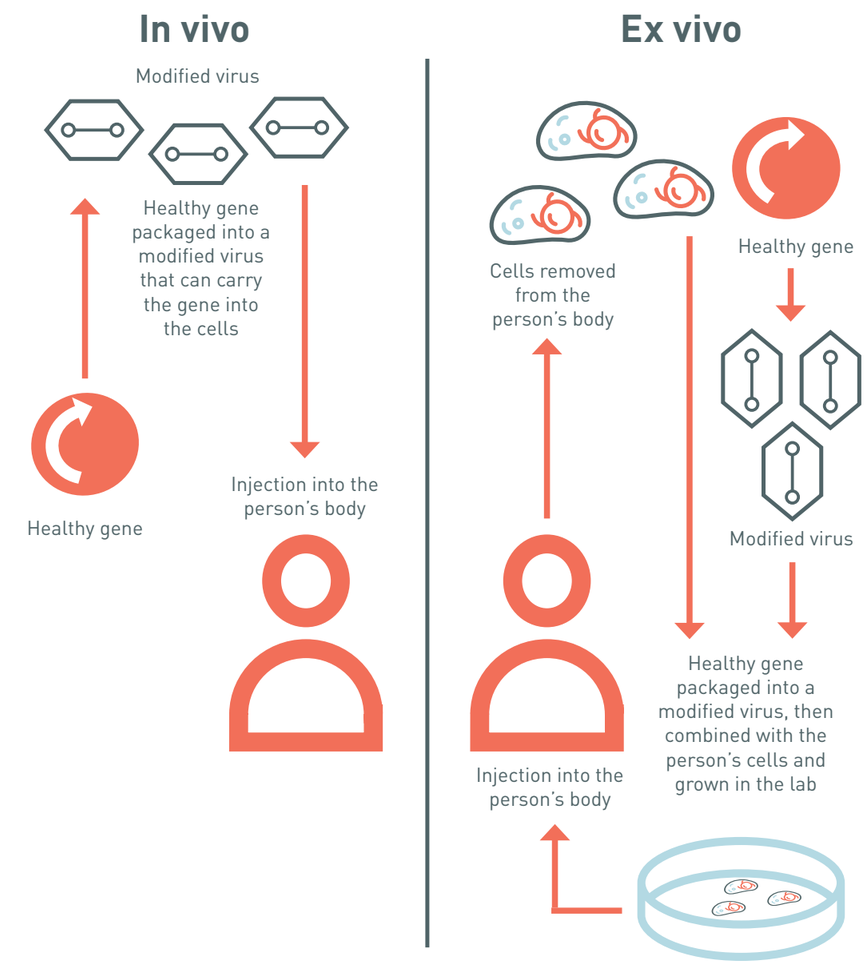
Informed consent is permission to proceed with therapy. Informed consent is given by a patient, parent or legal guardian, after receiving complete and adequate types of information about a therapy or procedure. There are two circumstances in which you may be asked to provide informed consent for gene therapy: when planning to receive gene therapy prescribed by your doctor or when planning to participate in a clinical study.[27,28] The informed consent process is subject to many rules about exactly what—and exactly how—information is provided. These rules or regulations are in place to protect the person being treated or participating in a clinical study. So, you need to listen closely to your doctor's explanations. If you are asked to sign any forms to give consent, read all forms carefully before signing. Ask questions or request more detailed information about anything you don't understand. (Please see the Amicus P&PA *Guide to Informed Consent* brochure for a more in-depth explanation.)

**How do people access gene therapy?**

Talk to your treatment team about ways to access gene therapy. Depending on the disease, there may be an approved gene therapy treatment or a clinical study available. Payment for an approved gene therapy varies by country. When gene therapy is given in a clinical study, the trial sponsor typically covers costs for the therapy and follow-up visits, but not the costs for additional routine care.[29]

## Gene therapy step-by-step

**How in vivo and ex vivo gene therapy transfers are carried out using viral vector technology[2,30-32]**




[a]Viral vectors are one type of vector. Other vectors include small organic particles and physical vectors (see page 4).[22]

# Glossary

**augmentation:** gene therapy that adds a properly functioning gene into cells that have poorly functioning gene variants

**chaperone:** a special protein molecule which may improve the effectiveness of gene therapy carried by a viral vector

**culture:** to grow cells in a laboratory

**DNA:** deoxyribonucleic acid—a biochemical that is the "building block" of genes

**ex vivo transfer:** transfer of genetic material outside of a person's body, into cells that are taken from the body, cultured, and then injected back into the body

**gene:** a distinct sequence of DNA that is the basic unit of a person's inherited traits

**genetic disease:** a disease caused by a variant gene

**genetic material:** typically DNA, but sometimes RNA (ribonucleic acid), a biochemical that helps DNA send its biological instructions for inherited traits

**gene variant:** (also known as mutations) a change to the structure of a gene that can alter the gene's function, sometimes resulting in diseases or conditions

**hereditary disease:** a disease passed from parent to child by means of a variant gene

**in vivo transfer:** transfer of genetic material directly into the body

**informed consent:** a person, parent or guardian's agreement to therapy, permission to proceed with therapy, approved medical procedure, or clinical study. Informed consent is given by a patient, parent or legal guardian, after receiving complete and adequate information

**liposome:** a small fat particle that is capable of carrying genetic material

**polymer:** a large molecule that consists of many similar chemical units, capable of carrying genetic material

**silencing:** gene therapy that turns off a gene variant that is not functioning properly

**suppression:** gene therapy that turns off a gene variant that is not functioning properly

**vector:** a biological agent (virus) or biochemical agent (liposome or polymer) that can carry and transfer genetic material into a cell

**virus:** a very small biological agent that can enter cells, and can be used to transfer genetic material; in gene therapy, the virus used is modified so it will not cause disease

## For further reading

Alliance for Regenerative Medicine

American Society of Gene & Cell Therapy. Gene therapy basics.

National Institutes of Health/Genetics Home Reference. What is gene therapy?

US Food and Drug Administration. What is gene therapy? How does it work?



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