Help Me Understand Genetics

Gene Therapy and Other Medical Advances

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1 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 being tested only for diseases that have no other cures.

For general information about gene therapy:

- MedlinePlus offers a list of links to information about genes and gene therapy (https://medlineplus.gov/genesandgenetherapy.html).
- The Genetic Science Learning Center at the University of Utah provides an interactive introduction to gene therapy (https://learn.genetics.utah.edu/content/genetherapy/) and a discussion of several diseases for which gene therapy has been successful (https://learn.genetics.utah.edu/content/genetherapy/success/).
- Your Genome from the Wellcome Genome Campus provides an introduction to gene therapy and describes several techniques (https://www.yourgenome.org/facts/what-is-gene-therapy).
2 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 inserted directly into a cell. A carrier called a vector is genetically engineered to deliver the gene. An adenovirus introduces the DNA into the nucleus of the cell, but the DNA is not integrated into a chromosome. (Figure 1)
FIGURE 1: A new gene is inserted directly into a cell. A carrier called a vector is genetically engineered to deliver the gene. An adenovirus introduces the DNA into the nucleus of the cell, but the DNA is not integrated into a chromosome.

For more information about how gene therapy works:

The Genetic Science Learning Center at the University of Utah provides information about various technical aspects of gene therapy in Gene Delivery: Tools of the Trade (https://learn.genetics.utah.edu/content/genetherapy/tools/). They also discuss other approaches to gene therapy (https://learn.genetics.utah.edu/content/genetherapy/approaches/) and offer a related learning activity called Space Doctor (https://learn.genetics.utah.edu/content/genetherapy/doctor/).

Penn Medicine’s OncoLink describes how gene therapy works and how it is administered to patients (https://www.oncolink.org/cancer-treatment/immunotherapy/what-is-gene-therapy).

Your Genome from the Wellcome Genome campus explains the first gene therapy trial to treat a condition called severe combined immunodeficiency (SCID) (https://www.yourgenome.org/stories/treating-the-bubble-babies-gene-therapy-in-use). It also describes other applications for gene therapy.
3 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:

The Genetic Science Learning Center at the University of Utah explains challenges related to gene therapy (https://learn.genetics.utah.edu/content/genetherapy/challenges/).

The NIH’s Office of Biotechnology Activities provides NIH guidelines for biosafety (https://osp.od.nih.gov/biotechnology/nih-guidelines/).
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 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 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:

A debate of the ethics of germline gene therapy (https://www.yourgenome.org/debates/is-germline-gene-therapy-ethical) is presented by yourgenome.org from the Wellcome Genome Campus.

A discussion of the ethics of gene therapy and genetic engineering (https://medicine.missouri.edu/centers-institutes-labs/health-ethics/faq/gene-therapy) is available from the University of Missouri Center for Health Ethics.
5 Is gene therapy available to treat my disorder?

Gene therapy is currently available primarily in a research setting. The U.S. Food and Drug Administration (FDA) has approved only a limited number of 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, a service of the National Institutes of Health, provides easy access to information about clinical trials. You can search for a specific clinical trial or browse by health condition or sponsor. You may wish to refer to a list of gene therapy clinical trials that are accepting (or will accept) participants.
What are mRNA vaccines and how do they work?

Vaccines help prepare the body to fight foreign invaders (pathogens such as bacteria or viruses), to prevent infection. All vaccines introduce into the body a harmless piece of a particular bacteria or virus, triggering an immune response. Most vaccines contain a weakened or dead bacteria or virus. However, scientists have developed a new type of vaccine that uses a molecule called messenger RNA (or mRNA for short) rather than part of an actual bacteria or virus. Messenger RNA is a type of RNA that is necessary for protein production. In cells, mRNA uses the information in genes to create a blueprint for making proteins. Once cells finish making a protein, they quickly break down the mRNA. mRNA from vaccines does not enter the nucleus and does not alter DNA.

mRNA vaccines work by introducing a piece of mRNA that corresponds to a viral protein, usually a small piece of a protein found on the virus’s outer membrane. (Individuals who get an mRNA vaccine are not exposed to the virus, nor can they become infected by the vaccine.) Using this mRNA blueprint, cells produce the viral protein. As part of a normal immune response, the immune system recognizes that the protein is foreign and produces specialized proteins called antibodies. Antibodies help protect the body against infection by recognizing individual viruses or other pathogens, attaching to them, and marking the pathogens for destruction. Once produced, antibodies remain in the body, even after the body has rid itself of the pathogen, so that the immune system can quickly respond if exposed again. If a person is exposed to a virus after receiving mRNA vaccination for it, antibodies can quickly recognize it, attach to it, and mark it for destruction before it can cause serious illness.

Like all vaccines in the United States, mRNA vaccines require authorization or approval from the Food and Drug Administration (FDA) before they can be used. Currently vaccines for COVID-19, the disease caused by the SARS-CoV-2 coronavirus, are the only authorized or approved mRNA vaccines. These vaccines use mRNA that directs cells to produce copies of a protein on the outside of the coronavirus known as the “spike protein”. Researchers are studying how mRNA might be used to develop vaccines for additional infectious diseases.

Scientific journal articles for further reading


Microscopic image of SARS-CoV-2, the virus that causes COVID-19. Spike proteins are seen surrounding the outer membrane of each virus particle. (Figure 2)
FIGURE 2: Microscopic image of four SARS-CoV-2 virus particles, the virus that causes COVID-19. Spike proteins are seen surrounding the outer membrane of each virus particle.

For more information about mRNA vaccines:

MedlinePlus offers many additional resources with information about mRNA vaccines, specifically relating to their use in COVID-19
