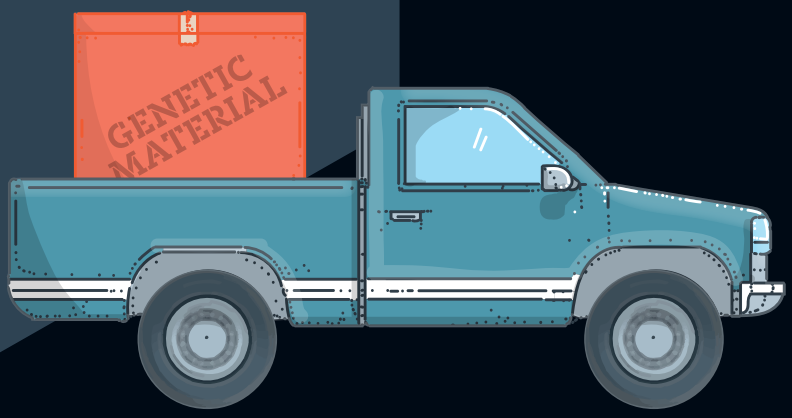
WHAT ARE **VECTORS**?

UNDERSTANDING HOW GENES ARE DELIVERED IN GENE THERAPY

One of the most important things to understand about gene therapy is how **genetic material** (such as the DNA that makes up a gene) is delivered to the cells of the person who is being treated.

Once the genetic material is delivered, it can have the intended therapeutic effect (the response that happens after treatment) in the person being treated.

In **gene therapy**, a vector is used to deliver genetic material to the cells.



FOR MORE INFORMATION ABOUT GENE THERAPY, VISIT **thegenehome.com**

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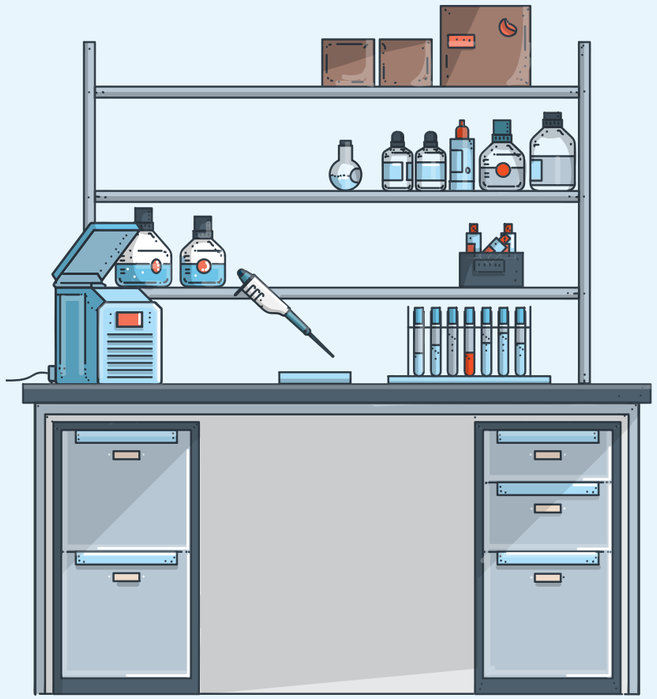
ALL GENE THERAPIES USE A VECTOR AS A DELIVERY METHOD. THIS BOOKLET WILL HELP TO ANSWER THE FOLLOWING QUESTIONS:

- What is gene therapy?
- What is a vector and how is it used in gene therapy?
- What role do viruses play in delivering gene therapy?
  - Can viral vectors cause viral infection?
  - How are viral vectors used in gene therapy?



WHAT IS GENE THERAPY?

GENE THERAPY IS A TREATMENT THAT USES GENETIC MATERIAL TO CHANGE THE COURSE OF A DISEASE

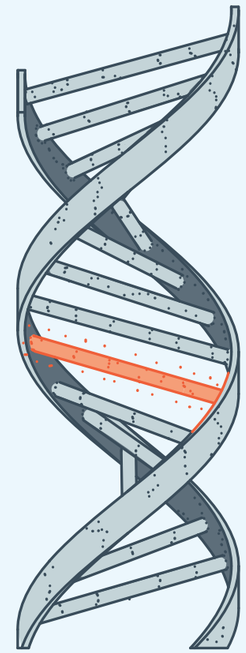
Gene therapy is an option that is being investigated for the treatment of multiple diseases. Although many gene therapies are currently in early stages of research or **clinical trials**, some have already been approved by the US Food and Drug Administration (FDA).

The goal of gene therapy is to change the course of a disease by treating the disease at the source. Usually, the source of a genetic disease is a change (or mutation) in a person's DNA that causes the disease.

Overall, there are 2 types of gene therapy being studied: **gene addition** and **gene editing**, and there are different approaches within these types.

Regardless of the type or approach, a gene therapy needs a way to deliver the genetic material to the target cell.

DNA TREATED BY GENE THERAPY



Genetic material consists of molecules (called DNA or RNA) that store information and provide instructions to the cell on what to do. For example, it may provide instructions for making a specific protein.

LEARN MORE ABOUT CELLS AND DNA AND THE ROLES THEY PLAY IN GENE THERAPY AT thegenehome.com

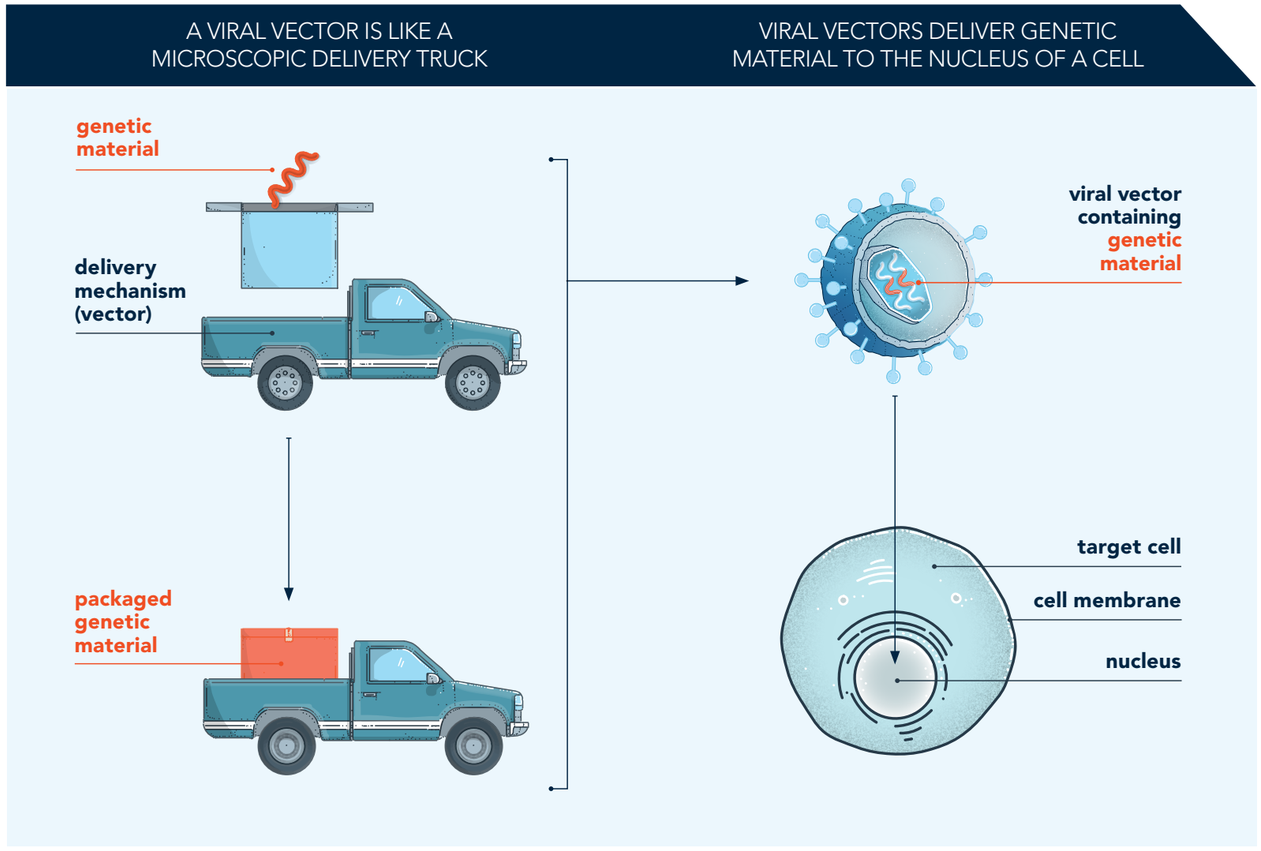
WHAT IS A VECTOR AND HOW IS IT USED IN GENE THERAPY?

VECTORS ARE USED TO DELIVER GENETIC MATERIAL TO SPECIFIC TARGET CELLS SO IT CAN HAVE A THERAPEUTIC EFFECT

There are 2 types of vectors:

1. **Viral vectors** are engineered from scratch using the blueprint of a **virus**. Viruses are used as blueprints to create vectors because they are naturally good at entering the nucleus of a cell and delivering genetic material. The rest of this brochure talks specifically about viral vectors
2. **Non-viral vectors** use other methods, either physical (such as a needle that goes into the cell) or chemical (which are created in a lab), to deliver genetic material to the cell

A **viral vector** is like a microscopic delivery truck that can transport and deliver a specific package (genetic material) directly to a target location (the nucleus of a cell). Like any delivery, the genetic material is packaged and loaded into the vehicle (the viral vector) for delivery.



HOW VIRAL VECTORS WORK IN GENE THERAPY

Viral vectors (microscopic delivery trucks) have information to help guide them to a specific type of cell (target cell).

When the viral vector reaches the target cell, it is able to:

- pass through the **cell membrane**, thereby entering the cell
- reach the nucleus

Once it reaches the nucleus, the vector:

- disassembles itself (the package is taken out of the delivery truck)
- delivers the genetic material (the package) into the nucleus

Once in the nucleus, the genetic material instructs the cell to provide the desired treatment effect to the person being treated.

After the vector enters the cell and delivers the genetic material, the cell naturally breaks down the vector and it is disposed of by the body.

VECTORS ARE ONLY ONE PART OF GENE THERAPY. VISIT **thegenehome.com** TO EXPLORE AND LEARN MORE

WHY ARE VIRUSES USED TO DELIVER GENE THERAPY?

VIRUSES ARE NATURE'S WAY OF GETTING GENETIC MATERIAL INTO CELLS. VIRAL VECTORS ARE BUILT USING VIRAL BLUEPRINTS SO THEY CAN DELIVER GENETIC MATERIAL FOR GENE THERAPY

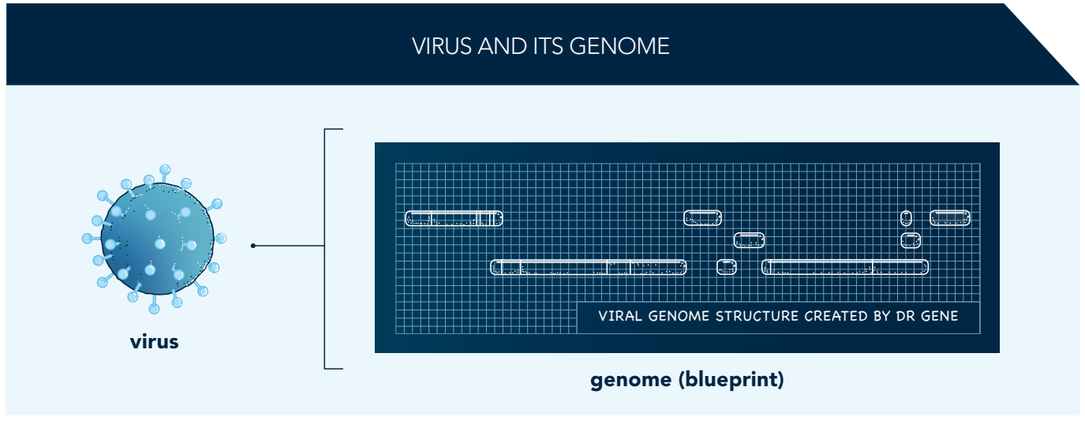
Scientists have created complete maps of the individual genetic parts of many different viruses. These maps are called **genomes** and are the blueprints that describe the parts of the virus.

Scientists create viral vectors from scratch by using these blueprints to build the parts of the virus that are good at packaging and delivering genetic material.

Then, specific information is added to help guide the vector to their target cells or to wherever the genetic material needs to be delivered.

Scientists leave out the parts of the viral blueprint that may lead to infection.

Viral genomes are used as the blueprints for creating viral vectors because viruses are naturally good at entering the nucleus of a cell and delivering genetic material.

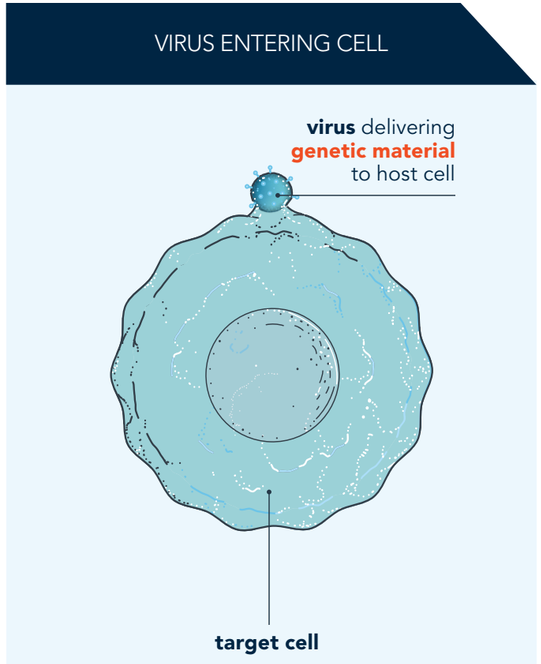


THE BLUEPRINTS OF SEVERAL DIFFERENT VIRUSES ARE USED TO CREATE VECTORS

Scientists can choose from **different types of viruses to create viral vectors**. The choice of the virus to be used depends on the specific needs of the disease being treated, such as:

- The amount of genetic material that needs to be delivered
- The target cell, or where the genetic material needs to be delivered (for example: a blood stem cell, liver cell, or an eye cell)
- Minimizing the possibility that the vector will trigger an immune system response (which is the body's response to something harmful)

Before any viral vector can be used, it needs to be reviewed by the FDA. Currently, viral vectors are used as the delivery vehicle in FDA-approved gene therapies.



Viruses are not only good at entering the nucleus of the cell, they are also good at targeting specific types of cells, such as stem cells or eye cells.

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CAN THE VIRAL VECTORS USED IN GENE THERAPY CAUSE A VIRAL INFECTION?

VIRAL VECTORS CANNOT CAUSE THE ORIGINAL INFECTION BECAUSE ONLY A FEW PARTS OF THE VIRUS ARE USED

Because scientists only use certain parts of the viral genome to create the vector, and never use all of the parts, the original virus is never recreated. This prevents a viral vector from causing the infection that would be caused by the original virus.

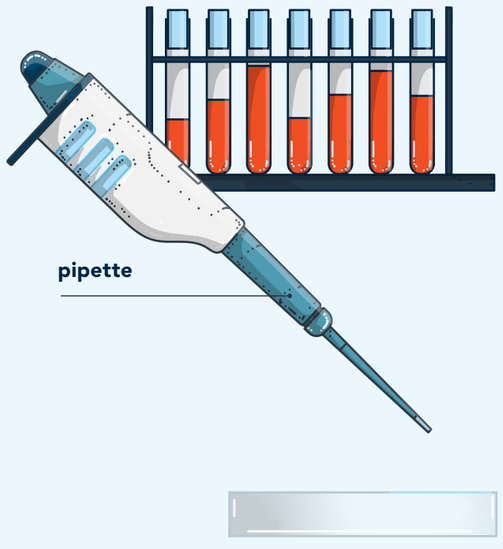
In other words, the viral vector is missing the parts of the original virus that are necessary to replicate or produce the infection that the original virus would have caused.

Which parts of the virus blueprint do scientists use when creating a vector?

Here are some examples:

- Parts that help target a specific cell
- Parts that may help a vector enter a cell

BULK OF RESEARCH IS DONE IN THE LAB



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LET'S LOOK AT THE DIAGRAM BELOW OF HOW A VECTOR IS CREATED FROM THE BLUEPRINT OF A VIRUS

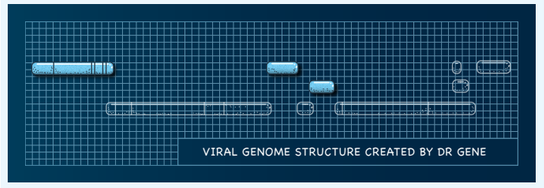
For this example, we will refer to a well-known virus, a **lentivirus**. Lentiviruses have been studied for decades. The most well-known lentivirus is HIV, which has a natural ability to deliver genetic materials into cells, specifically into stem cells.

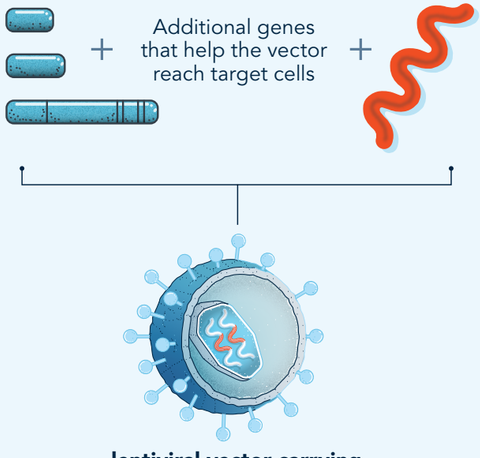
To create the lentiviral vector, a blueprint of the HIV virus is used. **HIV is made up of 9 genes**. To make the lentiviral vector, **scientists select 3 or 4 different genes from the blueprint of the HIV virus** to increase the vector's ability to deliver genetic material. At this point, other genes will be added to create the desired therapeutic effect.

Because only a specific few of the 9 genes from the original viral blueprint are used, the genome of the virus is not complete and an HIV infection cannot occur.

HIV GENOME AND LENTIVIRAL VECTOR

3 or 4 different genes from the HIV genome. The highlighted genes are responsible for the packaging and delivering of genetic materials to the cells.

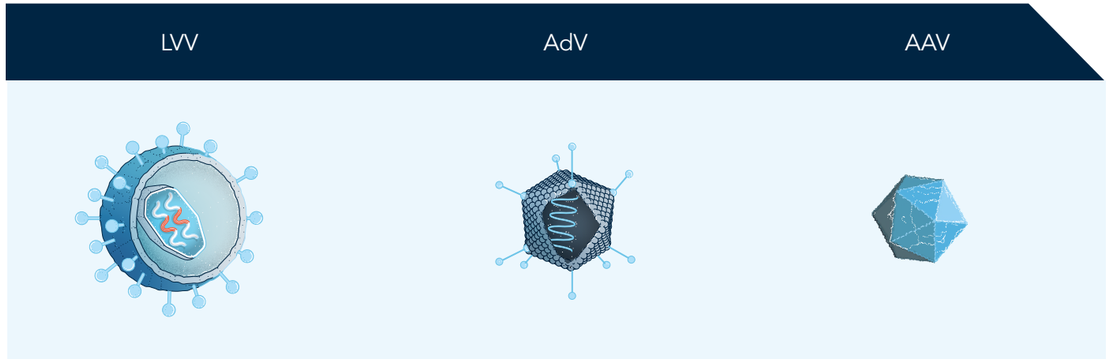




lentiviral vector carrying genetic material

EXAMPLES OF VIRAL VECTORS USED IN GENE THERAPY

DIFFERENT VIRAL VECTORS ARE USED FOR DIFFERENT GENE THERAPIES, DEPENDING ON THE CELL TYPE BEING TARGETED AND THE GENETIC DISEASE THEY ARE LOOKING TO TREAT



Lentiviral vectors (LVVs):

- Use of this type of vector became routine in research using mammalian cells in the mid-1980s
- Delivers genetic material into the DNA of a cell. This leads to a lasting genetic change that will be passed along to **daughter cells** during cell division
- Areas of research: blood diseases, liver diseases, cancer treatment

Adenoviral vectors (AdVs):

- First used for gene delivery in the late 1980s
- Highly effective at creating an immune system response
- Areas of research: treating cancer tumors, blood vessel treatments, vaccines

Adeno-associated viral vectors (AAVs):

- Discovered in 1965 with the help of electron microscopy
- Delivers genetic material in a way that does not permanently merge it into the cell DNA. This means that the changes cannot be passed down to **daughter cells** during cell division
- Areas of research: functional blindness, hemophilia, Parkinson's disease

GLOSSARY

The following terms have been defined within the context of gene therapy.

Cell membrane: Made up of 2 layers, the cell membrane separates the contents of the cell from the outside environment, while controlling what enters or exits the cell

Clinical trial: A study that measures the safety and effectiveness of a medication in humans

Daughter cells: Either of the two cells formed when a cell divides; daughter cells are genetically identical to the parent cell

Gene: Instructions made of DNA used to create the proteins the body needs to function

Gene addition: Adds functioning genetic material to do the work of a faulty gene

Gene editing: The creation of targeted double-stranded breaks in DNA, with or without repair instructions, to disrupt or correct the function of a gene

Gene expression: When the information that is part of a gene is expressed as an effect or trait

Gene therapy: A method of treating diseases at the genetic level (the source or mutation) with the goal of changing the course of a disease

Genome: The entire set of genetic instructions found in a cell nucleus

Lentivirus: A family of retroviruses used as vectors for gene therapy. A retrovirus uses RNA as its genetic material; when a retrovirus infects a host cell, the RNA changes into DNA, which then becomes part of the genome of the host cell

Non-viral vector: A way to deliver genetic material to a cell that is not based on a virus

Viral vectors: A way to deliver genetic material to a cell using the blueprint of a virus as a guide; it may be used to carry genes and change mutated cells to healthy ones

Virus: An infectious agent smaller than a bacteria consisting of a small RNA or DNA genome surrounded by a protein coat that is unable to grow or reproduce outside of a host cell

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GENEHOME IS YOUR SOURCE TO LEARN HOW GENE THERAPY WORKS AND HOW GENE THERAPY IS BEING USED TODAY. VISIT thegenehome.com

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