LEARN ABOUT **GENE THERAPY** FOR HEART CONDITIONS

TENAYA™ THERAPEUTICS

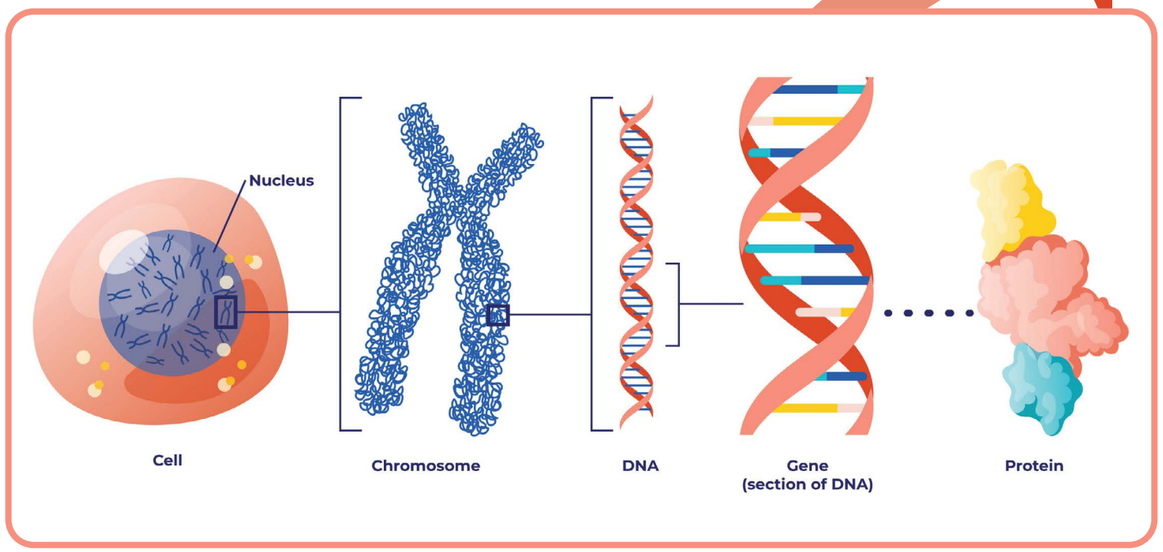
Tenaya Therapeutics is a biotechnology company using knowledge of genetics to discover and develop new medicines that may transform and extend the lives of people with heart disease.

The role of genetics

To understand how gene therapy may be a potential treatment for some heart conditions, it helps to know some basic information about genetics.

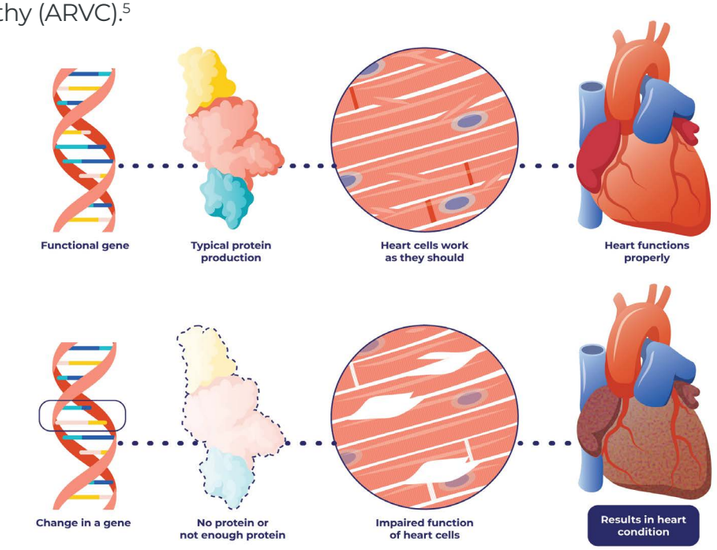
Many types of heart conditions are passed down within families (inherited). Changes in genes that lead to these conditions can come from one or both parents.

Your body is made up of **cells**.[1] Cells, in turn, contain different parts, like **chromosomes**. Chromosomes are long strands of **DNA**.[2] Within DNA are **genes**. Genes contain the instructions to make **proteins.** There are thousands of different proteins that work together to tell your body how to grow, develop and function.[3,4] For example, proteins are involved with making your organs, like your liver, lungs, and heart work.[4]



How changes in a gene cause genetic conditions

Mutations (also known as variations or changes) in a gene can affect that gene's ability to make a given protein the way it should or can affect whether that protein is made at all. For example, a gene mutation can prevent the heart muscles from making a specific protein needed for the heart to function as expected. Some examples of heart diseases frequently caused by genetic mutations include hypertrophic cardiomyopathy (HCM) and arrhythmogenic right ventricular cardiomyopathy (ARVC).[5]



Learn if you have gene variations through genetic testing

Genetic tests are usually performed by taking a sample of blood, saliva, or cells from inside of your cheek to identify changes in your genes. The results can help you understand your risk of developing a genetic condition. They can also help you and your doctor make decisions about your medical care.

As part of the genetic testing process, you may see a genetic counselor. This is a healthcare professional who can help you and your family understand the entire genetic testing process, including the possible outcome of the test and your test results. They can also explain how a genetic condition is inherited and your chance of passing it onto your children.

Did you know that genetic testing is recommended for people who have inherited heart conditions such as HCM and ARVC?[6] Ask your cardiologist about genetic testing for heart conditions.

Gene therapy for heart conditions

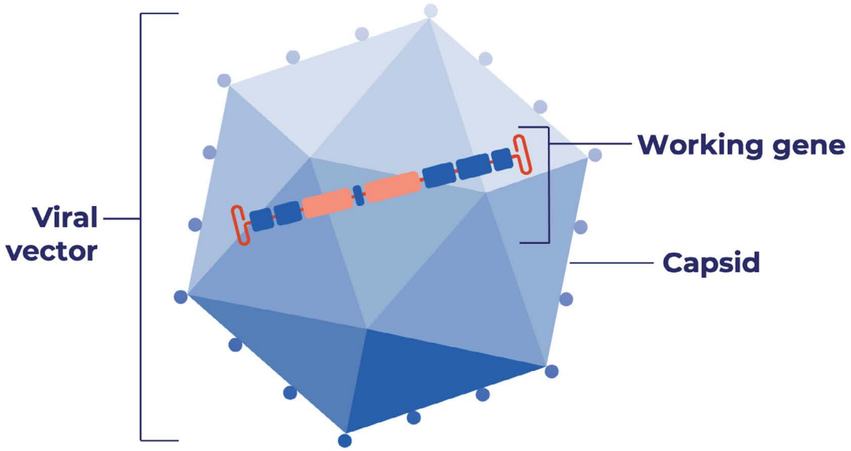
What is gene therapy?

Gene therapy is a way of treating or preventing conditions caused by genetic mutations. Gene therapy delivers a working gene into a cell to help the cell build the necessary protein to restore the expected function.[7]

What is AAV gene therapy?

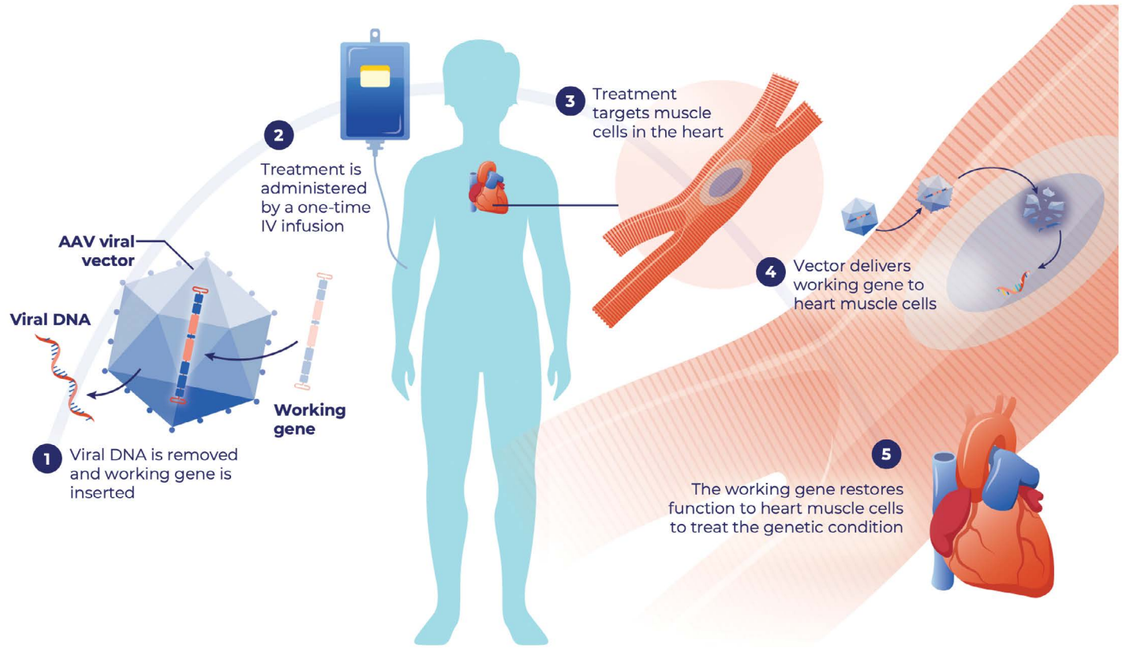
AAV gene therapy is an approach that uses an adeno-associated virus (AAV) as a vehicle (called a vector) to deliver a working gene into cells. AAV gene therapies have been studied in thousands of people for the treatment of many different genetic conditions for over 20 years.[8-11] Research on AAV gene therapies is ongoing, and there are currently several gene therapies approved by the U.S. Food and Drug Administration (FDA) and European Commission (EC) that use AAV for the treatment of genetic conditions.[12-16]

AAVs are a naturally occurring type of virus that is not known to cause symptoms or diseases in people. For this reason, AAV viruses are commonly used in gene therapy.[17]



Viruses are used because they are good at entering cells. When a virus is made into a vector, all viral genes are removed leaving the capsid.[18] A working human gene is then placed inside the capsid creating a vector.[19] The working gene is then packaged with specific instructions which tell the gene what to do in target cells and reduces potential effects on other cells.[19]

Once inside the body, the AAV vector can deliver the working gene into target cells, such as heart muscle cells. The goal of this approach is to address the underlying genetic condition and correct the problem, rather than only treating symptoms.



What is Tenaya's approach?

Tenaya is researching gene therapies for genetic heart conditions using AAV9 capsids. There are different types of vectors and capsids, and Tenaya selected AAV9 because of its proven ability to target heart muscle cells.[20] The AAV9 capsid is the most extensively studied gene therapy vector and has been used to treat more than 3,000 patients around the world.[21]

Tenaya's AAV9 gene therapies are intended to

- be delivered via a one-time intravenous (IV) infusion
- target specific types of muscle cells in the heart

Tenaya's gene therapies are investigational and have not been approved by the FDA or any other countries' health authority or regulatory agency.

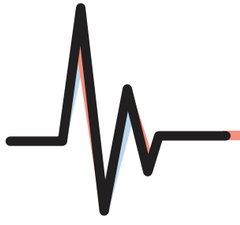
Common questions about gene therapy

What are the goals and potential benefits of AAV9 gene therapy for genetic heart conditions?

The goals of gene therapy for genetic heart conditions are to address the underlying genetic cause or root cause of the condition.

While gene therapy for inherited heart disease is still under investigation, it has several potential benefits:

- To stop or reverse genetic heart disease progression
- To stop or decrease the need for other medications and devices
- To increase quality of life
- A one-time therapy



What are the potential risks of AAV gene therapy?

Researchers are studying the potential risks of AAV gene therapy, which may include:

- The immune system may recognize the gene therapy as a harmful intruder. AAVs do not cause diseases in people. However, the immune system is designed to remove anything it does not recognize as part of a person's body. The immune system may react by attacking the treatment before it has a chance to work.[9,22]
  - Some studies of AAV and other forms of gene therapy show that immune system reactions may affect a person's liver[22]
  - Medicines that suppress or subdue the immune system are typically given before a person receives AAV gene therapy to help prevent or reduce this reaction[23]
- Currently, a person can receive AAV gene therapy only once; it cannot be re-dosed or administered in a larger dose at a later time[9,22]
  - After the first treatment with AAV gene therapy, a person's immune system makes antibodies to the AAV vector. If the body sees the same AAV again, it will attack it before it has a chance to work[24]
- AAV gene therapy may deliver a working gene to cell or tissue types that are not their intended target. This may cause illness or harm other cells.[9,22]
  - This is why the working gene is packaged with specific instructions which tell the gene what to do in target cells and reduces potential effects on other cells.[25]
- Participation in an AAV gene therapy clinical trial may prevent an individual from participating in clinical trials for other AAV gene therapies in the future
- Although many clinical trials of AAV gene therapies have been completed to date, other clinical trials of AAV gene therapies are still ongoing and not all of the risks are known

How long will AAV9 gene therapy work?

AAV9 gene therapy is designed to achieve permanent or long-lasting effects in the body. The FDA recommends that developers of gene therapies conduct long-term follow-up studies of at least five years. During this time, researchers will monitor patients for safety and to understand how well the gene therapy is working.

If a person receives AAV9 gene therapy, will they pass the new working gene to their children? Will AAV9 gene therapy protect a person's children from having their genetic heart condition?

AAV9 gene therapy does not make changes to genes in a person's reproductive cells (i.e., sperm or eggs).[26] The working gene cannot be passed from a parent to a child and so receiving AAV gene therapy will not change the risk of potentially passing on a genetic condition to children.

Where can I find more information about gene therapy?

These organizations can provide educational information about gene therapy:

American Society of Gene & Cell Therapy (ASGCT): www.asgct.org

HealingGenes: www.healinggenes.org

MedlinePlus Genetics: www.medlineplus.gov/genetics

National Human Genome Research Institute: www.genome.gov

Global Genes: www.globalgenes.org

National Organization for Rare Disorders (NORD): www.rarediseases.org

We encourage you to talk with your doctor if you have any questions about gene therapy. You may also share the information in this brochure with your doctor.

Gene therapy — words to know

AAV (adeno-associated virus): A naturally occurring virus that does not cause illness, infections, or diseases in people. It can be modified to carry genes into a person's cells.[2]

Capsid: The protective shell used to deliver a working gene and instructions into target cells. (see also vector)[18]

DNA (deoxyribonucleic acid): Genes are composed of segments of DNA. DNA carries the genetic information in cells.[2,3]

Gene: A segment of DNA that carries a cell's genetic information. Genes provide instructions for the structure and function of cells in the body. Some genes include instructions to make molecules called proteins.[3]

Gene therapy: A way to treat or prevent a disease or medical disorder using functional genes.[6]

Genetics: The scientific study of genes and inheritance.[27]

Genetic condition: A disease or disorder caused in whole or in part by a change in the typical DNA sequence of a gene, also called a gene mutation or variation.[5]

Immune response: The process by which a person's immune cells, also called white blood cells, find and fight an infection or a foreign substance in the body.[28]

Immune system: An organization of cells, tissues, and organs that work together to protect a person from infection, other diseases, or a foreign substance that it does not recognize as part of the body.[29]

Mutation: A change or variation in the typical DNA sequence of a gene.[30]

Protein: A large molecule made from the instructions of genes. Proteins are crucial to almost all the work done by cells in a person's body, and are required for the structure, function, and regulation of a person's tissues and organs.[4]

Vector: A vehicle or carrier used in gene therapy for delivering a working gene to target cells.[19]

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For more information about Tenaya and Tenaya's investigational gene therapies for genetic heart conditions:

Visit www.TenayaTherapeutics.com
Contact us at Patient.Advocacy@tenayathera.com

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