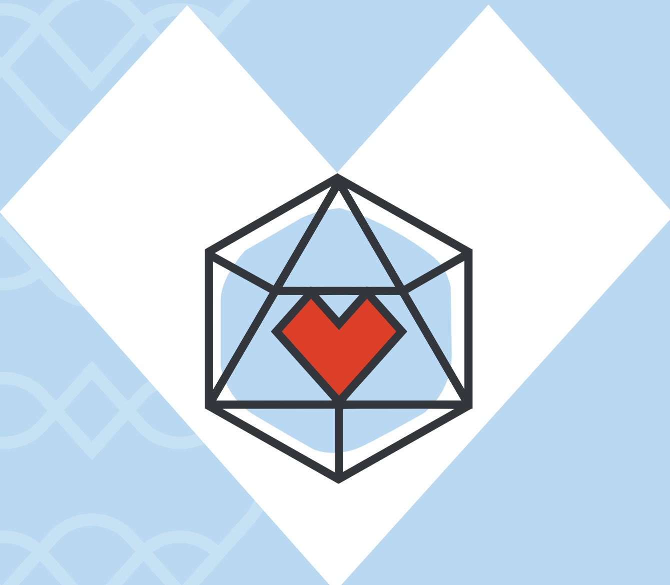
FROM GENE TO PROTEIN

A CLOSER LOOK AT GENE THERAPY FOR GENETIC HEART CONDITIONS



Background on gene therapy for genetic heart conditions

Hypertrophic cardiomyopathy (HCM) and arrhythmogenic right ventricular cardiomyopathy (ARVC) are commonly genetic heart conditions.[1,2]

- In both conditions, a gene mutation prevents the heart cells from making enough of a certain protein needed for the heart to work as it should.
- This leads to the signs and symptoms of these conditions.

Tenaya is researching AAV9 gene therapies for HCM and ARVC that **aim to restore the body's ability to make the proteins the heart needs to work as it should.**

- By delivering a working copy of the gene to heart muscle cells and helping the body make these important proteins, Tenaya's gene therapies have potential to stop the conditions from getting worse or may even reverse the conditions.

This brochure will help you understand how Tenaya's gene therapy may help heart cells make protein.

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.

Tenaya's AAV9 gene therapies for HCM and ARVC are investigational and have not been approved by the FDA or any other country's health authority or regulatory agency.

Genes contain the instructions cells need to make protein[3]

A **mutation** is a change or variation in the typical DNA sequence of a gene.

If a person has a certain gene mutation, such as *MYBPC3* in HCM or *PKP2* in ARVC, it can affect the heart cell's ability to make a protein the way it should or can affect whether the protein is made at all.[1,2]

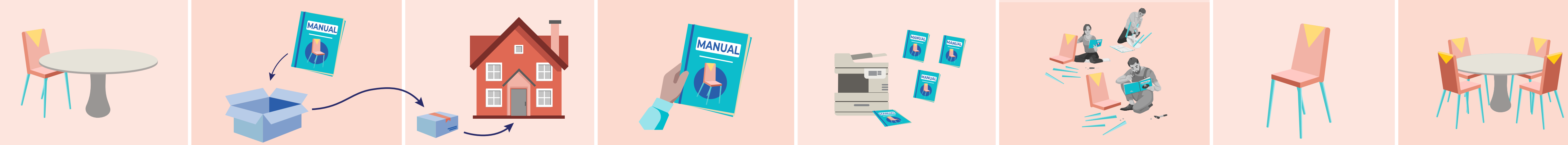
Tenaya's AAV9 gene therapy is intended to deliver a working gene, **or a new set of instructions,** to heart cells. The instructions help the cell build the necessary protein to restore the expected function.

To better understand how Tenaya's gene therapy is delivered and intended to work in heart cells, we compare the process to how someone might build chairs from a set of instructions.

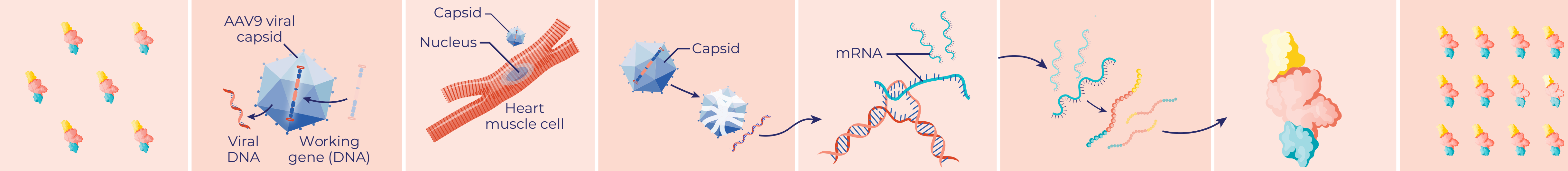
See the **resources section** on the back cover for more information about genetic mutations, gene therapy, HCM and ARVC

FROM GENE TO PROTEIN:

A Closer Look at How Gene Therapy Intends to Make Protein in Heart Cells



1. You do not have enough chairs for your table, so you order instructions to make them.
2. Instructions for making chairs are packaged in a box.
3. The box is delivered to your house.
4. You bring the box inside, open it, and take out the instructions.
5. You copy the instructions so your friends can help you.
6. You and your friends read the instructions and put the chairs together.
7. You make the chairs correctly.
8. You make enough chairs to go around the table.



1. There is not enough protein in heart cells for typical heart function. Gene therapy is designed to provide instructions for the heart to make the protein it needs.
2. A working gene (DNA) is placed inside a capsid (sometimes called a vector).
3. Gene therapy delivers capsids to heart muscle cells.
4. The capsids open and the working gene (DNA) is released.
5. The cell copies the working gene (DNA) to make mRNA.
6. The cell reads the mRNA and makes proteins.
7. The proteins are made as expected.
8. The process repeats to make the proteins needed for the heart muscle cells to work as expected.

A **capsid** is the shell of the AAV9 virus with all the viral genes removed. It is the package that delivers a working gene (DNA instructions) into cells.

Transduction: The process by which a working gene (DNA) is put into a cell using a viral vector (capsid).

mRNA expression: The process by which cells copy the working gene to make mRNA.

Protein expression: The process by which cells make protein from instructions in the mRNA.

The effects of gene therapy may take weeks, or even months to emerge, but if it works, the benefits following a single dose have potential to last for many years. `

In clinical trials, there are some early results that may give researchers insights that will allow them to determine if gene therapy is working as expected in the cells.

In Tenaya's clinical trials for HCM and ARVC, Tenaya will look at heart muscle cells to see if the:

- Working gene was delivered to heart cells (called **transduction**)[4]
- Heart cells are copying the working gene to make mRNA (called **mRNA expression**)[5]
- Heart cells are making the proteins needed for typical function (called **protein expression**)[6]

Gene therapy – words to know

DNA: Deoxyribonucleic acid, or DNA, is found in a cell's nucleus and contains all the genetic information for the cell, including how to make proteins.[3,7]

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]

mRNA: Messenger Ribonucleic acid, or mRNA, is a copy of a part of a cell's DNA that carries certain instructions, like how to make a protein.[5]

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.[8]

Resources to learn more about our gene therapy and research

Scan the QR codes for more information

Gene therapy brochure

HCMstudies.com
for *MYBPC3* associated HCM

ARVCstudies.com
for *PKP2* associated ARVC

References: [1]Crilley JG, et al. Hypertrophic cardiomyopathy due to sarcomeric gene mutations is characterized by impaired energy metabolism irrespective of the degree of hypertrophy. *J Am Coll Cardiol.* 2003;41:1776-1782. https://doi.org/10.1016/s0735-1097(02)03009-7. [2]Jacob KA, Noorman M, Cox MG, et al. Geographical distribution of plakophilin-2 mutation prevalence in patients with arrhythmogenic cardiomyopathy. *Neth Heart J.* 2012;20(5):234-239. https://doi.org/10.1007/s12471-012-0274-x. [3]U.S. Department of Health and Human Services, National Institutes of Health, National Human Genome Research Institute; 2024. https://www.genome.gov/genetics-glossary/Gene. Accessed January 24, 2025. [4]Choules MP, Bonate PL, Heo N, et al. Prospective approaches to gene therapy computational modeling – spotlight on viral gene therapy. *J Pharmacokinet Pharmacodyn.* 2024;51:399–416. https://doi.org/10.1007/s10928-023-09889-1. [5]Medlineplus Genetics. How do genes direct the production of proteins? Accessed January 24, 2025. https://medlineplus.gov/genetics/understanding/how-geneswork/makingprotein/. [6]NCI Dictionary of Cancer Terms. Comprehensive Cancer Information - NCI. Accessed January 24, 2025. https://www.cancer.gov/publications/dictionaries/cancer-terms/def/protein-expression. [7] American Society of Gene + Cell Therapy; 2023. https://asgct.org/education/more-resources/glossary. Accessed January 24, 2025. [8] U.S. Department of Health and Human Services, National Institutes of Health, National Human Genome Research Institute; 2024. https://www.genome.gov/genetics-glossary/Protein. Accessed January 24, 2025.

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 or 650-825-6990 option 4

Version 1, March 11, 2025

Tenaya Therapeutics
171 Oyster Point Blvd, Suite 500
South San Francisco, CA 94080

Follow us on Facebook and Instagram