

**Gene
therapy
aims at
the**

core
**of Huntington's
disease**

uniQure

GETTING STARTED

Before we describe an approach to gene therapy in Huntington's disease and the opportunity to participate in a clinical trial, we want to review some important terms.

Here are a few words that you need to understand before reading this brochure.

TERM	DEFINITION
Cell	The cells of your body – there are trillions of them – are considered the building blocks of all living things. They provide structure and function to all parts of your body. Cells contain DNA.
Chromosome	A bundle of DNA found within the nucleus of cells.
DNA	Material found in the nucleus of cells that contains instructions to direct the cell's activity. Your DNA contains a unique code that makes you, you.
Gene	A section of DNA that provides the instructions for the cell to make a certain protein.
Gene therapy	A variety of medical treatments that use genetic material to treat diseases.
Genetic disorder	An illness caused by 1 or more genes that are not working properly.
Inherit	To receive genetic material from parents.
Messenger RNA (mRNA)	Messenger RNA represents an intermediate step in the protein-making process and contains the instructions to direct the cell's activity. Typically, DNA is converted to messenger RNA, which is translated to proteins.
Mutant protein	A change in the structure of an encoded protein that alters the function.
Nucleus	The core of the cell that contains the DNA and provides instructions about how the cell should grow, mature, divide, or die.
Protein	Proteins provide structure to the parts of the body and serve a variety of functions; examples of types of proteins include antibodies, enzymes, and hormones.

Definitions are based on the literature and the following sources:

American Society of Gene and Cell Therapy: <https://www.asgct.org/education/glossary>

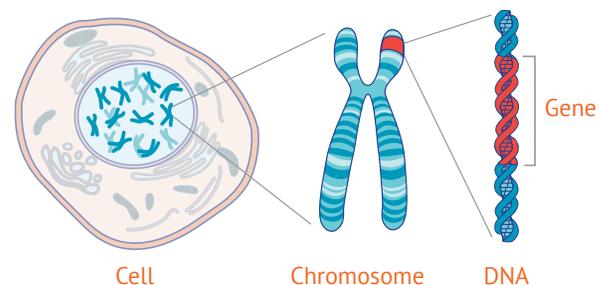
US National Genetics Home Reference: <https://ghr.nlm.nih.gov/primer>

INTRODUCTION TO GENETICS

What is a gene?

Genes make up the instruction manual used to make you into the person you are today.¹ Did you know that humans have about 30,000 genes?²

Each cell within your body contains 2 sets of chromosomes, or tightly packed bundles of genes. These chromosomes are passed down from generation to generation. You inherit 1 set of chromosomes from your mother and the other set from your father.¹



Chromosomes are tightly packed bundles of DNA, which provide cells instructions to make proteins. A gene is a segment of DNA.¹

GENETIC DISORDERS

What is a genetic disorder?

Genetic disorders result when an error or a change in a gene leads to a problem with the making of protein and causes a disease.³ Most of the time when we think about a genetic disorder we're talking about a disorder you inherit, or a congenital disorder.

TYPES OF GENE THERAPY

What is gene therapy?

Gene therapy is the method of using genetic material to treat or prevent disease.⁴ Gene therapy is being developed for the treatment of serious genetic disorders, such as Huntington's disease.⁵

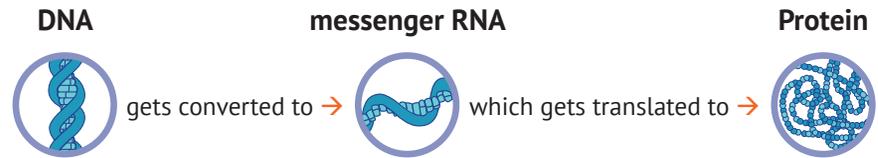
Are there other gene therapies approved?

There are approved gene therapies in the United States. One (ZOLGENSMA[®]) is for people with spinal muscular atrophy, an inherited genetic disorder that affects special cells within the spinal cord.⁶ The other (LUXTURN[®]) is for people with inherited retinal diseases.⁷ Both medicines use the same delivery system (AAV) that is used in the gene therapy for Huntington's disease.

What is the approach to gene therapy for Huntington's disease?

Gene regulation is the type of gene therapy being applied in the uniQure Huntington's disease clinical trial. It is designed to reduce the production of huntingtin protein. Build up of mutant huntingtin protein is thought to cause the symptoms of Huntington's disease.⁸

In order to reduce the levels of mutant huntingtin protein, multiple approaches are being studied that target different points of the protein-making process:



In the uniQure Huntington's disease clinical trial, gene therapy is targeting messenger RNA, which plays a role in how proteins get made. The gene therapy allows cells to produce blocking messenger RNA that interferes with Huntington's disease messenger RNA, preventing the production of huntingtin protein.⁸

What are the goals of gene therapy for Huntington's disease?

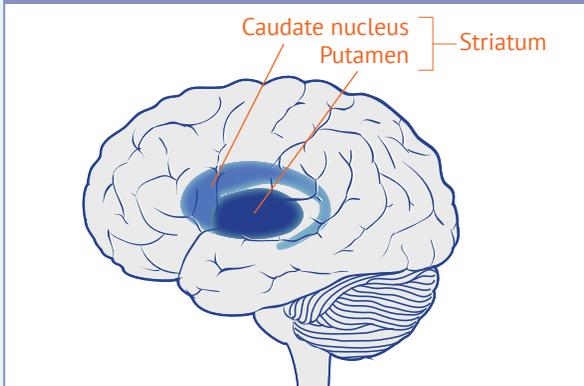
- Reduce the production of mutant huntingtin protein throughout the brain
- Preserve the function of brain cells
- Prevent or delay the progression of the symptoms of Huntington's disease
- Establish long-term, multiyear benefit from a 1-time procedure
- Maintain the patient's quality of life



UNDERSTANDING GENE THERAPY

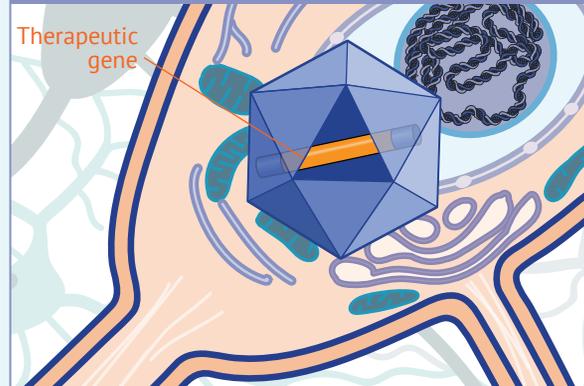
Follow along the 3 steps shown here for easy understanding.

1 Administering gene therapy



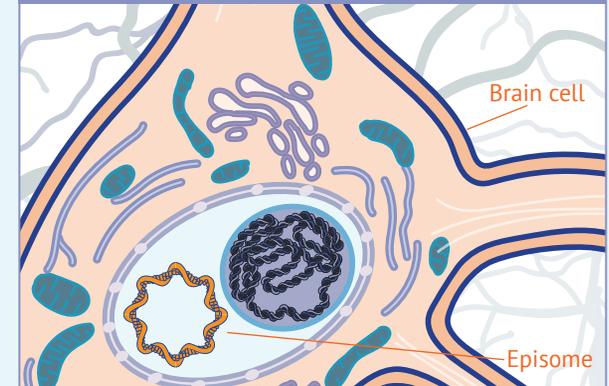
During a 1-time procedure, the gene therapy will be administered into the caudate nucleus and putamen, together known as the striatum, the areas most affected by mutant huntingtin protein.⁸

2 Entering the brain cell



The gene therapy delivers instructions to make blocking messenger RNA that interferes with Huntington's disease messenger RNA, preventing the production of huntingtin protein.⁸

3 Continuing to make blocking messenger RNA



The gene therapy may stay in brain cells and continue to make blocking messenger RNA, preventing the production of huntingtin protein over time.⁸



UNIQUIRE GENE THERAPY APPROACH IN HUNTINGTON'S DISEASE

uniQure is studying a new gene therapy in clinical trials to assess the safety, tolerability, and efficacy of a 1-time treatment in adults with Huntington's disease. The gene therapy is intended to reduce the production of mutant huntingtin protein, which may slow the progression of Huntington's disease.^{5,8} For more information about Huntington's Disease, please talk to your physician.

RESOURCES FOR THE HUNTINGTON'S DISEASE COMMUNITY

Huntington's Disease Society of America (HDSA)

<https://hdsa.org>

Helpline: 800-345-HDSA (4372)

National Office: 212-242-1968

Email: HDSAinfo@HDSA.org

Huntington's Disease Youth Organization (HDYO)

<https://en.hdyo.org/>

Email: support@hdyo.org

Postal address:

HDYO

PO Box 6371

Delray Beach, FL 33482

United States

For AMT-130 Clinical Trial Information Visit

Go to <https://clinicaltrials.gov> and search AMT-130 and uniQure

Comments or Questions

amt130_clinical_trials@uniquire.com or dial 1-339-970-7081

REFERENCES

1. Introduction to Genomics. Genome.gov. <https://www.genome.gov/About-Genomics/Introduction-to-Genomics>. Accessed December 18, 2019.
2. Human Genome Project FAQ. Genome.gov. <https://www.genome.gov/human-genome-project/Completion-FAQ>. Accessed December 18, 2019.
3. Genetics Home Reference. Do all gene mutations affect health and development? Genetics Home Reference. <https://ghr.nlm.nih.gov/primer/mutationsanddisorders/neutralmutations>. Accessed December 18, 2019.
4. Genetics Home Reference. What is gene therapy? <https://ghr.nlm.nih.gov/primer/therapy/genetherapy>. Accessed December 18, 2019.
5. Pfalzer A. Details emerge of first Huntington's disease gene therapy clinical trial. HD Buzz. <https://en.hdbuzz.net/274>. Accessed December 18, 2019.
6. Zolgensma(R) (onasemnogene abeparvovec-xioi). Prescribing information. AveXis, Inc.: Bannockburn, IL; 2019.
7. Luxturna (voretigene neparvovec-rzyl). Prescribing information. Spark Therapeutics, Inc.: Philadelphia, PA; 2017.
8. uniQure. Data on file. 2019.



About uniQure

uniQure delivers on the promise of gene therapy – single treatments with potentially curative results. The company is developing several gene therapies for the treatment of patients with liver/metabolic, central nervous system, and cardiovascular disease.

uniQure