Targeting Huntington's disease with Gene Therapy

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Understanding DNA, Genes, and Proteins

Genes: Your Body's Instructions

Genes are like the body's instruction guide—they help explain how you grow, develop, and become who you are.[1] Did you know that humans have about 20,000 genes?[2] Most cells within your body contain 2 sets of chromosomes, or tightly packed bundles of genes. These chromosomes are passed down from generation to generation. You inherit one set of chromosomes from your mother and the other set from your father.[1]

Chromosomes and DNA

Chromosomes are made of DNA, which stores the instructions for making proteins. A gene is a specific segment of DNA. Proteins are essential for the body to function, and DNA provides the instructions to produce them as needed. Some DNA sections code for proteins, while others control when, where, and how much is made.

RNA: The Messenger

RNA is a copy of the DNA instructions and helps cells make proteins. Messenger RNA (mRNA) carries these instructions from the nucleus to the cytoplasm, where proteins are built. Unlike DNA, mRNA is a single strand that can move freely through the cell.

Genetic Disorders – Huntington's Disease

What is Huntington's disease?

Huntington's disease is an inherited condition that causes the progressive breakdown of brain cells.[3] Buildup of mutant huntingtin protein is thought to cause Huntington's disease.[2] The striatum is a core structure of the brain that is first affected in people with Huntington's disease.[4] This structure is critical for motor function and reward- and goal-orientated behavior.[4] Loss of brain cells in the striatum can contribute to the following[4-6]:

- Motor function issues
- Cognitive dysfunction
- Changes in mood

What causes Huntington's disease?

Huntington's disease is driven by a mutation or change in your DNA. All cells contain genes or DNA (your individual genetic blueprint). In order to make proteins, including mutant huntingtin protein, DNA is converted to messenger RNA. Then, messenger RNA gets translated (or made) into proteins. In Huntington's disease, messenger RNA gets translated into mutant huntingtin protein.

References
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4. McColgan P, Tabrizi SJ. Huntington's disease: a clinical review. Eur J Neurol. 2018;25(1):24-34.
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Understanding Gene Therapy

What is Gene Therapy?

Gene therapy uses DNA or RNA to treat or prevent disease. It delivers instructions to correct problems with proteins—whether too much, too little, or malfunctioning.

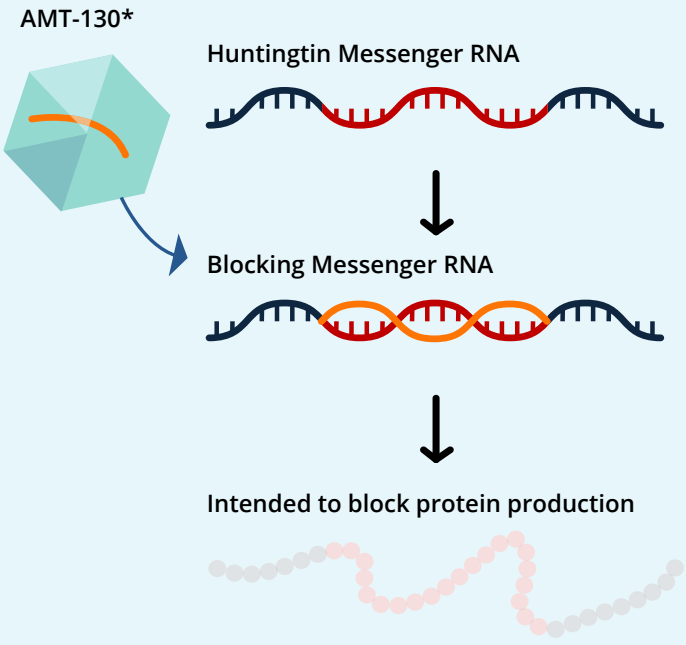
Each gene therapy is unique. How it's designed affects how well it may work and the potential side effects. That's why investigational therapies are rigorously tested in labs before entering clinical trials.

The Goals of Clinical Development of Gene Therapies for Huntington's disease

Researchers ask questions about symptoms, daily functioning, and overall health because they help determine whether the investigational therapy being studied is safe and effective for people with Huntington's disease. Clinical trials for investigational gene therapies also aim to understand whether a treatment could provide long-term benefit from a single or infrequent dose.

To support these goals, trials typically assess whether the investigational therapy or the way it is given causes any adverse reactions. They may also measure whether the therapy leads to changes in Huntington protein levels in brain tissue, signs of brain cell deterioration, the rate of disease progression, how long any effects last, or a patient's quality of life.

uniQure continues to study AMT-130, its investigational gene therapy treatment in patients with Huntington's disease.



A Look at uniQure's Approach To Gene Therapy

AMT-130 is an investigational gene therapy currently being studied to assess its safety, tolerability, and the efficacy of a single administration, in adults who have tested positive for the huntingtin gene and who have early-stage Huntington's disease.

STEP 1: Enters the brain cell
In clinical trials, AMT-130 is directly infused into the brain under real-time magnetic resonance imaging (MRI) guidance.[1]

STEP 2: Makes blocking messenger RNA
AMT-130 is intended to produce blocking messenger RNA which may interfere with the Huntingtin messenger RNA.[1,2]

STEP 3: May reduce the production of mutant huntingtin protein
AMT-130 is being studied to determine if it reduces the production of mutant huntingtin protein by assessing its impact on disease progression.[1,2]

* AMT-130 is an investigational agent currently being studied in the treatment of Huntington's Disease. Its safety and efficacy have not been established and it has not been approved by the United States Food and Drug Administration (FDA) or any other regulatory body. There is no guarantee that investigational agents will receive health authority approval or become commercially available.

References
1. uniQure. Data on file. 2019.
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