uniQure

What is Huntington's disease?

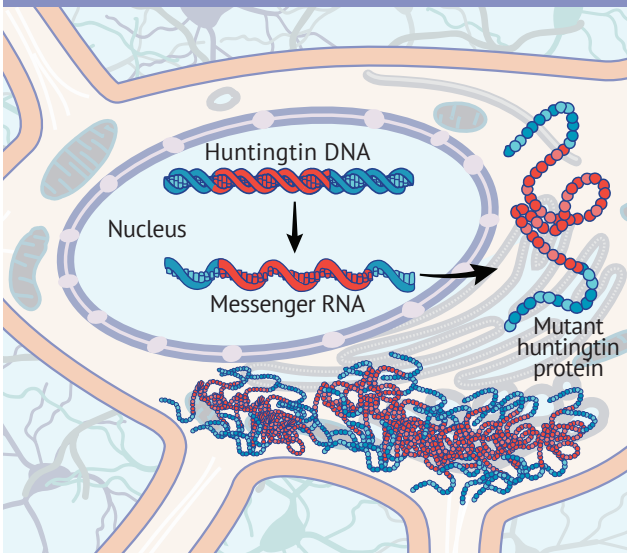
Huntington's disease is an inherited condition that causes the progressive breakdown of brain cells in the brain.[1] Buildup of mutant huntingtin protein is thought to cause Huntington's disease.[2] The striatum is a core structure of the brain that is first affected in people with Huntington's disease.[1] This structure is critical for motor function and reward- and goal-orientated behavior.[1] Loss of brain cells in the striatum leads to the following problems[3-5]:

- Motor function issues
- Cognitive dysfunction
- Psychiatric disturbances

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.

Brain cell with Huntington's disease



What should the ideal therapy for Huntington's disease look like?

The ideal Huntington's disease therapy should target the underlying cause—mutant huntingtin protein. An ideal Huntington's disease therapy would be able to do the following:

- Reduce the production of mutant huntingtin protein
- Be found throughout the brain
- Slow the production of Huntington's disease
- Be long lasting
- Be safe and tolerable

Introducing gene therapy with AMT-130

You may have heard about ways scientists are trying to create a gene therapy to treat Huntington's disease.[6] AMT-130 is an experimental (not approved by the FDA) gene therapy that is intended to slow the progression of your Huntington's disease.[6,7] AMT-130 has been tested in animal models but not in humans.[7,8]

What is AMT-130?

AMT-130 is a gene therapy currently being studied in a clinical trial to assess the safety, tolerability, and efficacy of a 1-time treatment in adults who have tested positive for the huntingtin gene and who have early-stage Huntington's disease.[7]

STEP 1: Entering the brain cell

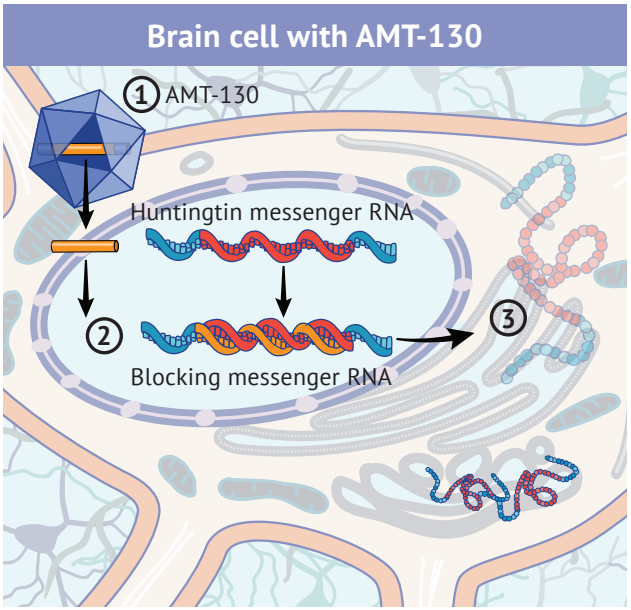
AMT-130 will be **directly infused** into the **brain** under real-time magnetic resonance imaging (MRI) guidance.[7]

STEP 2: Making blocking messenger RNA

AMT-130 is intended to allow the brain cells to produce **blocking messenger RNA** that interferes with the Huntington's disease messenger RNA.[7,9]

STEP 3: Reducing the production of mutant huntingtin protein

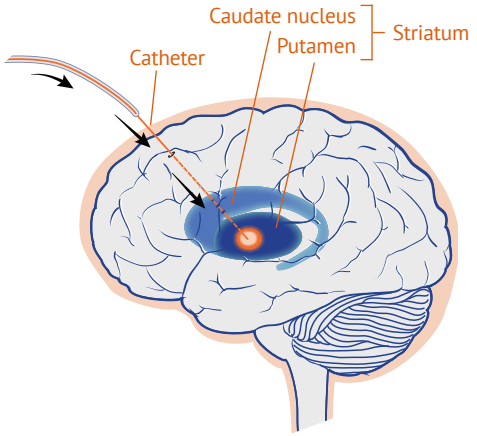
This process is intended to **reduce** the **production of mutant huntingtin protein**.[7,9]



Illustrations by Virginia Ferrante-Iqbal

How is AMT-130 administered?

During a single surgery, AMT-130 will be administered under general anesthesia by a skilled neurosurgeon who uses real-time MRI to guide delivery of AMT-130 into the caudate and putamen.[7]



How small is the catheter?

The size of the catheter may be more easily understood when it's compared to something more familiar. The catheter used to administer AMT-130 is a very thin catheter (~1/32″), or about the same thickness of a US penny.

What are the risks of brain surgery?

Common symptoms following brain surgery can include nausea, vomiting, headache, and incisional pain. Potential complications of AMT-130 administration include bleeding, infection, and brain swelling, which may prompt additional treatment and a longer hospital stay. uniQure is committed to the safety of all study participants and has procedures in place to prevent and minimize any and all risks.[7]

What are the potential benefits of AMT-130?

Huntington's disease is a slowly progressing disease for which there is currently no cure. Such signs and symptoms related to motor function, behavior and cognition, and the ability to function in daily activities are associated with the presence of mutant huntingtin protein. Gene therapy with AMT-130 offers the potential benefit of reducing the production of huntingtin protein in people with Huntington's disease.[7]

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