SAINTS PERSPECTIVES

Things Scientific and Technical

EDITORIAL PREAMBLE

This report has been created from a number of publications describing a possible breakthrough in the treatment of a crippling disease – Hungtington's Disease. In the US, a disease is considered rare if it affects fewer than 200,000 Americans. By this measure, Hungtington's disease, though deadly, is rare. This creates a challenge to develop an affordable treatment.

uniQure *(https://www.uniqure.com/), a biotechnology company based in Amsterdam is not intimidated by this challenge and specializes in developing gene therapies for genetic diseases such as Huntington's disease.*

A clever genetic technique may treat Huntington's Disease

It stops the toxic protein that causes it from forming

Huntington's disease is arguably the nastiest inherited illness around. The disease runs through families, relentlessly kills brain cells and resembles a combination of dementia, Parkinson's and motor neurone disease. Symptoms include involuntary jerking, difficulty swallowing and speaking, lapses of memory, lack of concentration, depression, anxiety, mood swings, irritability and personality changes. Eventually, the patient dies.

The first symptoms of Huntington's disease tend to appear in your 30s or 40s and is normally fatal within two decades – opening the possibility that earlier treatment could prevent symptoms from ever emerging.

Huntington's is the result of a strange mutation that amounts to a genetic stutter. Three letters of the genetic code, C, A and G, are repeated over and over again in the DNA that encodes a protein called huntingtin. Unlike most genetic disorders, for which a faulty gene must be inherited from both parents for someone to be affected, Huntington's requires only one parent to have the stutter for it to be passed on.

Everyone has some CAG repeats in their huntingtin genes, but if there are too many of them, trouble ensues. Something goes wrong with the resulting protein, causing it to accumulate in the cells that produce it, thereby wrecking them. These cells are in the brain.

But none of this happens immediately. Symptoms appear in later life, usually middle age, and are caused because, if the number of genetic repeats a person is born with exceeds 36, the repeat-chain may lengthen over the course of life until the resulting protein becomes toxic. If it is 40 or more repeats, this will definitely occur.

The exact mechanism is debated. But it seems likely that if production of the toxic protein could be suppressed, then the disease's progress might be slowed or halted.

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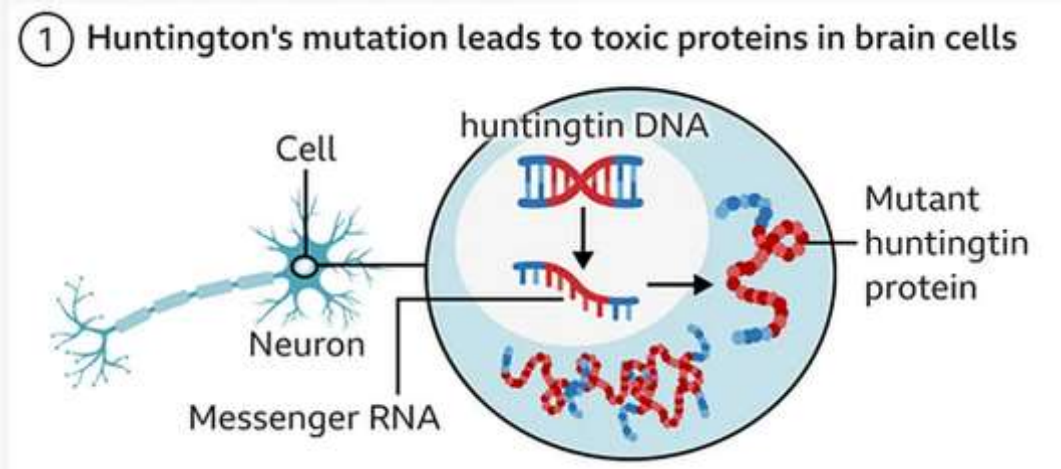
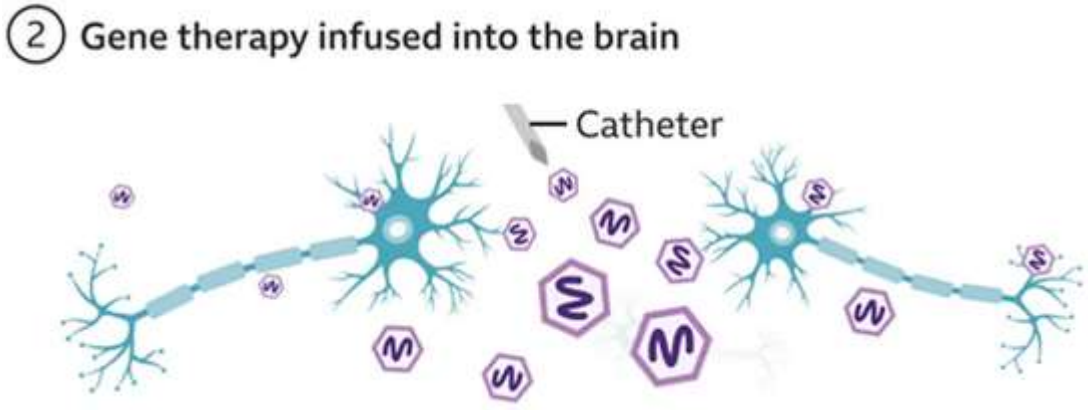
Technical Details

1) The Problem



Graphical illustration of how the therapy works separated into four tiles. The first (above) shows a spindly brain cell with a zoomed-in section showing a DNA double helix in blue with red section denoting the mutated DNA and the build up of toxic protein, also red, inside the brain cell.

2) Gene Therapy using microRNA



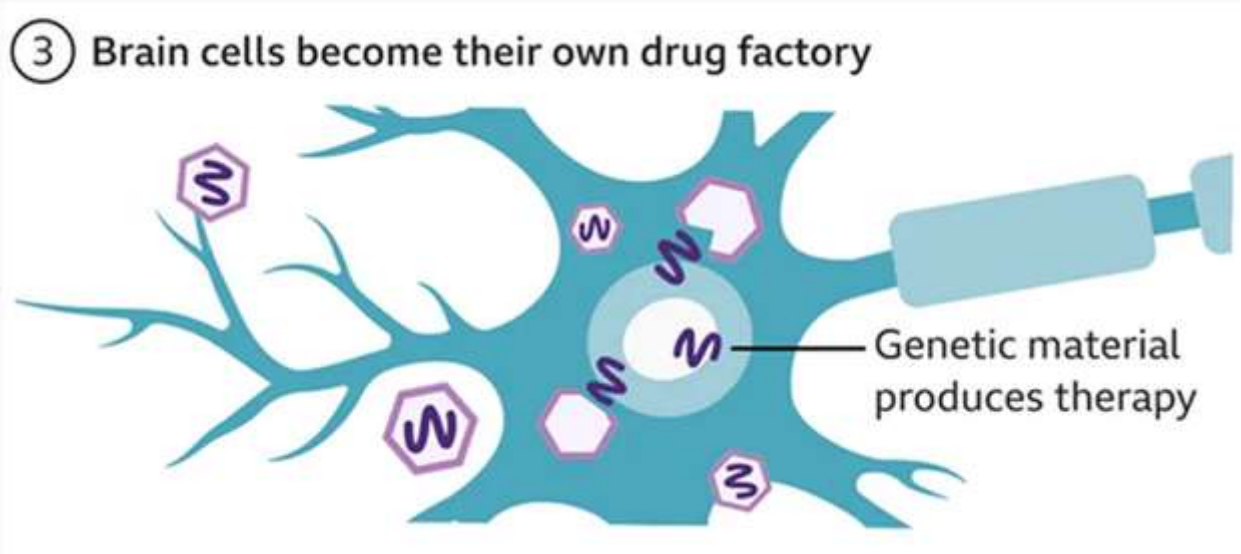
Tile 2 shows two neurons and hexagonal viruses with a purple line in the middle.

The research team at uniQure, a firm in Amsterdam, think they have been able to suppress this toxic protein using a type of genetic material called a **microRNA** that halts manufacture of the protein responsible for causing it. They dub their microRNA molecule **AMT-130**. It is generated by a genetically modified but harmless virus inserted into the brains of Huntington's patients using a trick **called MRI-guided, convection-enhanced stereotact delivery.** This is an established technique capable of great precision in the hands of a trained surgeon.

The targets of uniQure's initial experiments were the caudate nucleus and putamen areas of a deeply buried brain structure called the striatum. These are the places first affected by the illness.

The new treatment is a type of gene therapy given during 12 to 18 hours of delicate brain surgery.

3) Genetic Material transforms Brain Cells



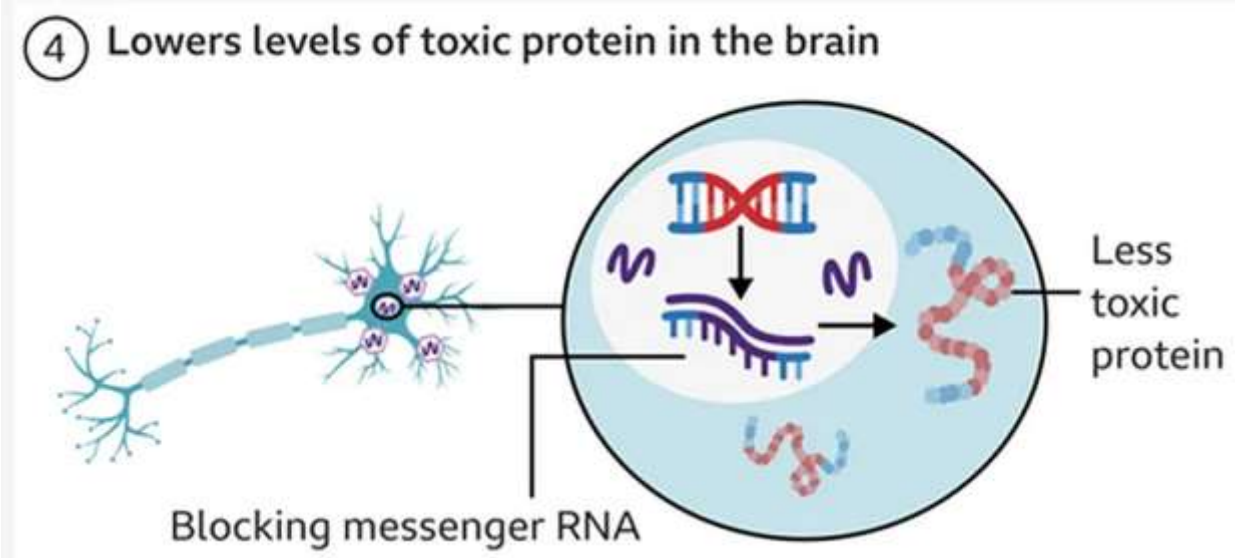
Tile 3 shows a close-up of the neurons from before with the viruses inside and releasing their purple squiggly line.

Once they have arrived in a cell's nucleus the viral genes turn out AMT-130. RNA is a molecule similar to DNA, though with a slightly different chemistry. Like DNA, two strands of RNA will bind together if their genetic letters complement each other.

AMT-130 is designed to glom onto the messenger RNA molecules that carry instructions about how to make huntingtin from the DNA in a cell's nucleus to its protein factories.

The resulting double-stranded RNA is quickly recognised by a cell as alien, and destroyed. As a bonus, the AMT-130 has a similar effect on what is known as the toxic exon-1 isoform. This is an additional toxic molecule which is a fragment of affected huntingtin.

4) The Brain Cells' Reaction



Tile 4 goes back to the same zoomed-in view of a neuron, but this time the purple squiggles are sticking to the previous genetic code so there is less toxic protein being made, represented by it being shaded out.

Note: Images copied from BBC News (see Reference 1)

The Trials

Results from the trial - which involved 29 patients - have been released in a statement by the company uniQure, but have not yet been published in full for review by other specialists.

UniQure's trial includes 29 people in America and Europe, and has been going on for three years. It reported a 75% slowing of disease progression, according to one widely used measure of Huntington's development, and a 60% slowing of progression by another. It reported, too, that a biochemical signal associated with disease severity, which can be sampled from the cerebrospinal fluid, was reduced. There were few worrying side-effects.

This is clearly good news, though there is no claim of a cure and if it can be turned into a treatment, that will surely be an expensive one. But uniQure estimates that 100,000 people in America alone carry the overlong repeat segments in their huntingtin genes, of whom 40,000 already have symptoms. This result will surely give them some hope.

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Seeing Light at the End of the Tunnel

Two scientists, Professors Ed Wild and Sarah Tabrizi led the UK part of the trial.
BBC/Fergus Walsh

Prof Tabrizi, director of the University College London Huntington's Disease Centre (UCLH), described the results as "spectacular". "We never in our wildest dreams would have expected a 75% slowing of clinical progression," she said.

None of the patients who have been treated are being identified, but one was medically retired and has returned to work. Others in the trial are still walking despite being expected to need a wheelchair.

The data showed that three years after surgery there was an average 75% slowing of the disease based on a measure which combines cognition, motor function and the ability to manage in daily life.

The data also shows the treatment is saving brain cells. Levels of neurofilaments in spinal fluid – a clear sign of brain cells dying – should have increased by a third if the disease continued to progress, but was actually lower than at the start of the trial.

"This is the result we've been waiting for," said Prof Ed Wild, consultant neurologist at the National Hospital for Neurology and Neurosurgery at UCLH. "There was every chance that we would never see a result like this, so to be living in a world where we know this is not only possible, but the actual magnitude of the effect is breathtaking, it's very difficult to fully encapsulate the emotion." He said he was "a bit teary" thinking about the impact it could have on families.

The treatment was considered safe, although some patients did develop inflammation from the virus that caused headaches and confusion that either resolved or needed steroid treatment.

Prof Wild anticipates the therapy "should last for life" because brain cells are not replaced by the body in the same manner as blood, bone and skin are constantly renewed.

Approximately 75,000 people have Huntington's disease in the UK, US and Europe with hundreds of thousands carrying the mutation meaning they will develop the disease.

UniQure says it will apply for a licence in the US in the first quarter of 2026 with the aim of launching the drug later that year. Conversations with authorities in the UK and Europe will start next year, but the initial focus is on the US.

Dr Walid Abi-Saab, the chief medical officer at uniQure, said he was "incredibly excited" about what the results mean for families, and added that the treatment had "the potential to fundamentally transform" Huntington's disease.

However, the drug will not be available for everyone due to the highly complex surgery and the anticipated cost

There isn't an official price for the drug. Gene therapies are often pricey, but their long-term impact means that can still be affordable. In the UK, the NHS does pay for a £2.6m-per-patient gene therapy for haemophilia B.

"It will be expensive for sure," says Prof Wild. Prof Tabrizi says this gene therapy "is the beginning" and will open the gates for therapies that can reach more people.

She paid tribute to the "truly brave" volunteers who took part in the trial, saying she was "overjoyed for the patients and families".

She is already working with a group of young people who know they have the gene, but don't yet have symptoms – known as stage zero Huntington's – and is aiming to do the first prevention trial to see if the disease can be significantly delayed or even stopped completely. ■.

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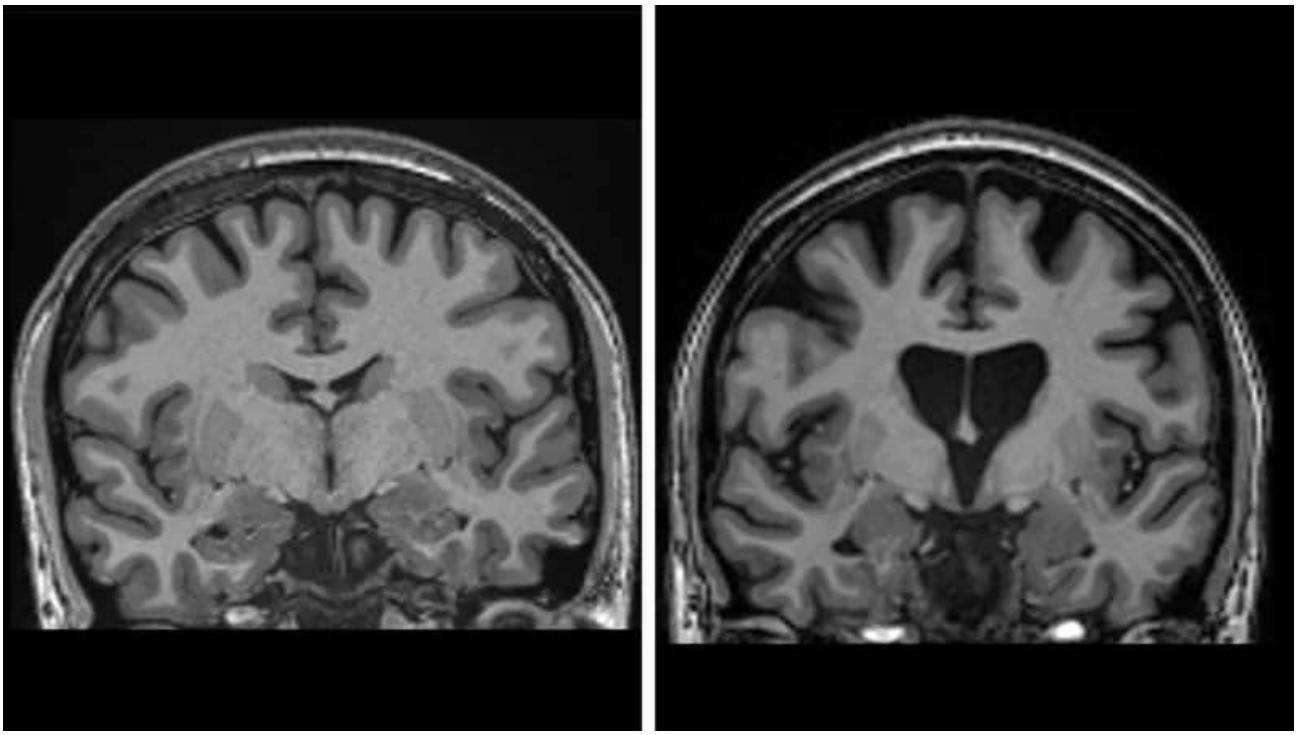

Two brain scans side-by-side. The one on the left is healthy, the one on the right shows loss of brain matter as neurons die in Huntington's disease.

The images show two cross sections of the human brain in black and white side- by-side. You can see the semi-circular outline of the skull. Inside is the folded brain matter. The key difference between the two images is the greater amount of dark space on the right demonstrating where brain tissue has died. UCLH

References

1) **Pivotal Phase I/II AMT-130 Huntington's Disease Update**
uniQure Presentation, Sept. 24, 2025

2) **Huntington's disease successfully treated for first time**
by James Gallagher, BBC NEWS Sep 24 2025

3) **A clever genetic technique may treat Huntington's Disease**
It stops the toxic protein that causes it from forming
The Economist, Sep 24th 2025