Research reveals Huntington's hope

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(Medical Xpress)—Researchers in Scotland and Germany have discovered a molecular mechanism that shows promise for developing a cure for Huntington's Disease (HD).

Scientists from the University of Dundee, the German Center for Neurodegenerative Diseases (DZNE) in Bonn, the Max-Planck Institute for Molecular Genetics in Berlin and the Johannes Gutenberg-Universität Mainz have found a mechanism that specifically stirs and induces the synthesis of disease-making protein in HD patients.

Their data lead to the conclusion that a selective overproduction of aberrant Huntington protein in patients is a key step in the establishment of the disease, which affects 1 in 10,000 people in Western countries and is so far incurable.

"This is a very promising strategy to develop a small molecule drug therapy that is able to inhibit the production of disease-making protein," said Professor Susann Schweiger of the University of Dundee and Johannes Gutenberg-Universität Mainz.

"Theoretically, if you don't have the disease-making protein then you don't have the disease. Obviously we still have work to do to develop a drug to target these mechanisms and inhibit the production of this protein but we think this research is attractive to drug discovery and ongoing work in this area is being carried out."

Huntington's Disease is a hereditary brain disorder that affects muscle

coordination and leads to cognitive decline and psychiatric problems. The disease is caused by an mutation in either of an individual's two copies of a gene called Huntingtin, which means any child of an affected person typically has a 50% chance of inheriting the disease.

The gene responsible for causing Huntington's Disease was first identified in 1993, leading to hopes that a specific therapy for HD would soon be on the market. However, cell biology and brain pathology of HD showed it to be more complicated than originally anticipated and only symptomatic treatments to slightly relieve the distress of single components of the disease are currently available.

The new discovery once again raises hopes that a curative therapy can be established. The scientists found that it was mainly three proteins - the mammalian target of rapamycin (mTOR), protein phosphatase 2A (PP2A) and Midline 1 (MID1) - that specifically drive the production of disease-making protein in HD patients.

As a result, more and more aberrant protein is produced with time, which leads to a protein overload in the cell. By interfering with the function of the three proteins it is possible to disrupt this circle and prevent the synthesis of aberrant protein in HD patients.

HD affects people of all races all over the world, and takes its name from Dr George Huntington, a US physician who first described what he called "hereditary chorea" in 1872. Chorea, from the Greek word for dance, refers to the involuntary movements which are a common symptom of HD.

It is a so-called late onset disorder. Most patients recognise first symptoms in their third to fifth decades. Within 10 to 15 years, the severity of the disease increases and patients can become confined to a wheelchair and fully dependent on carers.

The Dundee-Germany research is published in the latest edition of the *Nature Communications* journal.

Provided by University of Dundee