

New test measures deadly protein in Huntington's disease patients' spinal fluid

April 6 2015

A new test has been able to measure for the first time the build-up of a harmful mutant protein in the nervous system of patients during the progression of Huntington's disease (HD). Published today in the *Journal of Clinical Investigation*, the research team behind the findings hope that the new assay will enable the testing of drugs that aim to lower the production of the pathogenic mutant huntingtin protein that causes the disease, and could be useful in predicting or monitoring the progression of HD.

HD is a genetic neurodegenerative disease that usually develops in adulthood and causes abnormal involuntary movements, psychiatric symptoms, and dementia. It is caused by a single gene mutation that results in the production of mutant huntingtin protein. The mutated gene was identified in 1993 but until now it has not been possible to quantify the [mutant protein](#) in the [nervous system](#) of living HD patients.

The international team of scientists from University College London, IRBM Promidis, University of British Columbia, and CHDI Foundation developed a new ultra-sensitive test using the Singulex SMC Technology Erenna Immunoassay system that is able to detect mutant huntingtin in the cerebrospinal fluid (CSF) of HD patients, including some who carry the HD mutation but have not yet developed symptoms. The test, called a 'single molecule counting assay', combines fluorescent antibodies with a laser detection chamber to count individual molecules of mutant huntingtin with a very low detection threshold. The research team's findings were validated in CSF samples from two different groups of

volunteers in London and Vancouver.

CSF is a clear fluid produced by the brain that can be collected relatively easily with a needle, through a process known as a lumbar puncture or spinal tap. CSF is used in the diagnosis of other neurodegenerative diseases like Alzheimer's and Parkinson's, but until now the protein that causes HD had never been detected in CSF.

"We think the mutant huntingtin is being released into the CSF from the very brain cells it is killing," said Dr Edward Wild of UCL Institute of Neurology. "It may be a smoking gun that reflects the harm the protein is doing in the living human nervous system."

As well as detecting the protein for the first time, the researchers found that the level of mutant huntingtin was higher in volunteers with more advanced disease. What's more, the concentration of mutant huntingtin predicted the severity of movement and cognitive problems in patients.

"We do not yet have treatments that can slow the progression of Huntington's disease but, when we do, measuring the mutant protein in CSF could guide clinical decisions such as the best time to start a treatment," said Dr Douglas Macdonald at CHDI. "Measuring the amount of huntingtin may also be an essential biomarker for the upcoming trials of huntingtin-lowering therapeutics."

2015 will see the start of the first human clinical trial of a gene silencing or huntingtin-lowering drug, which specifically aims to reduce production of mutant huntingtin in the brains of HD patients. Being able to detect and measure the amount of mutant huntingtin present in the nervous system will be a valuable way of seeing whether the gene-silencing drug is hitting its target and has the intended effect, lowering the amount of disease causing mHTT protein. Meanwhile, this new technique will be an invaluable tool to help researchers study the effects

of this devastating disease in the living nervous system.

Provided by University College London

Citation: New test measures deadly protein in Huntington's disease patients' spinal fluid (2015, April 6) retrieved 21 May 2024 from <https://medicalxpress.com/news/2015-04-deadly-protein-huntington-disease-patients.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.