Scientists develop test to measure effectiveness of treatments for Huntington's disease

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Blair Leavitt of UBC's Centre for Molecular Medicine and Therapeutics

A new test developed by UBC researchers allows physicians to measure the effects of gene silencing therapy in Huntington's disease and will support the first human clinical trial of a drug that targets the genetic cause of the disease.

The gene silencing therapy being tested by UBC researchers aims to reduce the levels of a toxic protein in the brain that causes Huntington's

disease.

The test was developed by Amber Southwell, Michael Hayden, and Blair Leavitt of UBC's Centre for Molecular Medicine and Therapeutics and the Centre for Huntington Disease in collaboration with colleagues from Mayo Clinic. It was recently featured in a study published in *Scientific Reports*.

"This is an important breakthrough for several promising gene silencing therapies in Huntington's disease that are now moving from the bench to the bedside," said Leavitt. "We can move forward with these clinical trials and accurately measure whether our treatments are working."

Huntington's disease is a genetic disorder but symptoms generally don't appear until later in life. It affects the brain and gradually worsens, causing problems with coordination and movement, mental decline and psychiatric issues.

The genetic mutation responsible for Huntington's produces a toxic form of a protein called huntingtin, which progressively injures brain cells. Reducing brain levels of this toxic protein should prevent or delay the onset of symptoms. Several huntingtin-lowering therapies have already shown great promise in animal models of Huntington's disease and are rapidly approaching trials in humans.

The UBC research team found that they could accurately measure the levels of mutant huntingtin protein in the brain by collecting cerebrospinal fluid from a spinal tap. The ultrasensitive test detects small amounts of the toxic protein and can be used to follow changes in brain levels of the protein over time in response to new therapies.

This study enables Leavitt to initiate a new clinical trial of a huntingtin gene-silencing therapy for patients at the Centre for Huntington Disease

at the Djavad Mowafaghian Centre for Brain Health, a partnership between UBC and Vancouver Coastal Health. This trial will test the safety of a novel gene-silencing treatment in patients and is already in the process of screening patient candidates. The trial will be the first human study of a drug targeting mutant huntingtin.

More information: Ultrasensitive measurement of huntingtin protein in cerebrospinal fluid demonstrates increase with Huntington disease stage and decrease following brain huntingtin suppression, *Scientific Reports* 5, Article number: 12166 DOI: 10.1038/srep12166