Elucidating the Protective Mechanism of Phospho-N17 Huntingtin in Huntington’s disease

https://neurodegenerationresearch.eu/survey/elucidating-the-protective-mechanism-of-phospho-n17-huntingtin-in-huntingtons-disease/

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Country

Canada

Title of project or programme

Elucidating the Protective Mechanism of Phospho-N17 Huntingtin in Huntington's disease

Source of funding information

CIHR

Total sum awarded (Euro)

€ 581,466

Start date of award

01/04/2012

Total duration of award in years

5.0

The project/programme is most relevant to:

Huntington's disease

Keywords
Research Abstract

Huntington’s disease (HD) is one of a family of neurodegenerative diseases that occurs in mid-life that affects 1 in 6000. The exact cause of Huntington’s disease is a mutation in the gene that codes for the huntingtin protein. From the last 5 years of CIHR funding, we have discovered

important new functions for the huntingtin protein mediated by a small region of 17 amino acids (N17). N17 can be chemically modified in brain cells by kinase enzymes. This modification affects two amino acids that are located near the HD mutation. Based on our work, others have shown that if we can keep N17 modified, HD does not develop in the mouse. In 2011, we made two important new discoveries: that this critical modification can be prevented or increased by drugs called kinase inhibitors; and that huntingtin has an important role at the cell cytoskeleton during cell stress. We have discovered that mutant huntingtin is not properly modified in N17, but that drugs can restore this. These drugs are under development for other diseases by pharma, which has led to new collaborations. In the next 5 years, we will use sophisticated methods of microscopy that analyse properties of light behaviour in living cells, or Biophotonics. From these methods, we can watch in real time in live cells how the drugs we have identified can restore the mutant protein to a less toxic form. Our goals are to extend this technology to measure the shape of huntingtin protein from cells derived from HD patents, and eventually create an assay that can be used on patient blood samples. This assay can be used as a marker of disease progress, or to tell us if drugs are working in patients. There are tremendous advantages to studying neurodegeneration in Huntington’s disease, as there is a single defined cause, and this disease could be used to model drug discovery in more complex neurodegenerative diseases such as Alzheimer’s disease.

Lay Summary
Further information available at:

Types:
Investments > €500k

Member States:
Canada

Diseases:
Huntington's disease

Years:
2016

Database Categories:
N/A

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