

Targeting the innate immune system in Huntington's disease

<https://neurodegenerationresearch.eu/survey/targeting-the-innate-immune-system-in-huntingtons-disease/>

Principal Investigators

Professor SJ Tabrizi

Institution

University College London

Contact information of lead PI

Country

United Kingdom

Title of project or programme

Targeting the innate immune system in Huntington's disease

Source of funding information

MRC

Total sum awarded (Euro)

€ 1,457,420

Start date of award

01/09/2014

Total duration of award in years

4.0

The project/programme is most relevant to:

Huntington's disease

Keywords

Research Abstract

Huntington's disease (HD) is a fatal, inherited neurodegenerative disorder caused by a CAG repeat expansion in the huntingtin (HTT) gene, leading to an expanded poly-glutamine tract in the HTT protein. Considerable evidence suggests that HD is associated with increased systemic inflammation that may contribute to progression of the disease. We have shown previously that myeloid cells from HD patients are hyper-responsive to stimulation and that this is due to the

intrinsic expression of the mutant HTT protein in these cells. Our hypothesis is that mHTT primes myeloid cell hyper-reactivity to immune stimulation and that the resultant low-level systemic inflammation contributes to HD progression. We aim to determine the mechanisms by which mHTT affects myeloid cells isolated from the blood of HD patients as compared to those from non-HD individuals, by means of full-transcriptome sequencing and methods to monitor transcription factor activation and binding. We also aim to establish the extent to which components of the peripheral innate immune system contribute to HD and to determine whether systemic inflammation can be targeted to modify disease progression. We will specifically target cells and pathways by genetic and/or pharmacological means in ways that might ameliorate aspects of disease, allowing us to dissect the contribution of specific cell populations, signalling pathways and molecules to HD progression. We hope this will form the basis of further work seeking therapeutic intervention that targets in peripheral innate immune system and systemic inflammation in HD. Understanding the contribution that systemic inflammation makes to pathogenesis is essential in determining whether targeting it might be a viable therapeutic strategy in HD. A complete mechanistic understanding of these events may identify targets that lead to the development of novel therapies.

Lay Summary

Further information available at:

Types:

Investments > €500k

Member States:

United Kingdom

Diseases:

Huntington's disease

Years:

2016

Database Categories:

N/A

Database Tags:

N/A