Natural history and biomarker discovery in C9orf72 Amyotrophic lateral sclerosis and frontotemporal dementia

https://neurodegenerationresearch.eu/survey/natural-history-and-biomarker-discovery-in-c9orf72-amyotrophic-lateral-sclerosis-and-frontotemporal-dementia/

Principal Investigators

FLOETER, MARY KAY

Institution

National Institute of Neurological Disorders and Stroke

Contact information of lead PI
Country

USA

Title of project or programme

Natural history and biomarker discovery in C9orf72 Amyotrophic lateral sclerosis and frontotemporal dementia

Source of funding information

NIH (NIA)

Total sum awarded (Euro)

€ 1,188,325.69

Start date of award
Total duration of award in years

2

The project/programme is most relevant to:

Alzheimer's disease & other dementias|Motor neurone diseases

Keywords

ALS... Acquired Cognitive Impairment... Aging... Alzheimer's Disease Related Dementias (ADRD)... Alzheimer's Disease including Alzheimer's Disease Related Dementias (AD/ADRD)... Brain Disorders... Clinical Research... Clinical Research - Intramural... Clinical Trials and Supportive Activities... Dementia... Epidemiology And Longitudinal Studies... Frontotemporal

Dementia (FTD)... Neurodegenerative... Neurosciences... Rare Diseases... Translational Research

Research Abstract
Amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD) are adult-onset neurodegenerative disorders in which up to one-third of patients have overlapping clinical and pathological features. In 2011 a large hexanucleotide repeat expansion in the C9ORF72 gene was discovered that caused both ALS and FTD. The C9ORF72 expansion mutation is the commonest cause of familial ALS and familial FTD in the US and also accounts for a significant number of sporadic ALS cases. Despite the large number of patients identified from testing of stored samples, relatively little is known about the natural history of C9ORF72-related disease: how quickly the motor weakness and cognitive dysfunction progress, whether clinical presentation influences survival, and whether subtle motor or cognitive abnormalities are detectable prior to the onset of definite symptoms. Therefore, the first aim of this project is designed to fill this knowledge gap through a 3-year prospective longitudinal study of a cohort of symptomatic individuals carrying the C9ORF72 repeat expansion and asymptomatic carriers who are relatives of affected patients. The second aim of the study is to explore candidate biomarkers of disease progression. Biomarkers that can signal improvement or decline in disease activity before clinically evident deterioration would be valuable to speed the cycle of clinical trials. This is a highly collaborative study. Studies of biospecimens are coordinated by Dr. Bryan Traynor, a collaborative investigator in the National Institute of Aging. All participants consent to sharing of de-identified data and specimens. Participants undergo a structured battery of clinical ratings, neuropsychological tests, and motor measurements over a 2-4 day visit at NIH at enrollment and follow-up to assess disease severity and progression. Physiological, imaging, and biofluid biomarkers are obtained to examine their correlations with the clinical measures of progression. Skin biopsies are obtained at one visit for extramural collaborators studying disease mechanisms. The first participant was enrolled in FY14. As FY16 ends, 34 C9ORF72 mutation carriers have been enrolled and 91 visits have been carried out. To date, transcranial magnetic stimulation studies found evidence of cortical hyperexcitability in patients exhibiting lower motor neuron signs. Analysis of longitudinal physiological and imaging data is underway. CSF and plasma specimens have been shared with investigators at Johns Hopkins University, the Mayo Clinic Jacksonville, and pharmaceutical companies for exploring markers of disease activity and mechanisms of disease.

Lay Summary
Further information available at:

Types:
Investments > €500k

Member States:
United States of America

Diseases:
Alzheimer's disease & other dementias, Motor neurone diseases

Years:
2016

Database Categories:
N/A

Database Tags:
N/A