

# Genetic etiology of Fronto-Temporal Dementia

<https://www.neurodegenerationresearch.eu/survey/genetic-etiology-of-fronto-temporal-dementia/>

## Principal Investigators

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National Institute on Aging

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### Country

USA

## Title of project or programme

Genetic etiology of Fronto-Temporal Dementia

## Source of funding information

NIH (NIA)

## Total sum awarded (Euro)

€ 502,167.89

## Start date of award

## Total duration of award in years

8

## 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/ARD)... Biotechnology... Brain Disorders... Clinical Research... Clinical Research - Intramural... Dementia... Frontotemporal Dementia (FTD)... Genetics... Neurodegenerative... Neurosciences... Prevention... Rare Diseases

## Research Abstract

Amyotrophic lateral sclerosis (ALS; Lou Gehrig's disease) is a fatal neurodegenerative disorder that leads to rapidly progressive paralysis and respiratory failure. ALS is the third most common neurodegenerative disease in the Western World, and there are currently no effective therapies.

Frontotemporal dementia (FTD) is the most common form of dementia in the population under the age of 65. An overlap between these two clinically distinct neurological diseases has long been recognized, but the molecular basis of this intersection was unknown. In 2011, the Neuromuscular Diseases Research Section (NDRS), a part of the Laboratory of Neurogenetics at the National Institute on Aging, identified the major genetic cause of both ALS and FTD. To do this, Dr. Traynor (chief of NDRU) organized a worldwide consortium, bringing together groups that had previously been competitors to focus their efforts towards identifying this gene. This was made possible by the next generation sequencing technologies available at the NIH. This innovative approach worked, and his group published the cause of chromosome 9-linked ALS/FTD in the journal *Neuron* in September 2011. In these cases, the disease is caused by a six base pair segment of DNA that is pathologically repeated over and over again, up to several thousand times. This so-called large hexanucleotide repeat disrupts the C9ORF72 gene located on chromosome 9. This is the most common genetic cause of both ALS and FTD identified to date, accounting for approximately 40% of all familial cases of ALS and FTD in European and North American populations. Further, Dr. Traynor's group has shown that this mutation underlies about 8% of cases of sporadically occurring ALS and FTD that lack a family history. This represents the first time that a common genetic cause has been identified for the sporadic form of these diseases. In a separate publication in *The New England Journal of Medicine*, they have also shown that the same large hexanucleotide repeat expansion underlies 1% of patients clinically diagnosed with Alzheimer's disease. A one percent reduction in the number of AD cases would represent approximately \$1 billion in healthcare cost savings annually. The discovery of the C9ORF72 hexanucleotide repeat expansion is a landmark discovery in our understanding of neurodegenerative disease. It has already greatly effected how these diseases are diagnosed, investigated and perceived, and provides a mechanistic link between two clinically distinct disorders, ALS and FTD. It also provides a distinct therapeutic target for gene therapy efforts aimed at ameliorating the disease, and such efforts are already well underway. In summary, we have been successful in identifying genetic variants important in the pathogenesis of FTD using next generation sequencing. Our data also helps to unify FTD and ALS into a single disease rubric that encompasses two of the major late-onset neurodegenerative diseases. Each of the two studies employed large cohorts of research subjects, and utilized the sequencing and genotyping facilities available within the Laboratory of Neurogenetics, NIA.

### **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