UNDERSTANDING THE CAUSES OF THE RNA GAIN OF FUNCTION DISEASES

https://www.neurodegenerationresearch.eu/survey/understanding-the-causes-of-the-rna-gain-of-function-diseases/

Principal Investigators
Institution
Contact information of lead PI
Country

European Commission

Title of project or programme

UNDERSTANDING THE CAUSES OF THE RNA GAIN OF FUNCTION DISEASES

Source of funding information

European Commission FP7-Seventh Framework Programme

Total sum awarded (Euro)

€ 1,499,920

Start date of award

01/03/2013

Total duration of award in years

5.0

The project/programme is most relevant to:

Neurodegenerative disease in general

Keywords

Research Abstract

It is now increasingly clear that most of our genome is transcribed, but that only a small portion is associated with protein coding gene. Indeed, recent analysis indicate that long non-coding RNA outnumbered by five fold the coding RNA sequences. Despite this abundance, very little is known on the function of these long non-coding RNA.

The aim of this proposal is to understand the function of pathological long non-coding RNA. We will first focus our studies on the RNA gain-of-function diseases. These genetic diseases are caused by the pathogenic expansion of nucleotide repeats, which are transcribed into long non-coding RNA that titrate and sequester specific RNA-binding proteins, leading to molecular changes ultimately resulting in the symptoms of these pathologies. The RNA gain-of-function diseases include the most common muscular dystrophies in adult: the Myotonic Dystrophies of

type 1 and type 2 (DM), the common neurodegenerative Fragile X-Associated Tremor/Ataxia Syndrome (FXTAS) and the rare, but deleterious, Spinocerebellar Ataxia 10, 31 and 36 (SCA10, SCA31 and SC36).

We propose to :
1 – Identify the proteins sequestered by theses expanded RNA repeats.
2 – Identify the molecular causes of DM, FXTAS and SCA diseases in iPS neuronal cell model and mouse models.
3 – Identify pharmacological compounds able to reverse the toxic effects of these RNA.

Importantly, these RNA gain of function diseases present identical symptoms to other pathologies that are much more common and tremendously challenging to our society (for example the tremor in FXTAS is similar to the one observed in Parkinson; the cognitive impairment, the demence and the neurodegeneration found in FXTAS are present in Alzheimer Disease; the heart failure, which is a leading cause of morbidity in Europe is a cardinal symptom of DM; etc.).

THUS, ELUCIDATING THE MOLECULAR CAUSES OF THESE RNA DISEASES MAY HELP TO UNDERSTAND THE PATHOLOGY OF OTHER COMMON AND CHALLENGING DISEASES.

Lay Summary
Further information available at:

Types:
Investments > €500k

Member States:
European Commission

Diseases:
Neurodegenerative disease in general

Years:
2016

Database Categories:
N/A

Database Tags:
N/A