

# UNDERSTANDING THE CAUSES OF THE RNA GAIN OF FUNCTION DISEASES

<https://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 these 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 dementia 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