TOPIC: Targeting Cytotoxic Protein Oligomers

https://neurodegenerationresearch.eu/survey/topic-targeting-cytotoxic-protein-oligomers/

Name of Fellow
Institution
Funder

European Commission FP7-Seventh Framework Programme

Contact information of fellow
Country

EC

Title of project/programme

TOPIC: Targeting Cytotoxic Protein Oligomers

Source of funding information

European Commission FP7-Seventh Framework Programme

Total sum awarded (Euro)

€ 586,111

Start date of award

01/09/13

Total duration of award in years

4.0

The project/programme is most relevant to:

Huntington's disease

Keywords

Protein oligomer | cytotoxicity | aggregate | protein-protein interactions | small-molecule interaction disruptors

Research Abstract

Parkinson’s disease and Huntington’s disease are highly debilitating diseases for which no disease modifying treatment is available. This EID proposal, called TOPIC (Targeting Cytotoxic Protein Oligomers), will train 2 ESRs to target the oligomeric protein aggregate which accumulates in these diseases. These oligomers occur under conditions which eventually lead to the accumulation of fibrillar amyloid deposits. However, there is increasing consensus that

the amyloid state is biologically inert and the cytotoxic species is the oligomeric structure. Our approach rests on the working hypothesis that the cytotoxic oligomers engage in a number of unwanted interactions with proteins and membranes. The 2 ESRs will combine proprietary technology to stabilize these oligomers with state-of-the-art mass spectrometry and biophysical techniques to identify, quantitate and rank these interactions within the context of the cellular interactome. The next goal (building directly on the EID outcome but outside its present scope) is to develop small-molecule inhibitors of these interactions as a therapeutic strategy to eliminate cell death and disease progression. This training programme offers a unique opportunity for the 2 ESRs to carry out central parts of translational research in both an academic and SME setting, spanning a multitude of different cellular, biophysical and mass spectrometric techniques of general use in the life sciences.
Our target oligomeric proteins are ?-synuclein (Parkinson’s Disease) and the N-terminal part of exon 1 of huntingtin (Huntington’s Disease). By analysing two different proteins in parallel projects, we will be able to validate the robustness of our approach and potentially identify generic small molecules to target misfolded protein oligomers in general. Our approach will allow the ESRs to develop a general therapeutic strategy that targets a major class of devastating disease affecting the daily lives of millions of people throughout the world.

Types:
Fellowships

Member States:
N/A

Diseases:
Huntington's disease

Years:
2016

Database Categories:
N/A

Database Tags:
N/A