

Understanding the Molecular Origins of the Toxicity of Alpha-synuclein in Parkinson's Disease

<https://neurodegenerationresearch.eu/survey/understanding-the-molecular-origins-of-the-toxicity-of-alpha-synuclein-in-parkinsons-disease/>

Principal Investigators

Dr A De Simone

Institution

Imperial College London

Contact information of lead PI Country

United Kingdom

Title of project or programme

Understanding the Molecular Origins of the Toxicity of Alpha-synuclein in Parkinson's Disease

Source of funding information

MRC

Total sum awarded (Euro)

€ 576,077

Start date of award

01/01/2016

Total duration of award in years

3.0

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders|Alzheimer's disease & other dementias

Keywords

Research Abstract

In this project we assembled a cohort of complementary skills and combined our longterm research programmes to carry out an interdisciplinary study of the structural bases of the toxicity of prefibrillar alpha-synuclein oligomers in view of the crucial interaction with the membrane,

which represents the key step in the aetiology of Parkinson's disease. Our research proposal comes at a most opportune time, since we now have all the tools, background research and materials to perform such an ambitious study. The proposal is articulated on three independent and complementary streams of increasing scale of complexity (i.e. from oligomers structure to membrane interaction and to the effects of pathological mutations). To fulfil this ambitious goal, we will carry out an investigation of solid-state NMR (ssNMR), solution NMR and computational biology that will provide an accurate structural characterisation of toxic and non-toxic oligomers, previously individuated by a part of the team (Cremades et al, Cell, 2012 149:1048-59).

Moreover, to probe the selective interaction of the two types of oligomers with a variety of lipid membranes, we will adapt our recent approach that successfully unveiled the nature of the interaction between monomeric alpha-synuclein and lipid membranes (Fusco et al, Nature Communications, 2014 5:3827). The structural investigation will be complemented biophysical and cellular toxicity measurements to define the underlying structural bases of cellular toxicity of alpha-synuclein.

Lay Summary

Further information available at:

Types:

Investments > €500k

Member States:

United Kingdom

Diseases:

Alzheimer's disease & other dementias, Parkinson's disease & PD-related disorders

Years:

2016

Database Categories:

N/A

Database Tags:

N/A