The molecular mechanisms of structural conversion and toxicity in amyloid disease.

https://neurodegenerationresearch.eu/survey/the-molecular-mechanisms-of-structural-conversion-and-toxicity-in-amyloid-disease/

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United Kingdom

Title of project or programme

The molecular mechanisms of structural conversion and toxicity in amyloid disease.

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7.0

The project/programme is most relevant to:

Neurodegenerative disease in general

Keywords
Research Abstract

Despite the importance of amyloid disorders in today s population, attempts to inhibit the progress of amyloidosis have met with limited success. New therapeutic strategies require the structure, stability and dynamics of every species populated during assembly to be determined and the effects of individual species on cellular function deduced. Here we propose to combine biophysical, biochemical and cell biological approaches to address three questions that lie at the

heart of our quest to understand amyloidosis at a molecular level: (i) how does molecular self-recognition occur in the earliest stages of amyloid assembly; (ii) which species nucleate fibril formation and what is the structure of higher order oligomers and amyloid fibrils; and (iii) how do amyloid fibrils and fibril-associated species exert their toxic effects? Using beta2-microglobulin as a paradigm, and embracing other assembling proteins/peptides, our aim is characterise all species possible on an as sembly landscape in order to define the entire molecular assembly pathway from monomer to fibril. In parallel, by combining different strategies we aim to derive new understandings of the origins of amyloid-associated cytotoxicity. Together the programme will provide the much-needed structural, biophysical and cellular insights required for therapeutic intervention in the years ahead.

Lay Summary
Further information available at:

Types:
Investments > €500k

Member States:
United Kingdom

Diseases:
Neurodegenerative disease in general

Years:
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N/A

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