Molecular and cellular mechanisms of protein aggregation and toxicity in models of neurodegeneration.

https://neurodegenerationresearch.eu/survey/molecular-and-cellular-mechanisms-of-protein-aggregation-and-toxicity-in-models-of-neurodegeneration/

Name of Fellow

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Institution
Funder

Wellcome Trust

Contact information of fellow
Country

United Kingdom

Title of project/programme

Molecular and cellular mechanisms of protein aggregation and toxicity in models of neurodegeneration.

Source of funding information

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€ 1,626,217

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01/10/15

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The project/programme is most relevant to:

Neurodegenerative disease in general

Keywords

alzheimer | Cognitive impairment | Dementia | Neurodegen | Parkinson

Research Abstract
The proposed research focuses on the cellular machinery for removing and repairing damaged, aggregated proteins. During healthy life, protein quality control systems prevent the accumulation of these toxic aggregates. However, the repair systems become less effective with ageing, resulting in a increasing risk of degenerative diseases such as Alzheimers and Parkinsons. Recent advances in three-dimensional molecular and cellular electron microscopy will facilitate studies of the cellular machine ry for processing aggregates of incorrectly folded proteins which cause cell death. The broad question is how misfolding and aggregation are kept under control during the healthy lifespan of cells and tissues, and how these protein homeostasis functions eventually become ineffective in misfolding disease. The in vitro part of the proposed work focuses on how a family of protective proteins, the molecular chaperones, reverse the formation of damaging aggregates. We wish to examine how these chape rones engage with aggregated, non-native proteins and how the machinery operates in disaggregation. With the knowledge gained from in vitro structural and mechanistic studies, cell and animal models will help to address questions about the structural basis for disaggregation in vivo, as well as to identify common, underlying features of the toxicity resulting from protein aggregation.

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