Resolving ubiquitin-dependent degradation of misfolded proteins using advanced single-molecule techniques.

https://neurodegenerationresearch.eu/survey/resolving-ubiquitin-dependent-degradation-of-misfolded-proteins-using-advanced-single-molecule-techniques/

Name of Fellow

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Institution
Funder

Wellcome Trust

Contact information of fellow
Country

United Kingdom

Title of project/programme

Resolving ubiquitin-dependent degradation of misfolded proteins using advanced single-molecule techniques.

Source of funding information

Wellcome Trust

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€ 338,950

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01/06/14

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4.0

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords

alzheimer | Neurodegen

Research Abstract

My proposed research seeks to understand the links between degradation of protein aggregates and the ubiquitin-proteasome pathway. The project entails three goals. The first goal involves establishing a fluorescence-based system to detect individual interactions between aggregates and proteasomes. To achieve this, I will initially receive training on proteasome purification and examine how to modify proteins with specific ubiquitin chains. Subsequently, I will explore different fluorescence labe lling systems and optimise a labelling strategy for protein aggregates and the proteasome without disrupting their integrity. The fluorophores selected should be bright and photostable to be compatible with the single-molecule instruments. This single-molecule fluorescence system will be used to establish a method that can reveal interactions between individual protein aggregates and a single proteasome to determine the efficiency of degradation for different types of aggregates. The second goal will focus on aggregate degradation in cells using three-dimensional superresolution imaging. Heterogeneous interaction between aggregates and proteasomes can be resolved to determine whether certain types of aggregates can inhibit the proteasome. Finally, I will focus on cell lines with mutations on key Parkinson’s disease-related genes, and establish whether aggregate degradation is affected. Identifying altered degradation in these cells will relate proteasome functions directly to disease s tates.

Types:
Fellowships

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Diseases:
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