

# Studies on alpha-synuclein degradation and its relevance to Lewy body disease.

<https://www.neurodegenerationresearch.eu/survey/studies-on-alpha-synuclein-degradation-and-its-relevance-to-lewy-body-disease/>

## **Name of Fellow**

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## **Institution**

### **Funder**

Wellcome Trust

## **Contact information of fellow**

### **Country**

United Kingdom

## **Title of project/programme**

Studies on alpha-synuclein degradation and its relevance to Lewy body disease.

## **Source of funding information**

Wellcome Trust

## **Total sum awarded (Euro)**

€ 994,864

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## **Total duration of award in years**

5.0

## **The project/programme is most relevant to:**

Parkinson's disease & PD-related disorders

## **Keywords**

Cognitive impairment | Dementia | Neurodegen | Parkinson

## **Research Abstract**

Parkinsons disease (PD), is a common neurodegenerative disorder without pre-symptomatic

diagnosis or cure. Although it is established that an accumulation of alpha-synuclein in neurons contributes to PD pathogenesis, the factors influencing the content of this key protein in cells remain poorly understood. I have recently discovered that the ubiquitin-ligase Nedd4 robustly ubiquitinates alpha-synuclein and promotes its degradation by the endosomal-lysosomal pathway. I hypothesize that (a) impaired degradation of alpha-synuclein by this pathway contributes to the pathogenesis of PD and (b) this pathway can be targeted for neuroprotection. I have the following specific aims: 1. Study in cell models whether Nedd4 regulates the membrane-bound fraction of alpha-synuclein and whether this process involves further post-translational modifications. 2. Investigate using primary neurons whether Nedd4-mediated alpha-synuclein is a target for neuroprotection. 3. Understand how Nedd4 is regulated in normal and disease states. 4. Study the anatomical distribution, level of expression and post-translational modification of Nedd4 and other endosomal proteins in PD and control brain tissue.

**Types:**

Fellowships

**Member States:**

United Kingdom

**Diseases:**

Parkinson's disease & PD-related disorders

**Years:**

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