

# Role of Parkin in Familial and Idiopathic Parkinsons Disease

<https://www.neurodegenerationresearch.eu/survey/role-of-parkin-in-familial-and-idiopathic-parkinsons-disease/>

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### Country

USA

## Title of project or programme

Role of Parkin in Familial and Idiopathic Parkinsons Disease

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NIH (NINDS)

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01/08/2010

## Total duration of award in years

5

## The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

## Keywords

Idiopathic Parkinson Disease, parkin gene, , ,

## Research Abstract

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by both motor and non- motor disturbances. While the etiology of the disease is unknown, genetic mutations responsible for familial forms of PD likely provide critical molecular insights into the

underlying mechanisms of idiopathic disease. Loss-of-function mutations in the ubiquitin E3 ligase parkin are the most common cause of autosomal recessive PD. Parkin is now widely recognized as a pro-survival protein that possesses broad ranging effects on mitochondrial biology, and beyond. A more complete comprehension of these functions will lead to a better understanding of the neurodegenerative process in PD, as well as the identification of new pathways that may be targeted for disease modification. The long-term goal of our work is to uncover the molecular machinery responsible for parkin's protective effects in neurons. We propose that both the cytosolic and mitochondrial-localized pools of parkin play important roles in the maintenance of healthy neurons. This application will explore the role of cytosolic parkin in its neuro-protective function in human neurons. Using engineered isogenic and patient based WT and parkin null pluripotent stem cells differentiated to human neuronal fates, we will uncover the conditions that activate the cytoplasmic pool of parkin. We will identify the upstream proteins that control parkin activation and its protection against cell death in human neurons. Then, we will explore the role of BH3 domains in the recognition of an expanding class of putative substrates of cytoplasmic parkin E3 ligase activity. The pathways found to regulate neuronal parkin function may shed light on innovative targets for therapeutic intervention to up-regulate parkin activity and induce neuro-protection in neurologic disease.

### **Lay Summary**

Parkin is involved in a critically important protective, neuronal stress response and loss of parkin function is causally linked to neurodegeneration and Parkinson's disease. The goal of this study is to understand the precise mechanisms by which parkin protects neurons from stress, and identify new pathways that control its activity. These pathways, once discovered, may identify new therapeutic targets for the treatment of neurological disorders.

### **Further information available at:**

#### **Types:**

Investments > €500k

#### **Member States:**

United States of America

#### **Diseases:**

Parkinson's disease & PD-related disorders

#### **Years:**

2016

#### **Database Categories:**

N/A

#### **Database Tags:**

N/A