

# The Gut Microbiome in Neurodegenerative Disease

<https://www.neurodegenerationresearch.eu/survey/the-gut-microbiome-in-neurodegenerative-disease/>

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### Country

USA

## Title of project or programme

The Gut Microbiome in Neurodegenerative Disease

## Source of funding information

NIH (NINDS)

## Total sum awarded (Euro)

€ 1,218,963.30

## Start date of award

30/09/2013

## Total duration of award in years

1

## The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

## Keywords

gut microbiome, Parkinson Disease, microbiome, Neurodegenerative Disorders, Germ-Free

## Research Abstract

DESCRIPTION (provided by applicant): Beneficial bacteria permanently colonize many body sites, with a growing appreciation for the importance of the microbiome to human health. Pioneering research has revealed that changes in gut bacteria impact metabolic and

immunologic disorders such as obesity, inflammatory bowel disease (IBD) and multiple sclerosis (MS). Moreover, specific therapeutic bacterial molecules from the microbiome have been validated in experimental IBD and MS mouse models. Building on principles from the study of metabolism and immunity, reports have recently shown that the microbiome affects anxiety, nociception and aspects of brain development. These seminal studies may represent harbingers of extensive, currently undescribed, links between gut bacteria and the nervous system. Parkinson's disease (PD) results from neurodegeneration that leads to severe motor defects, with 3 million people worldwide suffering from this condition. Most cases are not hereditary; however, the contributions of environmental risk factors remain largely unknown. Based on the common occurrence of gastrointestinal (GI) symptoms and evidence supporting the hypothesis that neurodegeneration may initiate in the gut, examining a microbiome-brain connection in PD represents an exciting new frontier for research. Neurodegeneration in PD is believed to be caused by aggregation and/or accumulation of the prion-like protein, alpha-synuclein (alphaSyn). Disease symptoms can be modeled in mice by overexpression of human alpha-synuclein (Thy1-alphaSyn). To determine if the microbiome impacts disease, the first aim will test behavioral, cellular and functional features of disease in germ-free (gnotobiotic) Thy1-alphaSyn mice. Longitudinal analysis of disease progression will establish how gut bacteria contribute to neurodegeneration and aging. To test if changes in gut bacteria are relevant to PD, we will profile the microbiome of Thy1-alphaSyn mice using metagenomic (shotgun sequencing) and metatranscriptomic (RNAseq) analysis in the second aim. Differences between Thy1-alphaSyn and control mice may reveal specific microbes and microbial pathways that impact disease. Dopamine signaling is important for motor symptoms in PD, and the dopamine precursor L- DOPA is a mainline therapy. The final aim will employ a validated microfluidics approach to screen individual gut microbes for the potential to produce dopamine, and will test novel probiotic treatments in preclinical PD models. This project will investigate, for the first time, whether changes in gut bacteria affect the etiology of PD in mouse models. If successful, the key contribution of this project will be the transformative conceptual leap that PD may have a gut microbial origin, resulting in informed advances toward probiotic therapies for neurodegeneration.

### **Lay Summary**

**PUBLIC HEALTH RELEVANCE:** Parkinson's disease (PD) is a devastating neurodegenerative disorder that leads to motor and non-motor disabilities; despite improvements in symptomatic treatments, the etiology of PD remains unclear and there are no therapies to delay or prevent disease. The common occurrence of gastrointestinal complications and a critical role for environmental risk factors suggest that gut bacteria may contribute to PD; however, evidence for this theory is currently lacking. This project will test the innovative hypothesis that changes in the gut microbiome impact the onset and/or progression of PD in mouse models, and will apply a rational approach for uncovering novel probiotics that may revolutionize treatment options for neurodegeneration.

### **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