GBA pathway markers for Lewy body dementias

https://www.neurodegenerationresearch.eu/survey/gba-pathway-markers-for-lewy-body-dementias-2/

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Country

USA

Title of project or programme

GBA pathway markers for Lewy body dementias

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NIH (NINDS)

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30/09/2016

Total duration of award in years

5

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders|Alzheimer's disease & other dementias

Keywords

glucosylceramidase, Lewy Body Dementia, mutational status, phase II trial, Disease Progression

Research Abstract

Dysfunction of the ?-glucocerebrosidase gene (GBA) pathway is genetically, neuropathologically, and biochemically implicated in Lewy body dementias. GBA pathway-directed markers and treatments offer an opportunity for rapidly implementing proof-of-concept

trials of drugs designed to slow disease progression. A tool kit of tests is needed for biomarkers-guided go/no-go decisions that includes molecular biomarkers for target engagement, drug response, and disease progression. In Aim 1, we will determine, whether disruption of the GBA pathway in plasma and cerebrospinal fluid is specifically associated with Lewy body dementias in a large, cross-sectional study of 435 individuals with Lewy body dementias, healthy controls, and disease controls with other dementias using targeted, quantitative mass spectrometry assays for fifty pathway sphingolipids and an assay for ?-glucocerebrosidase activity. Moreover, we will explore whether quantitative or qualitative changes in the GBA pathway inform on GBA mutation status, clinical disease severity, and clinical diagnosis. In Aim 2, we will determine, whether GBA pathway markers longitudinally track disease progression in Lewy body dementias. In Aim 3, we will longitudinally collect clinical data, CSF, and blood samples of 100 patients with DLB, PDD and controls from Harvard-affiliated hospitals and expand the NINDS Parkinson’s Disease Biomarkers Program collection. These analyses will translate genetic clues into clinical trials markers. They will create the tools needed for innovative, genetics-inspired, biomarkers-guided phase II trials for Lewy body dementias and generally enrich the PDBP resource.

Lay Summary
Lewy body dementias are thought to account for up to 20% of all dementia cases. Dysfunction of the ?- glucocerebrosidase gene (GBA) pathway is genetically, neuropathologically, and biochemically implicated in Lewy body dementias. GBA pathway-directed markers are needed to rapidly implement proof-of-concept trials of drugs designed to slow disease progression.

Further information available at:

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Investments > €500k

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United States of America

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