Large Scale Biomarker Discovery and Validation for Parkinsons Disease

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Country

USA

Title of project or programme

Large Scale Biomarker Discovery and Validation for Parkinsons Disease

Source of funding information

NIH (NINDS)

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30/09/2012

Total duration of award in years

1

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords

biomarker discovery, Cerebrospinal Fluid, Parkinson Disease, Validation, Plasma

Research Abstract

DESCRIPTION (provided by applicant): Diagnosis of Parkinson’s disease (PD) is complicated by the overlap of its symptoms with those of other disorders, especially at early stages.

Additionally, clinical management of PD is hampered by a lack of objective assessment of disease progression. These factors make discovery of objective biomarkers an urgent priority, but a number of challenges have impeded their development. Although CSF levels of some PD-related proteins are altered in PD patients, none discovered so far are specific enough to differentiate between parkinsonian disorders, diagnose PD at early stages, or trace its progression. Profiling experiments have identified large numbers of potential candidates, but the development of protein-specific assays, which often depend on high-quality, well-characterized antibody sets that may not be available, presents a significant bottleneck in carrying these candidates through further development. Therefore, in this study, we propose a multi-pronged effort including a variety of complementary strategies to optimize the possibility of identifying P biomarkers. First, we will further explore the maximal utility of proteins previously observed to change in CSF in PD, by determining whether these proteins, or with post-translationally modified forms of them, perform well in disease diagnosis or monitoring progression. Second, we will expand the search for CSF biomarkers by using a newly developed peptide-based platform, which will allow us to perform high-throughput targeted discovery, followed by mass spectrometry-based measurement of specific peptide biomarkers in samples from human patients. Notably, we will make use of a unique combination of multiple large cohorts, including one in which samples are collected longitudinally, to allow independent validation and assessment of performance as progression markers of all promising candidates. Additionally, we will develop several novel techniques for biomarker discovery, including profiling based on aptamers, or based on RNA screening/sequencing. Further, we will attempt to extend the biomarker discovery process to a more easily collected sample type, plasma, by examining the performance of our best-performing candidates in plasma samples from the same cohorts. Finally, we will test the best candidate biomarkers, whether in plasma or CSF, in several cohorts selected to include an enriched population of subjects at risk for PD, in order to identify biomarkers capable of diagnosing PD at its earliest stages, when treatment is likely most effective. Importantly, each step of this process provides a novel step forward in biomarker research, providing the opportunity to improve the PD diagnostic process facilitate the search for better treatments.

Lay Summary
PUBLIC HEALTH RELEVANCE: Effective biomarkers, whether identified in CSF or plasma, will be extremely helpful to clinical diagnosis of Parkinson’s disease, following its progression a well as assessment of treatment effects.

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

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