Blood RNA biomarkers of Parkinsons disease and progressive supranuclear palsy

https://neurodegenerationresearch.eu/survey/blood-rna-biomarkers-of-parkinsons-disease-and-progressive-supranuclear-palsy/

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Country

USA

Title of project or programme

Blood RNA biomarkers of Parkinsons disease and progressive supranuclear palsy

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NIH (NIA)

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01/06/2016

Total duration of award in years

1

The project/programme is most relevant to:

Parkinson's disease

Keywords

Progressive Supranuclear Palsy, Parkinson Disease, Parkinsonian Disorders, RNA, PTPN1 gene

Research Abstract

DESCRIPTION (provided by applicant): Parkinson’s disease (PD) is the second most prevalent

neurodegenerative disease worldwide. PD is characterized by the progressive deterioration of the dopaminergic system in the substantia nigra pars compacta (SNpc). Approximately 95% of PD cases are idiopathic suggesting environmental factors and genetic susceptibility play a role in disease onset. Diagnosis of PD is currently based on clinical assessment of motor symptoms. Unfortunately, motor symptoms in PD patients are usually manifested later in the course of the disease, and by the time a patient is diagnosed, a substantial number of dopaminergic neurons are dead. Further, there is a 30% misdiagnosis between PD and atypical parkinsonian disorders (APD), in particular, with progressive supranuclear palsy (PSP). The high misdiagnosis rate observed between PD and PSP is due to the overlap in clinical symptoms and initial response to levodopa therapy in early stages of these diseases. To address these issues, we previously identified and replicated RNA biomarkers that can be used to distinguish early stage PD patients from healthy controls (HC) in whole blood samples obtained from two independent clinical studies. Specifically, 13 splice variants were useful to distinguish PD from HC and APD with 90% sensitivity and 94 % specificity. Subsequently, we identified APP, SOD2, HNF4A and PTBP1 as additional putative biomarkers in both clinical trials. The ideal diagnostic PD bio signature of the biomarkers has not yet been determined however. Eight of the original splice variants were useful to distinguish PD from APD, including PSP and multiple system atrophy (MSA) with similar diagnostic accuracy. In a separate study, we identified PTPN1 as a diagnostic biomarker for PSP. Nonetheless, the APD signature and PTPN1 have not been replicated in an independent set of samples. In the proposed studies, we will determine the diagnostic utility of these biomarkers in an additional independent cohort of participants using samples obtained from the Parkinson’s disease Biomarker Program (PDBP). This replication study is expected to identify a diagnostic PD and PSP bio signatures, which should advance the translation of these biomarkers into the clinic.

Lay Summary
PUBLIC HEALTH RELEVANCE: Diagnosis of Parkinson’s disease (PD) and progressive supranuclear palsy (PSP), both devastating neurodegenerative diseases, remains challenging and is currently based on the assessment of motor symptoms. Diagnosis of PD remains challenging and there is a high rate of misdiagnosis, reaching 30% between PD and PSP. Therefore, discovery and validation of sensitive and specific blood RNA biomarkers useful for distinguishing PD and PSP patients is expected to substantially improve the clinical management of both disorders.

Further information available at:

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Investments > €500k

Member States:
United States of America

Diseases:
Parkinson's disease & PD-related disorders

Years:
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Database Categories:
N/A

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