# Unbiased Approaches to Novel Biomarker Discovery in Parkinsons Disease

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**Principal Investigators**

CHEN-PLOTKIN, ALICE S

**Institution**

UNIVERSITY OF PENNSYLVANIA

**Contact information of lead PI**
**Country**

USA

**Title of project or programme**

Unbiased Approaches to Novel Biomarker Discovery in Parkinsons Disease

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1

**The project/programme is most relevant to:**

Parkinson's disease & PD-related disorders

**Keywords**

biomarker discovery, novel marker, Parkinson Disease, Epidermal Growth Factor, Biological Markers

**Research Abstract**
DESCRIPTION (provided by applicant): The need for well-validated, easily-accessible

biomarkers for Parkinson’s disease (PD) and endophenotypes within PD is great. Despite this need, candidate markers reported in the literature are few, and the most well-establishd biochemical biomarkers described to date in PD are cerebrospinal fluid (CSF) markers, creating a substantial barrier to widespread use. Until very recently, the search for biomarkes in PD and many other diseases was limited by the fact that a targeted approach was needed – that is, one could not find a biomarker unless there was a priori reason to believe that a particular gene/protein would be informative in the first place. In the past 10 years, however, technological advances have allowed the advent of large, unbiased screens of hundreds, if not thousands, of potential candidates, a radical change in approach pioneered in the world of genetics/genomics. We have previously used such an unbiased approach to discover, and subsequently replicate, a novel association between plasma levels of epidermal growth factor (EGF) and cognitive impairment in PD, demonstrating that low EGF levels may both correlate with and predate the onset of dementia in PD. In parallel, we hve found that low plasma Apolipoprotein A1 (ApoA1) levels may indicate increased risk for loss of dopaminergic system integrity and uncovered five potential plasma-based biomarkers correlating with rate of decline in PD. Here, we propose to build on this hands-on experience to move our findings forward in a pipeline towards clinical translation while also conducting a de novo discovery screen of 450 plasma proteins for additional biomarkers for PD and endophenotypes within PD. Embedded in our approach is an understanding that unbiased biomarker discovery methods require replication in additional cohorts of subjects, followed by validation through across-site replication of findings and investigations into biological mechanisms. Thus, our aims are: 1) To validate two previously-replicated plasma-based biomarkers in PD — determining whether plasma epidermal growth factor (EGF) levels are a biomarker for cognitive performance in PD, and whether plasma apolipoprotein A1 (ApoA1) levels are a biomarker for PD risk by evaluating their performance in additional cohorts of patients from independent clinical sites and exploring aspects of their biology and potential for clinical translation~ 2) To replicate five newly-discovered plasma-based biomarkers for rate of decline in PD — determining whether levels of AXL receptor tyrosine kinase (AXL), matrix metalloproteinase-2 (MMP-2), interleukin-7 (IL-7), EGF, and C-reactive protein (CRP) correlate with rate of PD motor decline in additional cohorts of UPenn patients, using alternative platforms for measurement~ and 3) To perform an unbiased discovery screen for plasma-based biomarkers of motor and cognitive disease progression in PD using a novel, protein-DNA-aptamer-based technology for simultaneous measurement of 450 plasma proteins.

**Lay Summary**
PUBLIC HEALTH RELEVANCE: Currently, the need for biomarkers in PD is great, but the field may be reaching the limits of what can be accomplished through a targeted approach to biomarker discovery. The studies proposed here may move two already-replicated biomarkers within striking distance of clinical translation, while promising to uncover additional, earlier-stge leads through unbiased discovery. As such, they have high potential to meet the goal of this RFA by developing practical, plasma-based biomarkers to improve the efficiency and outcome of Phase II clinical trials in PD.

**Further information available at:**

**Types:**
Investments > €500k

**Member States:**
United States of America

**Diseases:**
Parkinson's disease & PD-related disorders

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2016

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