

Parkinson's Research Program

Strategic Plan

INTRODUCTION

The Congressionally Directed Medical Research Programs (CDMRP) represents a unique partnership among the U.S. Congress, the military, and the public to fund innovative and impactful medical research in targeted program areas. In 2015, an ad hoc committee of the National Academies of Sciences, Engineering, and Medicine was assembled to evaluate the CDMRP's two-tier review process and its coordination of research priorities with the National Institutes of Health (NIH) and the Department of Veterans Affairs (VA). As part of their final report,¹ the committee recommended that each CDMRP program "... develop a strategic plan that identifies and evaluates research foci, benchmarks for success, and investment opportunities for 3-5 years into the future," and that these strategic plans "should specify the mission of the program, coordination activities with other organizations, research priorities, how those priorities will be addressed by future award mechanisms, how research outcomes will be tracked, and how outcomes will inform future research initiatives."

In response to these recommendations, this document presents the current strategy for the CDMRP's Parkinson's Research Program (PRP). The PRP Strategic Plan identifies the high-impact research goals most important to its stakeholders while providing a framework that is adaptable to changes in the medical research environment to address those goals. This plan has been formulated to provide greater clarity of the program's goals over time to the public and other stakeholders. Funding for the PRP is Congressionally appropriated on an annual basis; therefore, there is no guarantee of future funding. The PRP Strategic Plan will be reviewed during the program's annual Vision Setting meeting and updated as necessary.

PRP BACKGROUND AND OVERVIEW

The PRP is funded under the Neurotoxin Exposure Treatment Parkinson's Research Program appropriation. The appropriation was established by a Congressional Special Interest addition to the fiscal year 1997 (FY97) appropriation bill in October 1996. The program aims to provide support for research of exceptional scientific merit leading to an understanding of the cause, prevention, and treatment of Parkinson's disease (PD). Funded projects examine neurodegenerative mechanisms and compensatory effects that compromise motor, autonomic, and cognitive systems. Understanding these mechanisms and effects is the first step toward development of new treatments.

PRP VISION: To stop Parkinson's disease by funding research through a partnership of scientists and consumers

PRP MISSION: Support research to understand, prevent, diagnose, and treat Parkinson's disease in patients, including Service members and Veterans

FUNDING HISTORY

The PRP received funding of \$420.75 million in total appropriations from FY97 to FY17. Since its inception, the PRP has been funded at various amounts, as shown in **Figure 1**.



Figure 1. PRP Funding per Fiscal Year

RESEARCH PORTFOLIO

The PRP has taken a targeted approach to investing over its 20-year history. In recent years, the program has identified focus areas with the potential for the greatest impact for PD patients. From 2015 to 2017, focus areas for the program have been defined to drive understanding of the mechanisms of the disease and identification of disease-related biomarkers, as well as to increase understanding of neuroplasticity in the brain.

Biomarker research has received the most funding among the research areas in the PRP portfolio, as shown in **Figure 2**. The other major areas of research in the portfolio are pathogenesis, signal transduction, and therapies.



Figure 2. Dollars Invested per Focus Area (FY10-FY17)



RESEARCH AND FUNDING ENVIRONMENT

Today's medical research environment is dynamic. New research data sets are being created and made available to researchers at an ever-faster rate, and new technologies are emerging that will enable research that is impossible today. Funding for research comes from multiple sources and through a variety of programs. Many are funded by the government through the NIH, VA, CDMRP, and other Department of Defense organizations (**Figure 3**). In addition to the government, there are non-governmental organizations that are focused on disease-specific areas. The PRP must fit within this environment and effectively respond to changes in it to maximize the value and impact of PRP-funded research.





The PRP reviewed the research environment in the following three areas:

TRANSFORMATIONAL RESEARCH AND DATA

Ongoing research studies and initiatives that have the potential to make transformative progress toward understanding, treating, and curing PD are important for the program to monitor. The availability of new data or significant findings from groundbreaking studies could impact the direction of the PRP. New scientific technology and discoveries will be reviewed on a yearly basis to determine whether strategic adjustments are needed. Five areas of transformational research and data were identified as having particular importance to the PRP's mission: the Brain Initiative, the Million Veterans Study, the U.S. Department of Health and Human Services Tox 21 Program, the Parkinson's Progression Marker Initiative, and the NIH Parkinson's Biomarker Program.

EVOLVING TECHNOLOGIES

Technology advancements provide new research methods or enable the creation of data sets upon which new research can be conducted. The PRP identified a number of technology advances that currently provide or can provide significant new tools to the PRP research community and offer new avenues of research to address important questions. Five technological approaches were identified as relevant to the PRP's strategy and for annual review to determine whether strategic adjustments are needed: Human Cell Models, Whole Genome Sequencing, Microbiome Analysis, Novel Approaches to Analyzing Topology, and Alpha Synuclein Imaging/Marker.

ALIGNED/RELATED RESEARCH PROGRAMS

In order to maximize the PRP's ability to fill gaps and leverage the findings of others, it is important to understand the focus and successes of other programs funding PD research. The PRP will monitor and work closely with other funders like the National Institute of Neurological Disorders and Stroke programs; Morris K. Udall Centers for Excellence in Parkinson's Disease Research; Michael J. Fox Foundation; VA Centers; Parkinson's Disease Research, Education, and Clinical Centers; and American Parkinson Disease Association.

3



STRATEGIC DIRECTION

Considering the current state of PD research, the funding environment of both federal and private organizations, and the needs of the PD community, the PRP created its strategic plan.

The PRP Strategic Plan identifies the high-impact research goals with the potential to address major knowledge gaps and underfunded areas of research. The PRP believes that investing in strategic research goals will advance the field of PD research and benefit Service members, Veterans, and the general public.

STRATEGIC GOALS / PRIORITIES

LONG-TERM STRATEGIC GOALS – FY18 TO FY22

The PRP identified major research questions considered critical to advance potential treatments and cures for PD. The questions were prioritized to facilitate execution; the five questions below are the long-term priorities for the PRP.

What impact does the gut biome have on alpha-synuclein and other development and progression aspects of PD?

The gut biome is a vital, evolving, and understudied risk factor in PD. Dietary and environmental exposures have been shown to alter the gut microbiome. The gut and brain communicate through the nervous system, and the gut microbes also aids in immune response. Therefore, it is hypothesized that alterations in the microbiome may increase an individual's susceptibility to develop PD. Addressing this question has potential implications for Warfighters who are susceptible to both environmental and dietary changes, especially in the field. New discoveries could lead to non-drug strategies that may reduce risk and be potentially therapeutic for Service members, Veterans, and the general public.

What gene-environment interactions impact the development and progression of PD?

There are current challenges that need to be overcome in defining gene-environment effects, which are already a proposed risk factor for PD that is directly relevant to the military. Military Service members have high exposure to a variety of environmental hazards (e.g., herbicides and pesticides) that have been shown to alter the genome. Identifying the relationship between environmental hazards and the epigenetic changes leading to PD development is an understudied research area that could lead to novel therapeutics.

What are the mechanisms of the cognitive and psychiatric symptoms of PD?

The mechanisms of the cognitive and psychiatric symptoms of PD are an understudied research area with a potentially high impact. It is an extremely important topic from the patient perspective. Epidemiology, diagnosis, and management of common cognitive and psychiatric symptoms such as depression, anxiety, apathy, fatigue, and psychotic symptoms are areas that are understudied with respect to their relationship to PD.

What are the biological mechanisms of impact from exercise and other lifestyle modifications on neurodegeneration in PD?

Exercise and other lifestyle behaviors are modifiable risk factors with strong empirical data. There is a lack of biological mechanistic data, and the clinical evidence-based data are poorly defined to support lifestyle modifications and their benefit to those affected by PD.

How does traumatic brain injury (TBI) influence risk for PD?

The relationship between TBI and PD has a direct military relevance. Currently, there is difficulty conducting research on this relationship because of the span years between incurring a TBI and the diagnosis of PD. TBI is a hypothesized risk factor for PD that needs to be understood mechanistically. There are statistical correlations between Veterans with TBI and later diagnosis of PD. Increased research in the TBI-PD relationship will aid in preventative treatments and early onset diagnosis.

NEAR-TERM STRATEGIC GOALS – FY18 FOCUS AREAS

In the near term, the PRP will focus on addressing specific elements from three of the long-term strategic goals. These near-term focus areas are as follows:

- · Mechanisms of cognitive and psychiatric symptoms of PD
- Genetic stratification of suspected environment factors that are quantifiable regarding the risk of developing PD
- · Biological mechanisms of the impact from exercise on neurodegeneration in PD



INVESTMENT STRATEGY

NEAR-TERM INVESTMENT STRATEGY (1-3 YEARS)

The PRP seeks to invest in research through award mechanisms that emphasize high-impact projects that have the potential to make significant progress in the PD research field. Two award mechanisms are summarized below.

- Early Investigator Research Award
 - o Supports early-career investigators who have innovative, high-impact ideas or new technologies applicable to PD research and/or patient care.
 - o Principal Investigators must have a designated mentor who is an experienced PD researcher.
 - Investigator-Initiated Research Award
 - o Supports highly rigorous, high-impact research projects that have the potential to make an important contribution to PD research and/or patient care.
 - o The potential impact of research may be near-term or long-term, but it must be significant and go beyond an incremental advancement.

MEDIUM- TO LONGER-TERM INVESTMENT STRATEGY (4-5 YEARS)

Over this planning horizon, the PRP will consider projects across the research continuum and may consider offering other award mechanisms to make progress toward ending PD. The PRP envisions future research projects that will foster collaborations across industry, academia, and other research organizations.

The PRP will remain open to a wide range of award mechanisms to support both its strategic goals and its interest in funding highimpact projects that will benefit anyone with or at risk for PD.

MEASURING PROGRESS

The PRP will measure its success in the near term, 1 to 3 years (FY18-FY20), based on successful investments in the focus areas that have been identified as being important to the PRP strategy, as well as the outcomes of the funded research. In the longer-term, 4 to 5 years (FY21-FY22), success will be similarly evaluated based on contributions to the scientific community, follow-up research linked to PRP-funded projects, and the impact of PRP-funded projects on clinical treatments and interventions.

MEASURES OF SUCCESS

- Number of applications received and funded within each of the PRP focus areas
- Number of investigators that stay in PD research after the award
- Contributions to the scientific community, including the following:
 - o Publications
 - o Abstracts
 - o Presentations
- · Significant conceptual or technological advances (big discoveries) resulting from funded research
- · Subsequent downstream funding of ideas or concepts funded by the PRP
- Development of tools or methodologies from research funded by the PRP

REFERENCES

1. *Evaluation of the Congressionally Directed Medical Research Programs Review Process*. 2016. The National Academies of Sciences, Engineering, and Medicine. The National Academies Press. Washington, DC.