



Parkinson's Research Program

Strategic Plan

INTRODUCTION

The Congressionally Directed Medical Research Programs funds innovative and impactful biomedical research from basic science through clinical trials to transform health care for Service Members, their Families, Veterans and the American public.

The CDMRP Program Managers, in collaboration with stakeholders, develop formal strategic plans. The strategic plan includes program-specific research priorities, objectives, short- and long-term goals, investment strategies and requirements for program evaluation.

PRP BACKGROUND AND OVERVIEW

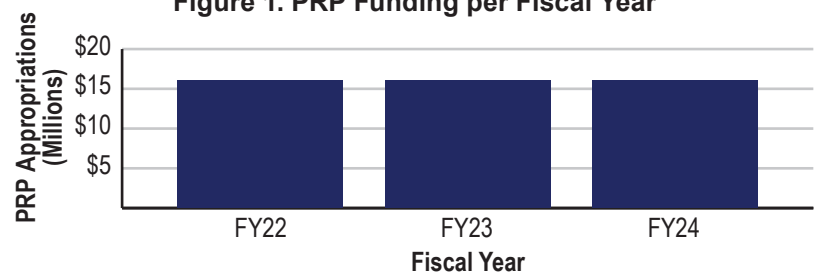
Between FY97-FY21, the CDMRP funded Parkinson's disease research through the Neurotoxin Exposure Treatment Parkinson's program. In FY22, Congress transitioned the NETP to the PRP and broadened the research from neurotoxin exposure treatment PD research to all types of PD research. The program aims to provide support for research of exceptional scientific merit leading to an understanding of the cause, prevention, and treatment of 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.

VISION: Improve the health and lives of people with Parkinson's disease through innovative, clinically meaningful treatments.

MISSION: To support high impact Parkinson's research that alters disease progression, improves disease symptoms, and develops treatments that benefit Service Members and their Families, Veterans, and the general public.

FUNDING HISTORY

Figure 1. PRP Funding per Fiscal Year

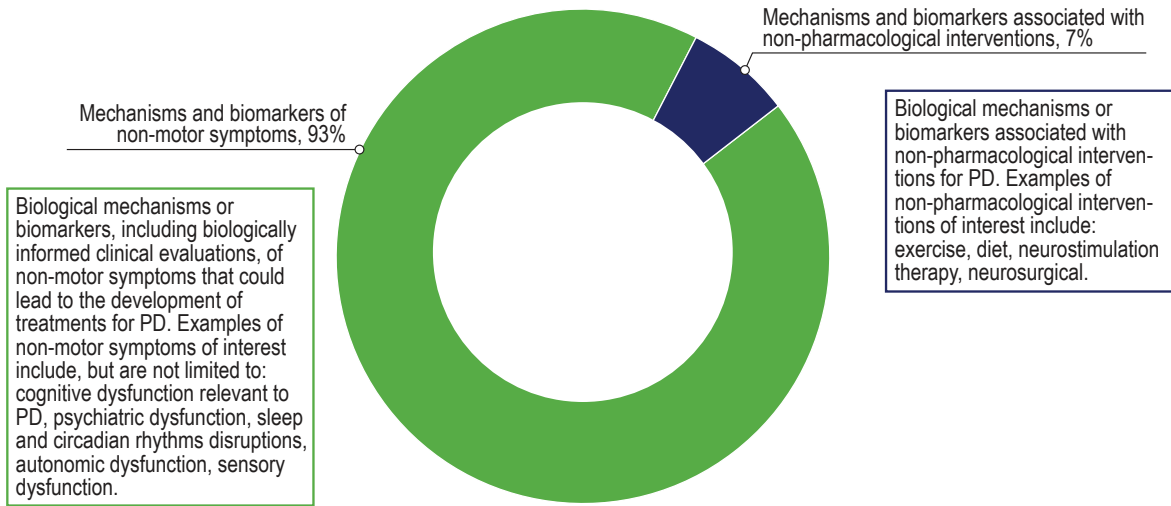




RESEARCH PORTFOLIO

CDMRP is currently managing PRP research as well as Parkinson's research funded in the NETP and Toxic Exposures Research Program (TERP). The CDMRP full portfolio includes unique approaches toward Parkinson's research and contributes to the overall research landscape. The program identified two focus areas with the potential for the greatest impact for PD patients. The following figure represents FY22-FY23 investments by focus area.

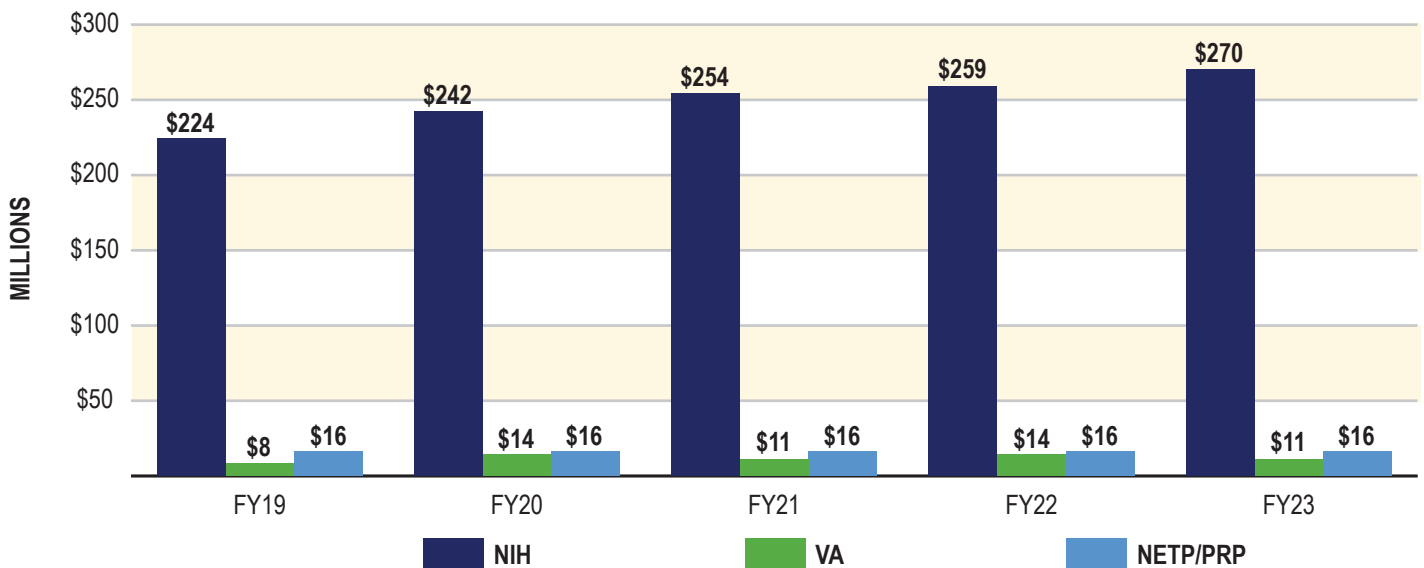
Figure 2. FY22 - FY23 Dollars Invested by Focus Area



RESEARCH AND FUNDING ENVIRONMENT

Today's medical research environment is dynamic. New research data sets are 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. The federal government funds a variety of programs through the CDMRP, National Institutes of Health, Veterans Affairs, and other DOD organizations. **(Figure 3)**. Additionally, there are non-governmental organizations that focus on disease-specific areas. The PRP must fit within this environment and effectively respond to changes in the environment to maximize the value and impact of PRP-funded research.

Figure 3. Federal Funding of PD Research (FY19-FY23)





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. Program panels convene once a year to review new scientific technology and discoveries and determine any strategic adjustments. Five areas of transformational research and data have 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 which scientists can use to conduct new research. The PRP identified a number of technological advancements that currently provide or can provide significant new tools to the PRP research community and offer new avenues of research to address important questions. The program identified five technological approaches as relevant to the PRP's strategy for annual review and adjustment as 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 monitors and works closely with other funding agencies like the National Institute of Neurological Disorders and Stroke programs; Morris K. Udall Centers for Excellence in Parkinson's Disease Research; The Michael J. Fox Foundation for Parkinson's Research; VA medical centers; Parkinson's Disease Research, Education, and Clinical Centers; and American Parkinson Disease Association.

STRATEGIC DIRECTION

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

The PRP Strategic Plan identifies 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, their Families, Veterans, and the general public.

LONG-TERM STRATEGIC GOALS – FY24-FY28

The PRP looks to support high-impact research that leads to a better understanding of PD to inform novel treatments. The following key areas are of interest:

Understand the neurobiological underpinnings of the cognitive, psychiatric, and other non-motor 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.

Understand the biological mechanisms or biomarkers of motor symptoms

The mechanisms of the motor symptoms of PD are a critical research area with a potentially high impact. By increasing the understanding of the biological mechanisms and biomarkers of motor symptoms, the program is establishing the foundation that should lead to the development of new treatments for PD.

Develop interventions that address unmet medical needs of PD

The program seeks intervention research that will directly improve the treatments for people with PD.

Delineate how gene-environmental interactions impact the development and progression of PD

There are current challenges to defining gene-environment effects, a known risk factor for PD development in the military. Research shows that Service Members have high exposure to a variety of environmental hazards that alter the genome, like herbicides and pesticides.¹ 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.



Determine mechanisms of dopamine refractory motor symptoms and treatment-associated adverse events of PD

A change or loss of motor function such as balance and coordination, muscle stiffness, or bodily tremors is one of the first observed symptoms of PD. The body relies on neurotransmitters like dopamine to regulate motor function; without a steady supply of dopamine, the body experiences a loss of these functions. Understanding the mechanism of dopamine refractory motor symptoms is important to retain normal motor function for patients. Treatments for these symptoms are available, but often come with unfavorable changes in health such as nausea, involuntary movement, and neurobiological symptoms. Understanding the mechanism behind the production of these symptoms post-treatment can provide insight in improving treatment options and treatment side effects for patients.

Expand PD research capacity through an investment in early career investigators

There is a great need for additional PD researchers to better address many understudied PD research areas. Since the transition from the NETP program to the PRP, the program has broadened the base of PD research with the continuation of the Early Investigator Research Award.

NEAR-TERM GOALS – FY24 FOCUS AREAS

- Identify biological mechanisms or biomarkers (e.g. fluid, imaging, tissue, devices) that could lead to the development of treatments for unmet medical needs of patients with PD. Examples of unmet medical needs of interest include, but are not limited to:
 - Non-motor
 - Cognitive
 - Psychiatric
 - Sleep and circadian rhythms disruptions
 - Autonomic
 - Motor
 - Tremor
 - Gait and balance
 - Dystonia
 - Dyskinesia
- Discover interventions that address unmet medical needs of patients with PD, including research involving both clinical and preclinical models. Examples of interventions of interest include, but are not limited to:
 - Pharmacological
 - Biologicals
 - Non-pharmacological
 - Surgical
 - Non-surgical devices
 - Non-invasive central nervous system stimulation

In the near term, the PRP will focus on addressing four of the six long-term strategic goals.

	Understand the neurobiological underpinnings of the cognitive, psychiatric, and other non-motor symptoms of PD	Understand the biological mechanisms or biomarkers of motor symptoms	Develop interventions that address unmet medical needs of PD	Delineate how gene-environmental interactions impact the development and progression of PD	Determine mechanisms of dopamine refractory motor symptoms and treatment-associated adverse events of PD	Expand PD research capacity through an investment in early career investigators
Long Term						
Near Term	Biological mechanisms or biomarkers (e.g. fluid, imaging, tissue, devices) of unmet medical needs that could lead to the development of treatments for non-motor symptoms of PD.	Biological mechanisms or biomarkers (e.g. fluid, imaging, tissue, devices) of unmet medical needs that could lead to the development of treatments for motor symptoms of PD.	Interventions that address unmet medical needs of PD that include both clinical and preclinical models.			The EIRA is expanding PD research capacity for early investigators.

INVESTMENT STRATEGY

NEAR-TERM INVESTMENT STRATEGY, 1-3 YEARS

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



- Early Investigator Research Award
 - Supports research opportunities for investigators in the early stages of their careers under the guidance of one or two designated Mentor(s) who have experience/expertise in PD research.
 - The Early Investigator is considered the Principal Investigator of the application and must exhibit strong potential for, and commitment to, pursuing a career as an investigator at the forefront of PD research.
- Investigator-Initiated Research Award
 - Supports highly rigorous, multidisciplinary, high-impact research impact projects that have the potential to make an important contribution to PD research.
 - This award mechanism supports the full spectrum of research from basic science through clinical research.

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 high-impact projects that will benefit anyone with or at risk for PD.

MEASURING PROGRESS

The PRP will measure its success in the near term, FY24-FY25, based on successful investments in the identified focus areas important to the PRP strategy and the outcomes of the funded research. In the longer term, 4-5 years, the program will evaluate success by considering 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 PROGRESS

- Number of applications received and funded within each of the PRP focus areas
- Number of investigators that stay in PD research after their PRP award ends
- Contributions to the scientific community, including the following:
 - Publications
 - Abstracts
 - Presentations
- Significant conceptual or technological advances
 - Altering disease progression
 - Improving disease symptoms
 - Developing novel treatments
- Subsequent downstream funding of ideas or concepts funded by the PRP
 - Altering disease progression
 - Improving disease symptoms
 - Developing novel treatments
- Development of tools or methodologies from research funded by the PRP

REFERENCES

1. Parkinson's Foundation. 2022. "Environmental Factors." <https://www.parkinson.org/understanding-parkinsons/causes/environmental-factors>.