CDMRP
Department of Defense

# Prostate Cancer 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 Prostate Cancer Research Program (PCRP). The PCRP 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 PCRP is Congressionally appropriated on an annual basis; therefore, there is no guarantee of future funding. The PCRP Strategic Plan will be reviewed during the program's annual Vision Setting meeting and updated as necessary.

### PCRP BACKGROUND AND OVERVIEW

In the United States, prostate cancer is the second most commonly diagnosed cancer in men and the second leading cause of death in men after lung cancer. An estimated 164,690 men in the United States will be diagnosed with prostate cancer in 2018, and an estimated 29,430 men will die from the disease.[2] Prostate cancer is a real threat to U.S. Service members, as 80% of the active duty population are men. According to the Defense Health Agency (DHA) Medical Surveillance Monthly Report (MSMR),[3] 8,973 new cancers were diagnosed among active duty members of the U.S. Armed Forces between 2005 and 2014, and of these, 1,046 (11.7%) were prostate cancer diagnoses. Prostate cancer incidence, morbidity, and mortality rates vary markedly by race and ethnicity, with African American (AA) men experiencing the highest rates in the United States.[4] Similarly, the DHA MSMR reported that, among active duty military personnel, prostate cancer occurred 2.5 times more frequently in AA Service members compared to Caucasian American (CA) Service members. The Prostate Cancer Foundation (PCF) estimates that more than 4 million American men are currently living with prostate cancer.[5]

The PCRP was established in 1997 through the efforts of dedicated and energized prostate cancer advocates and supporters who worked to realize additional federal research funds for prostate cancer. Initially funded by Joint Appropriations Bill 104-863, the PCRP was directed to promote innovative ideas and technology through both basic and clinical science in an effort to develop more effective therapies for patients in all stages of the disease. After consultation with other national prostate cancer research funding agencies (e.g., the National Cancer Institute [NCI], American Cancer Society [ACS], and PCF), the PCRP was designed to avoid overlap and target underrepresented avenues of research and novel applications of existing techniques.

Throughout its 22-year history, the vision, mission, and annual investment strategy of the PCRP have been shaped by recommendations from a Programmatic Panel of leading scientists, clinicians, and consumer advocates in the prostate cancer community. The CDMRP uses a two-tier review process for proposal evaluation. The first tier is a scientific peer review of proposals, measured against established criteria for determining their scientific merit. The second tier is a programmatic review that is conducted by the Programmatic Panel to compare applications and make funding recommendations based on scientific merit, portfolio balance, and relevance to the overall program goals.

This unique partnership among Congress, the Department of Defense (DoD), prostate cancer survivors, clinicians, and scientists has changed the landscape of prostate cancer research and energized the research community to conduct high-risk investigations that are more collaborative, innovative, and impactful, with the ultimate goal of conquering prostate cancer.

**VISION:** Conquer prostate cancer

**MISSION:** Fund research that will lead to the elimination of death from prostate cancer and enhance the well-being of Service members, Veterans, and all men experiencing the impact of the disease

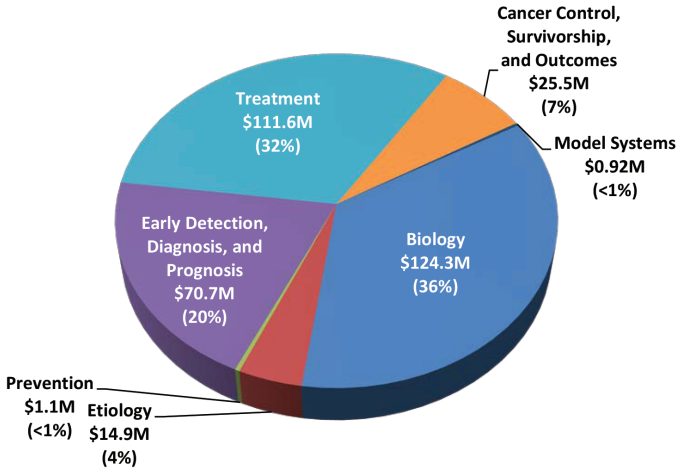
## FUNDING HISTORY

In 1997, $45 million (M) was appropriated to the DoD to conduct research specifically focused on prostate cancer. Since that initial appropriation, the PCRP has received Congressional appropriations totaling $1.72 billion (B), including $100M in fiscal year 2018 (FY18) to conduct research in prostate cancer.

## RESEARCH PORTFOLIO AND RESEARCH ACCOMPLISHMENTS

From FY97 through FY16, the PCRP received 17,743 applications and funded 3,158 awards totaling $1.32B. The research supported by the PCRP has historically been focused on better understanding the biology of prostate cancer and finding better ways to detect, diagnose, and treat men that develop the disease. Figure 1 depicts the distribution of PCRP-funded research from FY12 through FY16, as defined by the Common Scientific Outline (CSO) coding system, which is used by public and private organizations in the United States, United Kingdom, and Canada to describe research projects (https://www.icrpartnership.org/cso).

**Figure 1. PCRP-Funded Research by CSO Code, FY12-FY16**




### PCRP-Supported Research Resources

Part of the PCRP's investment has been to support the infrastructure necessary to develop several multi-institutional consortia that foster shared resources and collaborative projects to address the critical unmet needs of the prostate cancer research community. Leveraging these resources by the broader scientific community has led to significant achievements for prostate cancer research and patients, and the PCRP continues to encourage the research community to utilize these resources to their fullest extent to further enhance and facilitate the translation of research from bench to bedside.

*The North Carolina-Louisiana Prostate Cancer Project (PCaP)*

Initiated in FY02 with a PCRP investment of $14.1M, the PCaP represents the largest population-based study of newly diagnosed prostate cancer in AA and CA men ever conducted, with 2,256 participants. The study collected a significant amount of personal and medical information (e.g., income, health insurance coverage, treatments, and quality of life) at the time of initial diagnosis and 4 years after diagnosis. In addition, the PCaP collected a variety of biological samples from participants, including prostate cancer tissue, blood, and urine; these samples are now maintained in a large repository and continue to be used to investigate biological factors that contribute to prostate cancer health disparities. Additional information can be found at https://pcap.bioinf.unc.edu/.

*The Prostate Cancer Clinical Trials Consortium (PCCTC)*

The PCCTC was established in FY05 through the collective efforts of the PCRP and the PCF to facilitate rapid execution of collaborative Phase I or II clinical trials of promising new therapeutic agents or approaches for the management or treatment of prostate cancer. The PCCTC employs a team-based approach to more efficiently accrue patients to accelerate the development of promising drug candidates to Phase III clinical trials. The PCCTC now includes 10 PCRP-funded and 22 affiliated clinical research

sites across the United States and has been incorporated as a limited liability company. Through PCRP funding in the amount of $59.2M, centralized management of research activities, rational selection of investigational agents, and collaborative trial designs have resulted in the treatment of more than 7,400 prostate cancer patients in 214 clinical trials; advancement of 12 therapeutic candidates to Phase III studies; and approval by the U.S. Food and Drug Administration (FDA) of three treatments for prostate cancer patients. An interactive storyboard detailing the achievements of the PCCTC can be found through the CDMRP website (http://cdmrp.army.mil/pcrp_timeline/timeline), and additional information can be found at http://pcctc.org/.

*The Prostate Cancer Biorepository Network (PCBN)*
The PCBN was established in FY09 to provide infrastructure support for the development and maintenance of a prostate cancer biorepository through a collaborative network across multiple institutions. Through an initial PCRP investment of $2.59M, this network was tasked with facilitating the collection, processing, annotation, storage, and distribution of high-quality human prostate cancer biospecimens to prostate cancer investigators in a systematic, reproducible fashion, ultimately assuring researchers that PCBN-supplied samples are of the highest quality to address important questions in prostate cancer research. The PCBN has distributed over 3,000 de-identified patient samples to 83 investigators around the world, resulting in 39 manuscripts published in highly respected journals. Additional information can be found at http://prostatebiorepository.org/.

## PCRP-Supported Research Accomplishments

PCRP-funded projects have resulted in 8,600+ publications in highly respected scientific journals and 700+ patents, patent applications, and invention reports. In addition, the PCRP has contributed to the following breakthroughs in treatment, diagnostics and imaging, and molecular classification and subtyping:

***Treatment***

- Xtandi® (enzalutamide) – Anti-androgen therapy for the treatment of men with castration-resistant prostate cancer (CRPC)
- ZYTIGA® (abiraterone acetate) – Anti-androgen therapy for the treatment of men with metastatic CRPC
- Erleada® (apalutamide) – Anti-androgen therapy for the treatment of men with non metastatic CRPC
- XGEVA® (denosumab) – Monoclonal antibody therapy for the treatment of bone-related events in advanced prostate cancer; also FDA-approved as Prolia® for the prevention of treatment-induced bone loss
- EPI-506 – First and only small molecule inhibitor targeting the N-terminal domain of the androgen receptor
- pTVG-HP – DNA vaccine encoding prostatic acid phosphatase (PAP) for the treatment of men with non metastatic prostate cancer to inhibit disease recurrence
- Gamitrinib – First-in-class small molecular inhibitor of Hsp90 for the treatment of men with advanced castration-resistant and metastatic prostate cancer

***Diagnostics and Imaging***

- Elekta Synergy® – Computed tomography (CT) imaging system that pinpoints the exact position of the prostate to deliver high doses of radiation exclusively to the tumor
- Magnetic resonance imaging (MRI)-based treatment planning protocol for intensity-modulated radiation therapy (IMRT) that specifically targets prostate tumor tissue and avoids normal tissues
- Restricted spectrum imaging (RSI), a non-invasive MRI technique for detecting and distinguishing aggressive from indolent prostate cancer that is currently under investigation for detection of early metastatic disease and response to radiotherapy
- First-generation anti-prostate stem cell antigen (PSCA) radiolabeled minibody designed for optical detection of PSCA-expressing prostate cancers by positron emission tomography (PET) imaging, with an added potential as a targeted therapy

***Molecular Classification and Subtyping***

- NuSAP1 – A prognostic marker for early-stage prostate cancer that is now part of the Prolaris® and Decipher® commercial assays
- Oncotype IQ AR-V7 Nucleus Detect Test – A liquid biopsy assay that measures androgen receptor splice variant-7 (AR-V7) in circulating tumor cells and can help predict patient response to certain therapies
- 3BHSD1 – A gain-of-function mutation that was discovered to contribute to prostate cancer resistance to androgen deprivation therapy and is currently under development as a prognostic marker for predicting treatment response
- Microsatellite instability detection by next-generation sequencing (mSINGS) – A method for detecting microsatellite instability for prognosis and treatment of advanced prostate cancer

## 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 a variety of sources through a variety of programs. Many are funded by the government through the NIH, VA, CDMRP, and other DoD organizations, as well as non-government organizations focused on disease-specific areas. The PCRP must fit within this environment and effectively respond to changes in it to maximize the value and impact of PCRP-funded research.

The PCRP will continue to monitor and consider significant areas of crosscutting research, major studies, data set developments, and/or technology advances that could be important to PCRP-funded research, including the following:

- **All of Us Research Program**: Initiated and funded by the NIH, this program will gather large amounts of personal data and information from at least one million individuals in the United States, with the goal of developing more effective ways to treat disease, including cancer. This information can then be used to identify commonalities in lifestyle, environment, and biology that may contribute to prostate cancer incidence and mortality rates.
- **Million Veterans Program**: Funded by the VA Office of Research and Development (ORD), this program is building one of the world's largest medical databases of blood samples and health information from one million Veterans. This resource could be used to study a variety of diseases, including prostate cancer, and the information generated may help identify risk factors or differences in prostate cancer incidence and mortality that are specific to the military population.
- **Metastatic Prostate Cancer Project**: This nationwide, genomic research study plans to generate a comprehensive database of advanced prostate cancer treatment results based on the genetics of individual men and their tumors. This information is intended to be shared with the research community and could help determine which future treatments are pursued for advanced metastatic prostate cancer.
- **IRONMAN**: This international registry is focused on collecting information from 5,000 men with advanced prostate cancer from nine countries and ultimately aims to use the information collected to develop a better understanding of what causes prostate cancer, how to stop or slow disease progression, and how to provide the best possible care to enable men to live the best quality of life possible.

The PCRP is also cognizant of the impacts that technological advancements will have in both the prostate cancer research and patient communities and will continue to monitor the evolution of technologies including the following:

- Advances in cell therapy
- Artificial intelligence and machine learning
- Genomic analysis and improved turnaround times for sequencing and proteomics
- Improved antibody production for diagnosis and treatment
- Improved molecular imaging
- Liquid biopsy
- Radionuclides for targeted therapy
- Single cell technology

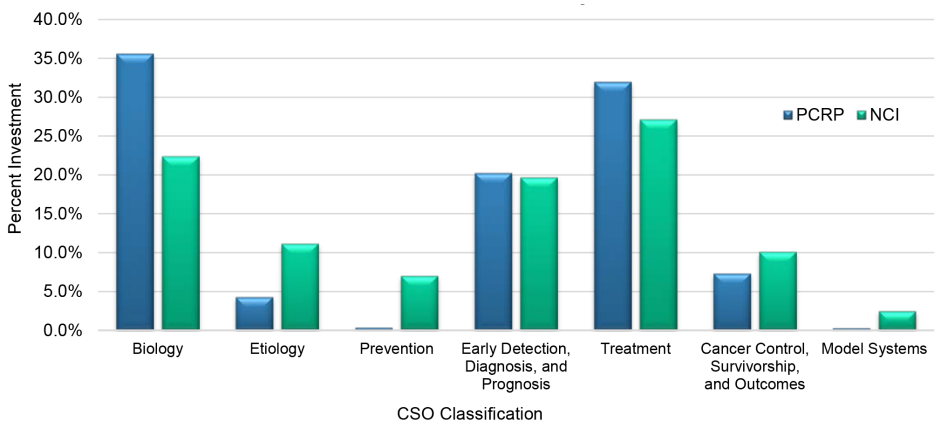
### RESEARCH FUNDING LANDSCAPE

In order to fund research of the highest scientific merit without duplicating the efforts of other funding agencies, the PCRP will continue to closely monitor other ongoing efforts in prostate cancer research. While not all inclusive, the primary agencies funding prostate cancer research include the following:

- ACS
- Movember Foundation
- NIH/NCI
- Patient-Centered Outcomes Research Institute (PCORI)
- PCF
- VA

From FY12-FY16, the NIH/NCI funded $1.18B in new extramural research projects related to prostate cancer, as reported on the NCI Funded Research Portfolio website (https://fundedresearch.cancer.gov/nciportfolio/). As shown in Figure 2, during this 5-year period, the PCRP invested mainly in biology (36%) and treatment (32%), while the NCI invested heavily in treatment (27%), biology (22%), and early detection, diagnosis, and prognosis (20%).

**Figure 2. Prostate Cancer Research Investment by CSO Code, FY12-FY16**




## STRATEGIC DIRECTION

Considering the major accomplishments resulting from PCRP-funded research and the priority research areas funded by other federal and non-federal organizations, the PCRP remains focused on addressing the knowledge, research, and clinical gaps that continue to make prostate cancer a global health issue.

The overall goal of the PCRP Strategic Plan is to establish a strategy for funding innovative and impactful ideas that will ultimately lead to the elimination of death from prostate cancer. It is expected that the outcomes of this research program will benefit Service members, Veterans, and the general public, all of whom are affected by and/or at risk for prostate cancer.

The PCRP has developed four overarching strategic goals that are critical to providing further advancements that will impact current and future prostate cancer patients. These FY18 Strategic Goals demonstrate a shift from the priorities of the program in recent years, resulting from new challenges currently facing prostate cancer disease management, including the development of resistance to prostate cancer therapies and the increased presentation of more advanced disease due to the decline in prostate-specific antigen (PSA) screenings. The funding flexibility offered by the CDMRP enables the Programmatic Panel to make recommendations on defined research topics and on projects for funding that directly address the PCRP's priority research areas. The FY18 PCRP Strategic Goals, which were developed based on recommendations from the Programmatic Panel, are described below in no particular order.

### STRATEGIC GOAL 1: DEVELOP TREATMENTS THAT IMPROVE OUTCOMES FOR MEN WITH LETHAL PROSTATE CANCER

A variety of treatment options are available for men facing a diagnosis of prostate cancer; however, the ACS estimates that, despite these treatment options, 29,430 men will die from prostate cancer in 2018. There are various reasons that deaths occur, despite there being a substantial number of treatment options. First, not all men have a positive response to the available treatments. For those patients that do respond positively to treatment, the disease takes longer to progress, but the delayed progression may only be measured in a few months. In many cases, the prostate cancer cells have already metastasized or stop responding to current treatments, leading these men to seek other treatment options to stop further disease progression and eventual lethality. It is the goal of the PCRP to invest in research to develop novel treatments for men with lethal prostate cancer that will far exceed the survival rates for currently available therapies and thereby ultimately improve the outcome for those patients that need better treatment options.

### STRATEGIC GOAL 2: REDUCE LETHAL PROSTATE CANCER IN AFRICAN AMERICANS, VETERANS, AND OTHER HIGH-RISK POPULATIONS

According to the ACS, approximately 11% of all men are expected to be diagnosed with prostate cancer in their lifetime. But certain populations are disproportionately affected by prostate cancer and have a higher risk of developing and/or succumbing to the disease. AA men are more than twice as likely to be diagnosed with prostate cancer and have a higher risk of dying from it.[6] Active duty Service members and Veterans have also been shown to have a higher rate of diagnosis compared to the general civilian population, which affects military readiness and places a burden on the Military Health System. While it is unclear whether the cause for these disparities are due to biological, socioeconomic, geographic, cultural, or other factors, these disparities are not well understood, and the knowledge gathered to date has not effectively reduced these disparities. The PCRP will focus research efforts on reducing lethal prostate cancer in high-risk populations, including, but not limited to, AA men and Veterans. Knowledge gained and advancements made from PCRP-funded research in these areas will also benefit the broader population of men at risk for prostate cancer and could create an opportunity for global collaboration with direct military and Veteran relevance. The PCRP has made prior investments in research resources such as the PCaP and PCBN data and sample repositories, which researchers are encouraged to leverage.

### STRATEGIC GOAL 3: DEFINE THE BIOLOGY OF LETHAL PROSTATE CANCER TO REDUCE DEATH

For men whose disease remains localized and who are successfully treated, the 5-year survival rate is close to 100%.[7] But for the greater than 10% of men whose disease is lethal, better detection methods and treatment options are urgently needed. A better understanding of the underlying biology of lethal prostate cancer must be investigated in order to identify new options for detection and treatment that will ultimately reduce death and suffering from the disease. The PCRP has a history of investing in innovative research ideas that often have a significant amount of potential risk, which is beneficial for investigating previously unexplored or undefined pathways that might be responsible for the development and progression of lethal prostate cancer. Flexibility to support basic, translational, and clinical research, as well as providing resources like the PCBN and tracking research against set goals and milestones, will increase the likelihood that promising discoveries will translate from bench to bedside.

### STRATEGIC GOAL 4: IMPROVE THE QUALITY OF LIFE FOR SURVIVORS OF PROSTATE CANCER

There are currently over 3 million prostate cancer survivors in the United States who have been successfully treated for prostate cancer, but now find themselves facing serious, potentially life-long side effects resulting from their treatment. These side effects can be both physical and psychological, affecting both prostate cancer patients and their family members. The PCRP intends to fund research that will improve the quality of life for those men who have undergone treatment and may be experiencing significant physical and/or psychological side effects. For those military Service members who have been treated for prostate cancer, improving their physical and psychological well-being is critical to enabling them to return to active duty Service. Progress toward this goal will not only improve the well-being of men facing these challenges, but may also reduce the psychological and economic burden on survivors, caregivers, and society.

## INVESTMENT STRATEGY

The investment strategy of the PCRP offers funding mechanisms that help drive research forward by supporting ideas that target innovation, impact, new investigators, and research resources. Award mechanisms offered by the PCRP are described below according to these general themes. The PCRP will review this investment strategy annually to ensure that it continues helping the program work toward accomplishing its strategic goals and will revise the strategy as needed.

### INNOVATION

- Idea Development Award

Research ideas proposing innovative, novel, and potentially high-risk approaches to important research questions could provide a significant impact, ultimately driving the field forward faster toward new advancements for patients.

### IMPACT

- Impact Award
- Health Disparity Research Award

Investing in research that has a high potential for direct impact for prostate cancer patients is critical for moving closer to the PCRP's vision of conquering prostate cancer. The PCRP seeks to fund research that will have a significant impact on patients that need advancements now, as well as support new avenues of research that have strong potential for making a significant long-term impact.

### NEW INVESTIGATORS

- Early Investigator Research Award
- Health Disparity Fellowship Award
- Physician Research Award
- New Investigator categories for Idea Development Award and Health Disparity Research Award

Investigators are the driving force behind the ideas that will propose and discover the clinical advancements of the future. The PCRP is committed to supporting the career development of new prostate cancer research investigators that will become future leaders of the field.

### RESOURCES

Research requires both great ideas and sufficient resources to pursue those ideas. The PCRP invests a portion of each year's appropriations to support the ongoing Clinical Consortium Awards and Prostate Cancer Pathology Resource Network Awards. As part of its investment strategy, the PCRP will evaluate the need for offering similar or new funding opportunities that bring together leading universities and cancer centers to help facilitate the translation of important findings from bench to bedside.

## MEASURING PROGRESS

**Short Term (3-5 years)**: Progress will be measured by evaluating the amount of funding invested in each PCRP Strategic Goal and how those investments have successfully generated publications and patents, follow-on funding, and the development of new clinical trials.

**Long Term (5-10 years)**: Progress will be measured by evaluating the numbers of publications, patents, and clinical trials, as well as the production of commercialized products and changes in the standard of care for prostate cancer.

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