DoD Prostate Cancer Research Program (PCRP)

Each year, the Department of Defense's office of the Congressionally Directed Medical Research Programs (CDMRP) assesses scientific opportunities to advance research in specific areas. The investigators supported by individual programs are making significant progress against targeted diseases, conditions, and injuries. This list is not intended to be a full representation of accomplishments, but rather a sampling of the broad portfolio of research and advances resulting from congressional appropriations.

Year	PCRP Research Contributions	Additional Information and Hyperlinks
1997	Dr. George Wilding determined the mechanism by which androgen induces reactive oxygen species (ROS) in prostate cancer cells. The discovery led to the development of APC-100, an antioxidant moiety of vitamin E that blocks ROS and delays prostate cancer progression. Clinical trials of an APC-100 derivative, APC-110, began in 2011.	• PCRP Research Highlight
1999	Dr. Samuel Denmeade developed plant-based agent thapsigargin as a pro-drug that can be cleaved into an active form after binding to prostate cancer cells and results in specific, localized cell killing. The agent is now in clinical trials for advanced prostate cancer.	• PCRP Research Highlight
2000	Dr. David Jaffray and colleagues developed cone-beam computed tomography with a flat-panel imager that later revolutionizes image-guided radiotherapy as the Elekta Synergy system, which was FDA-cleared in 2003 and is now used to treat prostate and other cancers in over 3,500 U.S. hospitals.	
2001	Dr. Eugene Kwon began clinical testing of ipilimumab, an antibody to stimulate the immune response to prostate cancer by targeting the protein CTLA-4. Androgen deprivation plus ipilimumab results in 70%–100% response in some patients and advances to Phase 3 clinical trials for advanced prostate cancer.	• PCRP Video Highlight from the 2011 IMPaCT Meeting
2001	Dr. Kim Chi developed and completed the first clinical testing of OGX-011, an agent that targets the protein clusterin and results in death of prostate cancer cells. The agent has now progressed to Phase 3 clinical trials.	
2002	Dr. Evan Keller demonstrated that blocking the activity of RANKL slows the progression of prostate cancer growth in bone. The monoclonal antibody against RANKL, denosumab, was later synthesized and in 2010 attained FDA approval as XGEVA, which became the standard of care for the treatment of bone-related events in advanced prostate cancer.	• PCRP Research Highlight
2002	The North Carolina–Louisiana Prostate Cancer Project (PCaP) was initiated as a landmark collaboration to study racial disparities in prostate cancer and ultimately recruited over 2,500 Caucasian and African American men. After surviving major setbacks due to Hurricane Katrina in 2005, the study concluded in 2010 with key discoveries related to health care access and other socioeconomic factors.	• PCRP Video Highlight from the 2011 IMPaCT Meeting
2002	Dr. David Curiel invented a method to enhance gene therapy for prostate cancer by genetically modifying the cell surface receptor CAR. The enhanced therapeutic approach has now entered Phase 1 clinical trials.	

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2003	Dr. Michael Karin made the key discovery that castration-recurrent prostate cancer results from an inflammatory response involving lymphotoxin and NF-kB, opening new opportunities for targeted therapies for advanced disease.	
2004	Dr. Marianne Sadar discovered an extract from marine sponges that blocks activation of androgen receptors. The synthetic version, EPI-001, shrinks prostate tumors without toxicity in animal models, and shows promise for greater efficacy than currently available therapies. The optimized agent, EPI-506, has entered Phase I/II clinical trials for the treatment of patients with castration-resistant prostate cancer.	• PCRP Video Highlight from the 2011 IMPaCT Meeting • PCRP Research Highlight
2005	The Prostate Cancer Clinical Trials Consortium (PCCTC) was initiated, bringing together 10 renowned cancer centers, led by Dr. Howard Scher, to accelerate the clinical testing of new drugs for prostate cancer. The PCCTC has expanded with the addition of new sites over the years, and in 2014 established themselves as a limited liability company - the Prostate Cancer Clinical Trials Consortium, LLC. As of 2014, the consortium has accrued over 4,400 prostate cancer patients to more than 100 Phase I and Phase II clinical trials, studying more than 50 new drugs. The PCCTC rapidly advanced nine therapeutic candidates to Phase III clinical testing, including abiraterone acetate (ZYTIGA) and enzalutamide (XTANDI), both of which are now FDA-approved and part of the standard of care for the treatment of advanced prostate cancer. The PCCTC has executed over 20 service agreements with outside sponsors and has been recognized as a qualified vendor by Novartis.	• PCRP Video Highlight featuring Maha Hussain, M.D. from the 2011 IMPaCT Meeting • PCRP Video Highlight featuring Howard I. Scher, M.D. from the 2011 IMPaCT Meeting • PCRP Video Highlight featuring Tia S. Higano, M.D., FACP from the 2011 IMPaCT Meeting • PCRP Research Highlight: The Prostate Cancer Clinical Trials Consortium – Multicenter Trials Made Easy • PCRP Research Highlight: PCRP Clinical Consortium Accelerates Enzalutamide to FDA Approval • PCRP Research Highlight: Critical Role of the PCRP in FDA Approval of Abiraterone Acetate • http://pcctc.org
2005	Dr. Martin Pomper developed a series of PET radiotracers that target prostate membrane-specific antigen, a protein on the surface of prostate cells. The radiotracers were later commercialized and are now in Phase 1 clinical trials to significantly improve imaging for patients with newly diagnosed or recurrent prostate cancer.	
2005	Dr. Cynthia Menard developed an MRI table to allow needle placement for prostate cancer patients lying on their backs (rather than side or stomach) to improve prostate gland stability during prostate biopsies, visualization of local prostate cancer recurrence after radiation treatment, and treatment to areas of recurrent tumor growth after radiotherapy.	• PCRP Research Highlight
2005	Dr. Arul Chinnaiyan discovered that the protein SPINK1 is associated with the more aggressive forms of prostate cancer and later used it as part of a panel of biomarkers in urine that can outperform PSA in the detection of prostate cancer.	• PCRP Research Highlight
2005	Dr. Douglas McNeel developed an immunotherapy-based DNA vaccine to inhibit prostate cancer recurrence in patients after treatment for primary disease. The agent is later successful in Phase 1 clinical testing and enters Phase 2.	• PCRP Research Highlight

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2006	Dr. Fazlul Sarkar identified a compound from cruciferous vegetables (e.g., broccoli, cauliflower, brussels sprouts, and cabbage) that inhibits prostate cancer cell growth. Dr. K.M. Rahman later showed that this compound, 3,3'-diindolylmethane (DIM), in combination with docetaxel, inhibits tumor growth by 80% in animal models. DIM has now moved into Phase 1 clinical trials.	
2007	Dr. Karen Cichowski discovered a key mechanism for the development of prostate cancer metastasis whereby the protein nuclear factor kB (NF-kB) is constitutively activated via loss of the protein disabled homolog 2 interacting protein (DAB2IP). DAB2IP expression and activity, which control cell signaling to NF-kB, are blocked by the EZH2 protein, which has long been implicated in prostate cancer metastasis.	• PCRP Research Highlight
2007	Dr. Michael Rosenfeld discovered a mechanism involving androgen receptor recruitment to sites of chromosomal breakage that brings the TMPRSSS2 gene close to ETS family genes, enabling the gene fusion found to be common in prostate cancers. The discovery provides key strategies for the development of prostate cancer biomarkers and therapeutic agents.	• PCRP Research Highlight
2008	Dr. Lloyd Trotman discovered a new tumor suppressor gene, PHLPP1 ("flip 1"), which cooperates with the gene PTEN to prevent prostate cancer progression to aggressive disease, providing new insight for therapeutic targeting of this pathway.	• PCRP Research Highlight
2008	Dr. Paul Cho developed an innovative system incorporating fluoroscopy, ultrasound, and an advanced probe, which made major improvements to the efficacy of prostate cancer brachytherapy.	
2009	The Prostate Cancer Biorepository Network (PCBN) was initiated, bringing together Johns Hopkins University and New York University, to deliver high-quality biospecimens for wide usage by the research community. By 2012, the PCBN accumulates over 2,000 samples, resulting in the discovery of a link between the SPARCL1 protein and aggressive prostate cancer.	• PCRP Research Highlight
2010	Dr. Michael Pollack pioneered work with silibinin, a protein from milk thistle plants, which inhibits prostate tumor growth and has now entered clinical testing.	
2011	Utilizing the PCRP-supported Prostate Cancer Biorepository Network (PCBN), Dr. Jun Luo analyzed AR-V7 expression in metastatic tissue samples and found that detection of AR-V7 in circulating tumor cells of patients with CRPC indicated resistance to enzalutamide and abiraterone. The PCRP is now funding him and his colleagues to perform a multi-institutional validation of a blood-based assay to predict resistance to androgen deprivation therapy.	• PCRP Research Highlight
2012	Dr. Michael Milosevic's research in identifying hypoxia in prostate cancer culminated in the finding that prostate cancer hypoxia is an indicator for disease recurrence after therapy, providing key insight on intermediate-risk disease and better therapies.	