



**UNDER SECRETARY OF DEFENSE**  
4000 DEFENSE PENTAGON  
WASHINGTON, D.C. 20301-4000

PERSONNEL AND  
READINESS

The Honorable Jon Tester  
Chairman  
Subcommittee on Defense  
Committee on Appropriations  
United States Senate  
Washington, DC 20510

**MAR 21 2024**

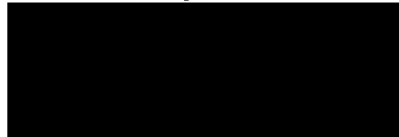
Dear Mr. Chairman:

The Department's response to House Report 117-88, pages 329-330, accompanying H.R. 4432, the Department of Defense Appropriations Bill, 2022, "Peer-Reviewed Cancer Research Programs," is enclosed.

The report covers Fiscal Year (FY) 2022 appropriations for the Peer-Reviewed Cancer Research Programs (PRCRP) (\$130 million), discusses key PRCRP research efforts, outcomes, and summarizes the projects selected for FY 2022 funding. This includes topic areas and their relevance to military health. The FY 2022 PRCRP Programmatic Panel selected 82 applications for funding, representing 99 separate awards (20.4 percent funding rate), based on scientific peer-review ratings, a balanced portfolio, programmatic intent, and relevance to military health. Through evaluations including, but not limited to, gap analyses of military health needs, topic area research, and patient outcomes, the FY 2022 PRCRP funded innovative and impactful research to support Service members and their families.

Thank you for your continued strong support for the health and well-being of our Service members, veterans, and their families. I am sending similar letters to the other congressional defense committees.

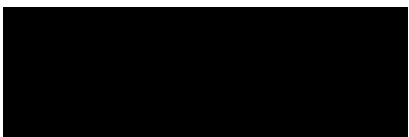
Sincerely,



Ashish S. Vazirani  
Acting

Enclosure:  
As stated

The Honorable Susan Collins  
Ranking Member





**UNDER SECRETARY OF DEFENSE**  
4000 DEFENSE PENTAGON  
WASHINGTON, D.C. 20301-4000

PERSONNEL AND  
READINESS

The Honorable Ken Calvert  
Chairman  
Subcommittee on Defense  
Committee on Appropriations  
U.S. House of Representatives  
Washington, DC 20515

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Ashish S. Vazirani  
Acting

Enclosure:  
As stated

cc:  
The Honorable Betty McCollum  
Ranking Member



**UNDER SECRETARY OF DEFENSE**  
4000 DEFENSE PENTAGON  
WASHINGTON, D.C. 20301-4000

PERSONNEL AND  
READINESS

The Honorable Jack Reed  
Chairman  
Committee on Armed Services  
United States Senate  
Washington, DC 20510

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Ashish S. Vazirani  
Acting

Enclosure:  
As stated

cc:  
The Honorable Roger F. Wicker  
Ranking Member



UNDER SECRETARY OF DEFENSE  
4000 DEFENSE PENTAGON  
WASHINGTON, D.C. 20301-4000

PERSONNEL AND  
READINESS

The Honorable Mike D. Rogers  
Chairman  
Committee on Armed Services  
U.S. House of Representatives  
Washington, DC 20515

MAR 21 2024

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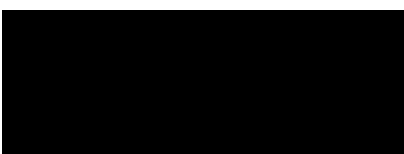
Sincerely,



Ashish S. Vazirani  
Acting

Enclosure:  
As stated

cc:  
The Honorable Adam Smith  
Ranking Member



# Report to the Congressional Defense Committees



## Peer-Reviewed Cancer Research Program

**March 2024**

The estimated cost of this report for the Department of Defense (DoD) is approximately \$1,300.00 for Fiscal Years 2023–2024. This includes \$500.00 in expenses and \$800.00 in DoD labor.

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## BACKGROUND AND PURPOSE

This report is in response to House Report 117–88, pages 329-330, accompanying H.R. 4432, the Department of Defense Appropriations Bill, 2022, which directs the Assistant Secretary of Defense for Health Affairs to provide a report to the congressional defense committees on the status of the Peer-Reviewed Cancer Research Program (PRCRP). For each research area, the report includes the funding amount awarded, progress of the research, and relevance of the research to Service members and their families.

The Defense Health Agency manages the Defense Health Program (DHP) Research, Development, Test and Evaluation (RDT&E) appropriations. The U.S. Army Medical Research and Development Command (USAMRDC) Congressionally Directed Medical Research Programs (CDMRP) provides execution management for the DHP RDT&E PRCRP Congressional Special Interest funds.

## FISCAL YEAR 2022 PRCRP INTRODUCTION AND STATUS

Congress initiated the PRCRP in 2009 to research cancers relevant to military health and not already addressed in the cancer programs currently executed and managed by CDMRP. For Fiscal Year (FY) 2022, the Consolidated Appropriations Act, 2022 (Public Law 117–103) provided \$130 million for the PRCRP and specified 20 different Topic Areas (Table 1).

**Table 1. FY 2022 PRCRP Topic Areas**

• Bladder Cancer	• Head and Neck Cancers	• Pediatric, Adolescent, and Young Adult Cancers <sup>¥</sup>
• Blood Cancers	• Liver Cancer	• Pediatric Brain Tumors <sup>¥</sup>
• Brain Cancer	• Lymphoma	• Sarcoma
• Colorectal Cancer	• Mesothelioma	• Stomach Cancer
• Endometrial Cancer	• Metastatic Cancers	• Thyroid Cancer
• Esophageal Cancer	• Myeloma*	• Von Hippel-Lindau Syndrome Malignancies <sup>±</sup>
• Germ Cell Cancers	• Neuroblastoma	

<sup>¥</sup>Research focused on children (ages 0–14 years), adolescents (ages 15–24 years), and/or young adults (ages 25–39 years).

\*Topic area not congressionally directed in FY 2021; returned in FY 2022.

<sup>±</sup>New for FY 2022; excludes cancers of the kidney and pancreas.

The PRCRP holds an annual Vision Setting meeting to review the research landscape, including Federal and non-Federal research funding of the specified topic areas for that FY, the knowledge and product gaps in cancer research and care, and the relevance of cancer research to military

health. Coordination with other Federal and non-Federal funding organizations enables the PRCRP to identify research areas for investment, optimize the impact of cancer research and care efforts, and develop an investment strategy for the current year's PRCRP appropriation.

During the FY 2022 Vision Setting, the PRCRP Programmatic Panel members (comprised of clinicians, scientists, veterans, active duty military oncologists, and patients), identified a list of overarching challenges in the current spectrum of cancer research. The PRCRP Overarching Challenges represent a focused strategy to close gaps in cancer research and patient care and ultimately make an impact across the different topic areas. Each PRCRP application must address at least one PRCRP Overarching Challenge.

#### FY 2022 PRCRP Overarching Research Challenges:

##### **Prevention**

- Develop innovative prevention strategies and early detection methods to decrease cancer burden in diverse different populations.
- Identify and elucidate the mechanisms behind cancer epigenetics/genetics and cancer development to improve prevention methods.

##### **Diagnostics/Prognostics**

- Identify strategies to predict treatment resistance, cancer recurrence, and development of advanced disease.
- Distinguish unique features driving cancer occurrence across the spectrum of ages (e.g., children, adolescents, young adults, older adults).
- Develop and improve minimally invasive methods to detect cancer initiation, progression, and recurrence.

##### **Therapeutics**

- Transform cancer treatment through identification of new targets, especially for advanced disease and metastasis.
- Advance immunotherapy across the different PRCRP Topic Areas.
- Evaluate a longitudinal collection of deep, multidimensional characterizations of clinically annotated research biospecimens during disease progression and/or treatment.
- Identify and elucidate the mechanisms behind cancer epigenetics/genetics and cancer development to improve treatment methods.

##### **Behavioral Science**

- Develop strategies to address survivorship issues including quality of life, overall mental health, psychological impact of recurrence, and/or survivor permanent disability.



- Develop strategies to reduce short- and long-term treatment effects, including neurocognitive deficits.

**Disparity**

- Improve prevention strategies, diagnosis, treatment, and outcomes for patients in underserved or under recognized populations.
- Develop strategies to improve accessibility to care and address survivorship.

**Resources**

- Develop open access platform(s) or methods/tools to coordinate and integrate multiple databases, biorepositories, and data-sharing interfaces.

**FY 2022 PRCRP Award Mechanisms**

During the FY 2022 Vision Setting meeting, the PRCRP Programmatic Panel recommended seven award mechanisms to achieve the vision of the PRCRP and most effectively address the FY 2022 PRCRP Overarching Challenges. Table 2 discusses the PRCRP award mechanisms offered in FY 2022.

**Table 2. FY 2022 PRCRP Funding Opportunities**

<b>FY 2022 Award Mechanism</b>	<b>Intent</b>	<b>Maximum Direct Costs per Award</b>
Idea Award	Support innovative, high-risk/high-reward research	\$400,000
Career Development Award – Fellow Option	Advance cancer research capacity by developing early-career investigators	\$400,000
Career Development Award – Scholar Option	Advance cancer research capacity by developing exceptional early-career investigators with potential for leadership in cancer research	\$800,000
Impact Award	Support mature studies with near-term clinical impact	\$1,000,000
Translational Team Science Award	Support correlative studies focused on the next phase of a clinical trial or future clinical application	\$2,500,000
Convergent Science Cancer Consortium Development Award	Promote novel approaches to ending cancer through convergent science cancer research	\$2,500,000
Behavioral Health Science Award	Support studies to improve survivorship and patient outcomes	\$1,000,000

## **FY 2022 APPLICATION REVIEW PROCESS AND INVESTMENTS**

The PRCRP uses a two-tier review process to evaluate and recommend awards for funding. To ensure that each program's research portfolio reflects not only highly meritorious science, but also the most programmatically relevant research, the CDMRP developed this two-tier model based upon recommendations from a 1993 report issued by the National Academy of Medicine (formerly the Institute of Medicine). Both tiers of review incorporate the expertise of scientists, clinicians, military Service members, and consumers (lay persons with experience in cancer either as patients or caregivers).

The first tier of review entails a scientific peer review of the applications received for funding. An external panel, recruited specifically for each peer review session, conducts these reviews. The peer review process evaluates the applications based on established scientific and technical criteria as delineated in each program announcement/funding opportunity.

The second tier of review, the programmatic review, involves a programmatic panel. The PRCRP Programmatic Panel (<https://cdmrp.health.mil/prcrp/panels/panels22>) assesses the applications based on their scientific peer-reviewed ratings, the funding landscape, portfolio composition, programmatic intent, and relevance to congressional language.

During October-November 2022, CDMRP convened 39 FY 2022 PRCRP peer review panels. The panels used peer review criteria to evaluate applications that included technical merit and impact on patient outcomes. During December 2022-February 2023, CDMRP convened the FY 2022 PRCRP Programmatic Panel to conduct programmatic review. The Programmatic Panel considered each FY 2022 PRCRP Topic Area, Overarching Challenges, and award mechanism-specific criteria to ensure a balanced portfolio. Following deliberation, the Programmatic Panel recommended 99 applications that were scientifically sound and best met the program's goals. The USAMRDC Commanding General reviewed and approved the funding recommendations.

In FY 2022, the PRCRP funded 82 applications (representing 99 separate awards) of the 484 full applications received, for a 20.4 percent funding rate totaling \$114,201,395. An additional \$663,262 in research funds was added to budgets for the two FY 2020 Convergent Science Virtual Cancer Center (CSVCC) Director awards to fund competitive subawards for the FY 2022 cohort of CSVCC Scholars (Career Development Award – Scholar Option awardees.) The remaining \$15,135,343 of the FY 2022 PRCRP appropriation is directed toward administrative and management costs in support of these PRCRP projects and Department of Defense (DoD) withholds, including USAMRDC withholds, Small Business Innovation Research (SBIR)/Small Business Technology Transfer Programs (STTR) allocations, and CDMRP management costs (Table 3).

**Table 3. FY 2022 PRCRP Budget**

<b>Budget Allocations</b>	<b>Amount</b>
FY 2022 PRCRP Congressional Appropriation	\$130,000,000
Less: SBIR/STTR Withholds	(\$4,336,000)
Less: USAMRDC Withholds	(\$2,511,183)
Less: CDMRP Management Costs	(\$8,288,160)
Amount Available for FY 2022 Research	\$114,864,657

Table 4 presents total research recommended for FY 2022 funding, by Topic Area.

**Table 4. FY 2022 Total Research Dollars Invested per PRCRP Topic Area\***

<b>Topic Area</b>	<b>Number of Awards</b>	<b>Total Award Amount</b>
<b>Bladder Cancer</b>	6	\$7,804,489
<b>Blood Cancers</b>	7	\$12,368,950
<b>Brain Cancer</b>	15	\$19,254,798
<b>Colorectal cancer</b>	7	\$8,366,492
<b>Endometrial cancer</b>	7	\$8,200,215
<b>Esophageal cancer</b>	6	\$5,930,215
<b>Germ cell cancers</b>	5	\$5,693,666
<b>Head and neck cancers</b>	5	\$6,858,962
<b>Liver Cancer</b>	7	\$8,039,463
<b>Lymphoma</b>	8	\$7,963,314
<b>Mesothelioma</b>	1	\$676,000
<b>Metastatic cancers</b>	1	\$1,575,806
<b>Myeloma</b>	2	\$2,357,541
<b>Neuroblastoma</b>	1	\$642,000
<b>Pediatric Brain Tumors</b>	5	\$4,753,139
<b>Pediatric, adolescent, and young adult cancers</b>	7	\$6,440,495
<b>Sarcoma</b>	6	\$5,368,127
<b>Stomach Cancer</b>	2	\$656,272
<b>Thyroid cancer</b>	1	\$1,251,451
<b>Von Hippel-Lindau syndrome malignancies<sup>†</sup></b>	0	0

\*An additional \$663,262 in research funds was added to budgets for the two FY 2020 CSVCC Director awards, which are topic-agnostic.

<sup>†</sup>No awards were made for this topic area. Applications received were either not meritorious as determined during the two-tier review or not compliant with congressional language.

The PRCRP awarded all FY 2022 research funds by September 30, 2023. The Department expects outcomes by the end of each period of performance, which spans 2 to 4 years from the start date of an award.

## **FY 2022 PRCRP TOPIC AREAS: RELEVANCE TO MILITARY HEALTH**

Cancer research profoundly impacts the reduction of cancer burden on military families and improves force readiness. Tables 5a and 5b show potential cancer risks and effects on military health. Successful studies may lead to innovative approaches for the prevention of cancer development, improved diagnostic/detection methods, new prognostic information, potentially novel treatments, and better ways to cope with quality-of-life issues.

### **Environmental Exposures**

The Department of Veterans Affairs (VA) has acknowledged certain exposures increase cancer risk among Service members and their families.<sup>1,2</sup> Service members operate in environments that may increase the incidence of multiple cancers immediately or years, if not decades, later. Exposures linked to increased cancer risk include, but are not limited to, chemical weapons, including storage; ionizing radiation; herbicides; electromagnetic fields; jet fuel; organic materials; biological agents; environmental hazards; herbicides; pesticides; air pollutants; burn pits; chemical and biological warfare weapons; and other occupational hazards. Tables 5a and 5b detail the potential carcinogenic agents implicated in cancer and military health. Specific risk levels of exposures may vary depending on the deployment environment. For example, use of exposed asbestos as building material declined in the United States; however, many countries where Service members deploy still use asbestos as key material for housing and building manufacturing.<sup>3</sup> Cancers that develop due to asbestos exposure include mesothelioma, cancer of the larynx, pharynx (throat), stomach, colon, and rectum.<sup>4</sup> A study by the Centers for Disease Control and Prevention reported a rise in mesothelioma deaths by five percent from 1999 to 2015.<sup>5</sup> Asbestos and other elongated mineral particles remain a relevant exposure for military members.




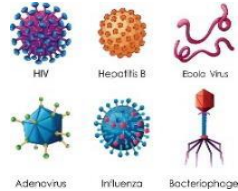
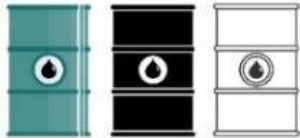
The VA currently recognizes seven categories of associated cancers with Agent Orange exposure. Although the Vietnam War ended in 1975, C-123 airplanes responsible for spraying the pesticide known as Agent Orange stayed in commission until 1982.<sup>6</sup> The National Academy of Medicine determined that Service members who were not involved in the Vietnam conflict may have been exposed to Agent Orange residue. Reservists who served on these planes are eligible for the Agent Orange Registry and benefits.<sup>7</sup>



The VA recently recognized airborne hazards as a risk factor for many rare respiratory tract cancers. Due to the rarity of some of these cancers, such as cancers of the head and neck, data may not directly demonstrate a causation of military service with cancer incidence. Nonetheless, the VA took action to acknowledge the cancer risk potential for these cancers.<sup>8</sup>

Infectious agents such as *Helicobacter pylori* (stomach cancer), human papillomavirus virus (associated with head and neck cancers, and cancers of the genital tract), and hepatitis (liver cancer) present another area of cancer risk.<sup>9-11</sup>

The incidence of cancer diagnosis and mortality among military aviators and aircraft support personnel is higher compared to individuals in the U.S. population, including an increased rate of brain and nervous system cancers.<sup>12</sup>

**Table 5a. Exposure-Related Cancer Risks\***


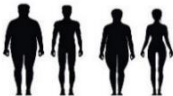

Environmental or Occupational Exposure-Related Cancer Risks	
Risk	Related Cancer
Agent Orange and other herbicides 	Soft tissue sarcoma, Hodgkin’s lymphoma, non-Hodgkin’s lymphoma, chronic lymphocytic leukemia, multiple myeloma, respiratory, thyroid, bladder cancer
Asbestos 	Mesothelioma, bladder cancer
Radiation 	Leukemias (except chronic lymphocytic leukemia), thyroid, bone, liver, esophageal, stomach, colorectal, bladder, salivary gland, multiple myeloma, brain, lymphoma (except Hodgkin’s lymphoma), endometrial/uterine cancers
Infectious Agents 	<b>Epstein-Barr virus:</b> Lymphoma, oral cavity <b>Hepatitis B and hepatitis C viruses:</b> Liver cancer <b>Human immunodeficiency virus:</b> Kaposi sarcoma, lymphoma, cervical, anal, throat, liver cancer <b>Human papilloma virus:</b> Cervical, head and neck, vulvar, vaginal, penal, anal cancers <b>Human T-cell lymphotropic virus type 1:</b> Adult T-cell lymphoma <b>Helicobacter pylori:</b> Gastric cancer
Industrial Solvents 	Liver, bladder, gastric, blood (leukemia, lymphoma), nasopharyngeal, bone, brain, adrenal cancer

Environmental or Occupational Exposure-Related Cancer Risks	
Risk	Related Cancer
Contaminated Water: Camp Lejeune (1953–1987) 	Leukemia, bladder, esophageal, multiple myeloma, non-Hodgkin's lymphoma
Chemical Weapons 	Nasopharyngeal, laryngeal, squamous cell carcinoma, acute myeloid leukemia

\*See “References for Tables 5a and 5b” section.

Service members, their families, veterans, and the American public are also at risk for developing various cancers due to lifestyle choices (Table 5b). The PRCRP remains committed to decreasing the burden of cancer on these populations by funding innovative and high-impact research.

**Table 5b. Cancer Risk Factors and Lifestyle\***

Additional Cancer Risks	
Risk	Related Cancer
Alcohol 	Oral, esophageal, liver, head and neck, colorectal cancer
Obesity 	Endometrial, esophageal, gastric, liver, colorectal, thyroid cancer
Tobacco 	Oral cavity, esophageal, bladder, stomach, colorectal, cervical, head and neck, adrenal cancers

\*See “References for Tables 5a and 5b.” section.

## Mission Readiness

Congressional language requested that PRCRP-funded research be relevant to Service members and their families. The PRCRP devised a FY 2022 investment strategy to address military health concerns that prioritizes protection against force vulnerabilities. The FY 2022 PRCRP addressed these core capabilities by *requiring* that all applications address at least one of the FY 2022 PRCRP relevant military health Focus Areas, presented in Table 6.

**Table 6. FY 2022 Relevance to Military Health Focus Areas**

<b>Environmental Exposures</b>	<ul style="list-style-type: none"> <li>• Environmental/exposure risk factors associated with cancer.</li> </ul>
<b>Mission Readiness</b>	<ul style="list-style-type: none"> <li>• Gaps in cancer prevention, early detection/diagnosis, prognosis, and/or treatment that may impact mission readiness and the health and well-being of military members, veterans, their beneficiaries, and the general public.</li> <li>• Gaps in quality of life and/or survivorship that may impact mission readiness and the health and well-being of military members, veterans, their beneficiaries, and the general public.</li> </ul>

A Service member’s cancer diagnosis affects not only the individual Service member, but also the Service member’s entire unit and mission. Each Service member plays a crucial role in mission readiness that may be affected by a cancer diagnosis of the Service member or family member. Research that improves survival, while minimizing side effects, will have a major impact on mission readiness by enabling an active duty Service member to return to full duty. Additionally, mission readiness includes ensuring that family members receive world-class health care. Service members become affected when a member of their family or support system receives a cancer diagnosis. Time off to assist in the care, recovery, and well-being of family members will affect overall unit force readiness and vulnerabilities.

Cancer not only directly affects the military’s capabilities, but also indirectly places a burden on the Military Health System (MHS). Data provided by the Armed Forces Health Surveillance Division (AFHSD) (formerly the Armed Forces Health Surveillance Branch), based on electronic records within Defense Medical Surveillance System (DMSS), demonstrated the impact of cancer care on the MHS. Table 7 presents MHS medical encounters for select cancer types (2010-2019) within the PRCRP’s Topic Areas.

**Table 7. MHS Medical Encounters for Select Cancers (2010-2019)\***

<b>Cancer Type</b>	<b>Patient Category</b>	<b>Number of Patients</b>	<b>Number of Outpatient Encounters</b>	<b>Number of Hospital Bed Days</b>
Bladder Cancer	Active Service Members	427	3,107	269
	Other DoD Beneficiaries	66,887	940,960	88,263
Leukemia	Active Service Members	1,059	48,162	17,793
	Other DoD Beneficiaries	46,407	1,110,000	194,538
Osteosarcoma	Active Service Members	717	10,457	3,064
	Other DoD Beneficiaries	15,020	90,505	24,590
Stomach Cancer	Active Service Members	236	3,417	1,737
	Other DoD Beneficiaries	16,546	198,188	64,973
<b>Totals</b>		<b>147,299</b>	<b>2,404,796</b>	<b>395,227</b>

\*Data provided by the AFHSD based on electronic records within DMSS. Does not include care received outside the MHS. Includes all MHS inpatient and outpatient encounters where the first (primary) diagnosis was for leukemia. Active Component Service members (ACSMs) does not include Activated Reserve and Activated National Guard. This does not include care received while deployed or any care received outside of the MHS that was not processed through TRICARE (i.e., care covered by other insurance sources or care paid for entirely out of pocket). Other DoD beneficiaries include: National Guard/Reserve members; family members of ACSMs and National Guard/Reserve members; former Service members; and family members of former Service members.

A report commissioned by the Leukemia & Lymphoma Society found that treatment cost for blood cancers during the first year following diagnosis is \$156,000 per patient.<sup>13</sup> Costs for 3 years of follow-on care vary, depending on blood cancer type (e.g., \$200,000 for chronic leukemia to over \$800,000 for acute leukemia). Other cancers, such as bladder cancer, have mean lifetime costs that can exceed \$200,000.<sup>14,15</sup> Studies show the costs of national cancer care in 2020 were \$208 billion.<sup>15</sup> The MHS and VA burden includes costs for active duty Service members, their families, veterans, and other military beneficiaries.

## **PRCRP RESEARCH PROGRESS AND OUTCOMES**

The PRCRP has funded several clinical pipeline projects with potential to have a profound impact on the health of active duty Service members and their families, veterans, and the American public. Table 8 summarizes a select representation of awards.



**Table 8. Select PRCRP Clinical Pipeline Projects**

Cancer Type	Organization	Summary
<b>Head and Neck Cancer</b>	University of Pennsylvania	Researchers are conducting a three-year, multi-site, randomized clinical trial of head and neck cancer survivors with lymphedema and fibrosis, long-term and late toxicities that cause disfiguration and impair functions like swallowing and breathing. The study aims to develop a comprehensive intervention to reduce symptom burden and improve quality of life.
<b>Neurological Cancers</b>	University of Alabama at Birmingham	This project focuses on malignant glioma, a type of brain cancer, including investigation of potential treatment with oncolytic viral therapy, a less toxic treatment that targets tumor cells and spares healthy cells. Findings identified therapeutic biomarkers for predicting which patients with brain tumors will likely benefit from oncolytic viral therapy.
	University of North Carolina (UNC)	Utilizing a promising Chimeric Antigen Receptor T cell therapy (CAR-T) approach, the team at UNC plans to attack solid pediatric tumors. Though CAR-T continues to remain an elusive therapy for solid tumors, the approach being tested may improve the antitumor activity of CAR-T cells through enhanced survival and efficacy at the tumor site. A Phase 1 trial currently underway tests this new method on children with relapsed/refractory neuroblastoma.
	Virginia Commonwealth University	An evidence-based psychotherapeutic intervention, Managing Cancer and Living Meaningfully is being tested in a pilot clinical trial. Researchers hope to better understand the potential benefits of this intervention on brain tumor patients' mood and quality of life. This may lead to improvements in health care providers' understanding of how to enhance brain tumor patients' well-being and overall functioning.
<b>Gastrointestinal Cancers</b>	Brigham and Women's Hospital	Using messenger ribonucleic acid (mRNA) nanoparticles to reprogram the tumor microenvironment of liver cancer, this team restored the function of the tumor suppressor, p53, in preclinical laboratory work. This work demonstrated that in combination with immune checkpoint blockade, the p53 mRNA nanoparticle technology led to significantly increased antitumor immune responses in liver cancer models.

Cancer Type	Organization	Summary
	Cleveland VA Medical Center	Researchers are conducting a clinical study testing a non-invasive screening method available in primary care offices for esophageal adenocarcinoma and its precursor lesion, Barrett's esophagus among the veteran population. The EsoCheck device is a small retrievable capsule that can sample the lower part of the esophagus. Collected samples will be assayed for deoxyribonucleic acid (DNA) mutations that are common in EAC. The EsoCheck test will be evaluated for its sensitivity and specificity as a detection method.
	Thomas Jefferson University/ Institute for Cancer Research/ Seattle Institute for Biomedical and Clinical Research	A multi-institutional team of researchers are evaluating the use of oral linaclotide, a drug used to treat irritable bowel syndrome, as a potential treatment for colorectal cancer. A Phase 2 clinical trial of oral linaclotide is underway to examine its ability to inhibit the development and spread of CRC in patients with established adenomas or invasive carcinomas.
<b>Pediatric and Young Adult Cancers</b>	Fred Hutchinson Cancer Center	A pilot clinical trial is being conducted to investigate the feasibility of administering gonadotropin-releasing hormone analogs as an intervention among newly diagnosed adolescent and young adult cancer patients who are at increased risk of premature menopause, and consequently experience reduced fertility due to their cancer treatment.
	City of Hope	This project supported the preclinical development of a vaccine to prevent and treat Epstein-Barr virus (EBV)-driven lymphomas targeting five glycoproteins important for viral entry into diverse cell types. The results strongly suggest that the vaccine induces serum antibodies with protective properties both in vitro and in vivo, providing necessary proof to support a Phase 1 clinical trial. This vaccine could reduce rates of EBV infection, thus reducing rates of infectious mononucleosis and EBV-associated lymphomas.

Cancer Type	Organization	Summary
	Children’s Hospital of Philadelphia (CHOP)	Researchers at CHOP are conducting a multi-site observational cohort study of pediatric patients with differentiated thyroid cancer that has metastasized to their lungs. The study will examine how radioiodine (RAI) therapy, a standard of care, interacts with recently developed therapies targeted against driver oncogenes. Among adults, the interaction of targeted therapies with RAI has demonstrated to increase sensitivity of the disease to RAI. This study will help confirm if the same effects are observed among children and adolescents.
<b>Genitourinary Cancers</b>	Cedars-Sinai Medical Center	This team investigated improving outcomes for patients with advanced bladder cancer. Inflammatory mediators released by chemotherapy often cause immunogenic cell death (ICD) or the ability to invoke an immune response to cause cell death. Gemcitabine, a bladder cancer treatment, initiates the inflammatory response, but not ICD, due to inhibition by prostaglandin E2 (PGE2). Using the PGE2 inhibitor celecoxib in combination with gemcitabine, this team overcame the inhibition and sensitized bladder cancer cells to ICD.

**SELECTED MAJOR RESEARCH OUTCOMES AND PRODUCTS**

**Outcome with Promise**

The diagnosis of a child with Diffuse Intrinsic Pontine Glioma (DIPG), also known as Diffuse Midline Glioma, is devastating due to its inoperability. DIPG has a 1 percent survival rate. Research conducted at Weill Cornell Medicine resulted in the development of a peptide nanofiber precursor (NFP), a highly stable structure shown to improve tissue penetration in DIPG. NFPs were conjugated with emtansine (DM1), an approved drug for breast cancer treatment with demonstrated effectiveness in treating other brain cancers. DM1-NFP exhibited selective toxicity toward glioma cells in mice implanted with human-derived DIPG tumors. A single treatment with the intervention increased survival time.

**Outcome Advancing Cancer Research**

Conventional cancer treatments rely on a one-size-fits-all approach that disregards the complexity and heterogeneity of tumors composed of diverse cell types. The PRCRP funded formative research in the development of **CIBERSORTx** (Cell-type Identification By Estimating Relative Subsets Of RNA Transcripts), an analytical tool for characterizing tumor cell subsets in individual tumor samples. The data generated using CIBERSORTx are essential for the development of personalized medicine and are being widely used by cancer researchers exploring precision medicine with the potential to enter the clinic and revolutionize cancer treatment.

## **Product in Phase 1 Clinical Trial**

In the fight against CRC, the team at Thomas Jefferson University used *Listeria*-based cancer vaccine to optimize the immune response in a CRC model. Results demonstrated protection against metastatic spread of CRC to the lungs, and findings led to a Phase 1 clinical trial for CRC patients with minimal residual disease. This *Listeria*-based vaccine may be the first step in protecting against disease recurrence in CRC but could also lead to more positive outcomes for other cancers, as well.

## **Product in Phase 2 and 3 Clinical Trials**

Novel combinations of immunotherapies are at the leading edge of new cancer treatment regimens. A study conducted at UNC focused on a key mediator of immunotherapy and resulted in ongoing Phase 2 and Phase 3 clinical trials for the combination of denosumab and other immunotherapeutic agents for patients with rare and metastatic melanoma.

## **Product in Clinical Practice**

The PRCRP contributed to a groundbreaking achievement for cancer research and military health. The Ohio State University conducted seminal work on the overexpression of a protein called exportin (XPO1), which led to clinical trials to test selinexor as a new treatment for blood cancers. In 2020, the findings led to approval by the U.S. Food and Drug Administration of **XPOVIO**® (selinexor), in combination with ibrutinib, as an oral treatment of multiple myeloma and relapsed or refractory diffuse large B-cell lymphoma. As of August 2023, there are 72 active clinical trials utilizing selinexor as an intervention.<sup>17</sup> In an ongoing clinical trial of patients with advanced or recurrent endometrial cancer, exploratory analyses showed selinexor increased the length of progression-free survival for a subgroup of patients.<sup>18</sup>

Other accomplishments may be reviewed at the PRCRP webpage for research highlights (<https://cdmrp.health.mil/prcrp/highlights>).

## **SUMMARY**

The PRCRP's vision is to advance mission readiness of U.S. military members affected by cancer and improve quality of life by decreasing the burden of cancer among Service members, their families, veterans, and the American public. Through analyses of military health needs, gaps in topic area research and patient outcomes, and Federal and non-Federal funding landscapes, the FY 2022 PRCRP responded to congressional language by funding innovative and impactful science. In FY 2022, the PRCRP funded 82 applications (representing 99 separate awards) of the 484 full applications received, for a 20.4 percent funding rate totaling \$114,201,395. The FY 2022 PRCRP investment in these awards represents its commitment to advancing the health and well-being of Service members, their families, veterans, and the American public.

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**APPENDIX A: FY 2009–FY 2021 PRCRP APPROPRIATIONS AND TOPIC AREAS**

<b>Fiscal Year</b>	<b>Appropriation / (Awards)‡</b>	<b>Topic Areas*</b>
<b>2009</b>	\$16M (38)	\$4M, Melanoma and other skin cancers as related to deployments of Service members to areas of high exposure; \$2M, Pediatric brain tumors within the field of childhood cancer research; \$8M, Genetic cancer and its relation to exposure to the various environments that are unique to a military lifestyle; and \$2M, Noninvasive cancer ablation treatment, including selective targeting with nanoparticles
<b>2010</b>	\$15M (30)	Melanoma and other skin cancers; Pediatric brain tumors within the field of childhood cancer research; Genetic cancer research and genomic medicine; Kidney cancer; Blood cancer; Colorectal cancer; <i>Listeria</i> vaccine for cancer; and Radiation protection utilizing nanotechnology
<b>2011</b>	\$16M (44)	Melanoma and other skin cancers; Pediatric cancer research; Genetic cancer research; Kidney cancer; Blood cancer; Colorectal cancer; Pancreatic cancer; Mesothelioma; <i>Listeria</i> vaccine for cancer; and Radiation protection utilizing nanotechnology
<b>2012</b>	\$12.8M (27)	Melanoma and other skin cancers; Pediatric brain tumors; Genetic cancer; Pancreatic cancer; Kidney cancer; Blood cancer; Colorectal cancer; Mesothelioma; and <i>Listeria</i> vaccine for cancer
<b>2013</b>	\$15M (27)	Melanoma and other skin cancers; Pediatric brain tumors; Genetic cancer; Pancreatic cancer; Kidney cancer; Blood cancer; Colorectal cancer; Mesothelioma; and Neuroblastoma
<b>2014</b>	\$25M (47)	Blood cancer; Colorectal cancer; Genetic cancer research; Kidney cancer; <i>Listeria</i> vaccine for cancer; Melanoma and other skin cancers; Mesothelioma; Myeloproliferative disorders; Neuroblastoma; Pancreatic cancer; Pediatric brain tumors; and Cancers related to radiation exposure
<b>2015</b>	\$50M (110)	Colorectal cancer; Genetic cancer research; Kidney cancer; <i>Listeria</i> vaccine for cancer; Liver cancer; Melanoma and other skin cancers; Mesothelioma; Myeloproliferative disorders; Neuroblastoma; Pancreatic cancer; and Stomach cancer
<b>2016</b>	\$50M (89)	Bladder cancer; Colorectal cancer; Immunotherapy; Kidney cancer; <i>Listeria</i> vaccine for cancer; Liver cancer; Lymphoma; Melanoma and other skin cancers; Mesothelioma; Myeloproliferative disorders; Neuroblastoma; Pancreatic cancer; Pediatric brain tumor; and Stomach cancer
<b>2017</b>	\$60M (92)	Bladder cancer; Brain cancer; Cancer in children, adolescents, and young adults; Colorectal cancer; Immunotherapy; <i>Listeria</i> -based regimens for cancer; Liver cancer; Lymphoma; Melanoma and other skin cancers; Mesothelioma; Neuroblastoma; Pancreatic cancer; Pediatric brain tumor; and Stomach cancer

<b>Fiscal Year</b>	<b>Appropriation / (Awards)‡</b>	<b>Topic Areas*</b>
<b>2018</b>	\$80M (114)	Adrenal cancer; Bladder cancer; Blood cancers; Brain cancer; Cancer in children, adolescents, and young adults; Colorectal cancer; Immunotherapy; <i>Listeria</i> -based regimens for cancer; Liver cancer; Lymphoma; Melanoma and other skin cancers; Mesothelioma; Myeloma; Neuroblastoma; Pancreatic cancer; Pediatric brain tumor; and Stomach cancer
<b>2019</b>	\$90M (103)	Bladder cancer; Blood cancers; Brain cancer; Cancer in children, adolescents, and young adults; Colorectal cancer; Immunotherapy; <i>Listeria</i> -based vaccines for cancer; Liver cancer; Lymphoma; Mesothelioma; Neuroblastoma; Pancreatic cancer; Pediatric brain tumor; Rare cancers; and Stomach cancer
<b>2020</b>	\$110.0M (98)	Bladder cancer; Blood cancers; Brain cancer; Colorectal cancer; Esophageal cancer; Head and neck cancer; Immunotherapy; Liver cancer; Mesothelioma; Metastatic cancers; Neuroblastoma; Pediatric, adolescent, and young adult cancers; Pediatric brain tumor; and Stomach cancer
<b>2021</b>	\$115.0M (86)	Bladder cancer; Blood cancers; Brain cancer; Cancers Associated with the Use of Beryllium; Colorectal cancer; Endometrial Cancer; Esophageal cancer; Germ Cell Cancers; Head and neck cancer; Link between Scleroderma and Cancer; Liver cancer; Lymphoma; Mesothelioma; Metastatic cancers; Neuroblastoma; Pediatric, adolescent, and young adult cancers; Pediatric brain tumor; Sarcoma; Stomach cancer; and Thyroid cancer

\*Congressional language designates topic areas (as published in the Public Law, Congressional Record, and post-Presidential signature communications for clarification on language).

‡Number of awards represents all open, pending closeout, and closed awards, and does not include withdrawals.