Pancreatic Cancer Research Program

CDMRP
DEPARTMENT OF DEFENSE
CONGRESSIONALLY DIRECTED MEDICAL RESEARCH PROGRAMS

Vision:

Reduce the burden of pancreatic cancer among Service Members, Veterans, their families, and the American public

Mission:

Promote rigorous, innovative, high-impact research that leads to earlier pancreatic cancer diagnosis, new therapeutic tools, and improved outcomes

"The PCARP program's investment in innovative collaborations and in young investigators will transform prevention, early detection, and treatment. In turn, these will have an impact by increasing survival and improving care for pancreatic cancer."

Dr. Gloria Petersen, *PCARP Programmatic Panel Member*

Pancreatic Cancer Research Program

Program History

Based on 2021 Surveillance, Epidemiology, and End Results Program data, over 60,000 new cases of pancreatic cancer were diagnosed in the U.S. that year making it the third leading cause of cancer deaths in the country. Over 26,500 active duty and former Service Members and their beneficiaries were diagnosed with pancreatic cancer within the Military Health System from 2010-2019.

In fiscal year 2020 (FY20), the U.S. Congress established the Peer Reviewed Pancreatic Cancer Research Program (PCARP) in the Department of Defense (DOD) appropriation, allocating $6 million (M) to the new program. Congress appropriated $15M to PCARP in FY21 and again in FY22. Since its inception in 2020, the PCARP has funded 33 awards that promote innovative, high impact research that will lead to new therapies and earlier detection for pancreatic cancer.

The PCARP has developed a multifaceted strategic direction based upon the current state of pancreatic cancer research and the needs of the pancreatic cancer community. The PCARP will: (1) fill gaps and advance knowledge that will drive new and innovative clinical trials for pancreatic cancer, (2) expand pancreatic cancer expertise by bridging diverse scientific fields, (3) facilitate a multidisciplinary approach to advancing scientific knowledge of pancreatic cancer, and (4) recruit and retain young investigators dedicated to pancreatic cancer research.

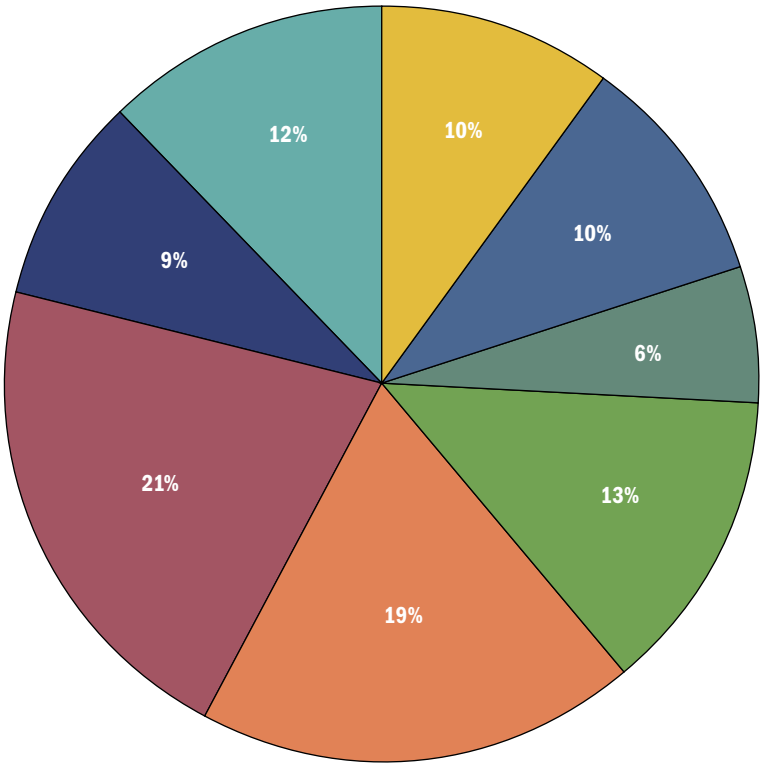
Number of PCARP Awards & Appropriations by Fiscal Year

PCARP Focus Areas

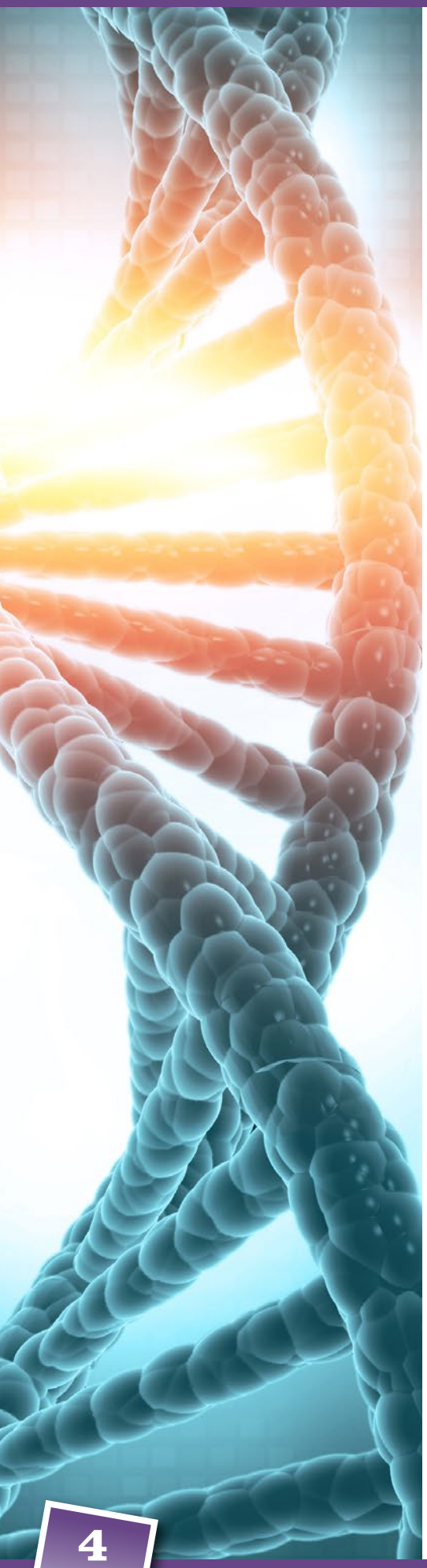
To fulfill its strategic direction, the PCARP created nine focus areas:

- Early detection research for pancreatic cancer, including the prevalence in individuals with pre-diabetes and diabetes and/or those in underserved ethnic and minority communities
- Supportive care interventions, patient-reported outcomes, quality of life, and perspectives during diagnosis, treatment, and survivorship
- Barriers to the implementation of health care, including ways to overcome socioeconomic, geographic, or ethnic and racial disparities
- Identification and characterization of pancreatic cancer risk including genetic and environmental risk factors, such as diet, obesity, and microbiome
- Understanding the relationship between metabolic disruptions in pancreatic cancer and their systemic effects, including diabetes and cachexia
- Understanding tumor development and progression, from precursors to metastasis
- Understanding the relationship between oncogenic signaling and the tumor microenvironment that drives drug resistance and therapeutic response
- Biomarkers to predict therapeutic response and guide management strategies
- New drug development targeted toward cancer sensitivity and resistance mechanisms including immune mechanisms of resistance

PCARP Funded Awards FY20-FY21



- Development of pharmacological, immunological, or genetic interception approaches, **10%**
- Early detection research, including studies of individuals with pre-diabetes and diabetes and/or underserved ethnic minority communities, **10%**
- Integration of biologic and imaging biomarkers to drive more precise and earlier detection an prognosis, **6%**
- New drug development targeted toward cancer sensitivity and resistance mechanisms, **13%**
- Understanding precursors, origins and early progression of pancreatic cancer, **19%**
- Understanding the events that promote pancreatic cancer metastasis, **21%**
- Understanding the relationship between metabolic disruptions in pancreatic cancer and their systemic effects, **9%**
- Understanding the relationship between oncogenic signaling and the tumor microenvironment, **12%**



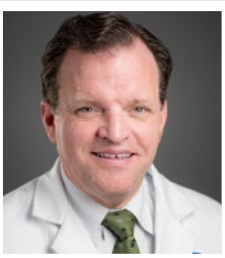
Translational Studies: Achieving Excellence from the Bench to the Bedside

The PCARP Translational Research Partnership Award (TRPA) supports collaborations between two investigators – a clinician and a research scientist – to translate promising ideas generated during hypothesis-driven, basic laboratory research and preclinical (animal) studies into clinical applications that directly benefit patients with pancreatic cancer.

Novel DZ-Artemisinin for Treatment of Pancreatic Cancer

Mouad Edderkaoui, Ph.D., and Steven Pandol, M.D., Cedars-Sinai Medical Center

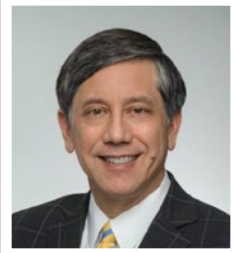
Drs. Edderkaoui and Pandol received an FY21 TRPA to investigate artemisinin (ART), a malarial drug that has been shown to kill cancer cells, as a potentially more effective and less toxic chemotherapeutic agent for pancreatic ductal adenocarcinoma (PDAC). The Principal Investigators (PIs) aim to increase the effectiveness of ART and its analogs by conjugating them to biomedical imaging dyes that specifically target cancer cells. The PIs will evaluate the biological activities of these conjugates in PDAC cell lines and compare them to conventional therapies by testing their safety and effectiveness in animal models. If successful, the study could generate preclinical efficacy data and preliminary safety and pharmacokinetic data to support pilot clinical trials.

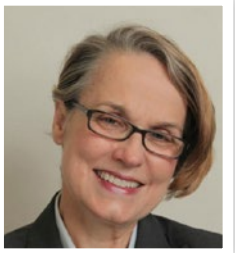


Evaluating Obesity-Mediated Mechanisms of Pancreatic Carcinogenesis in Minority Populations

Jennifer Permuth, Ph.D., and Jason Fleming, M.D., H. Lee Moffitt Cancer Center and Research Institute

Pancreatic cancer incidence and mortality rates are significantly higher in the African American (AA) population compared to other groups. In addition, obesity confers a 30% increase in risk for pancreatic ductal adenocarcinoma (PDAC). Drs. Permuth and Fleming were awarded an FY21 TRPA to collect and characterize molecular and imaging data from paired PDAC and adipose tissue (AT) samples donated by AA patients living in high-risk geographic regions in Florida and Mississippi. The PIs aim to determine if AT dysfunction contributes to malignant transformation, therapeutic resistance, and poor survival among obese AA pancreatic cancer patients using in vitro, in vivo, and ex vivo models. If successful, this work could help identify therapeutic targets and potential new therapies for pancreatic cancer.





Modulating Neural Signaling in the Treatment of Pancreatic Cancer

Timothy Wang, Ph.D., and Susan Bates, M.D., Columbia University Medical Center

Drs. Wang and Bates have previously studied the direct contribution of the vagus nerve, cholinergic signaling, and muscarinic receptors to PDAC and its progression. They were awarded an FY20 TRPA to investigate the effects of cholinergic signaling in suppressing cancer growth and determine if muscarinic agonists (anti-cholinergic agents) can act as an effective treatment option for PDAC. They plan to conduct mechanistic studies in cell lines and examine cholinergic signaling on antitumor immune response in animal models. In addition, the PIs will conduct a Phase 2A clinical trial of bethanechol, a cholinergic agent, given in combination with gemcitabine plus nab-paclitaxel prior to surgical resection of tumors to determine if the combination can improve patient outcomes. As bethanechol is a drug already approved by the U.S. Food and Drug Administration for other indications, a positive finding from this award could support larger clinical trials and swiftly contribute to a change in clinical treatment of PDAC.

For more information, visit:
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