Congressionally Directed Medical Research Programs

CDMRP

Department of Defense

https://cdmrp.army.mil

Peer Reviewed Cancer Research Program

VISION

To advance mission readiness of U.S. military members affected by cancer and to improve quality of life by decreasing the burden of cancer on Service members, their families and the American public

MISSION

To successfully promote high-impact research for cancer prevention, detection, treatment, and survivorship

PROGRAM HISTORY

Since fiscal year 2009 (FY09), Congress has appropriated $429.8 million (M) to the Department of Defense Peer Review Cancer Research Program (PRCRP), which in turn has invested in cancer research covering over 20 topic areas. Each year, Congress determines which topic areas will be funded through the program. The PRCRP offers a variety of funding mechanisms.

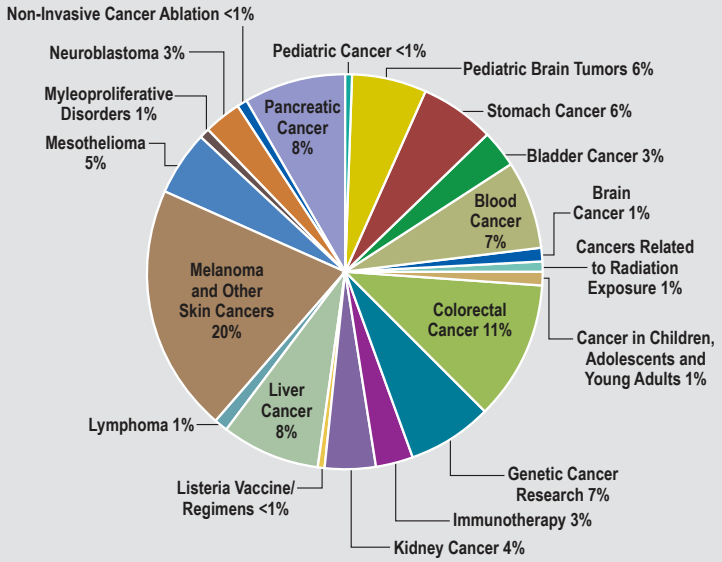
PRCRP MILITARY HEALTH FOCUS AREAS

- Exposure Research: Addresses risks associated with environmental exposures due to deployment.
- Mission Readiness Research: Addresses knowledge gaps in cancer research or patient care that may affect mission-readiness and the health of all military beneficiaries.

HIGH-IMPACT ADVANCES SUPPORTED BY THE PRCRP

- A combination of CXCL12/CXCR4 blockade with a mesothelin targeted immunotherapy produced two provisional patents for treatment of mesothelioma and ovarian cancer.
- A combination of anti-RANKL antibody and checkpoint inhibitors produced a phase II clinical trial for the treatment of metastatic melanoma.

PROGRAM PORTFOLIO



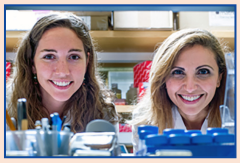
TOPIC AREAS[1]

- Adrenal Cancer[2]
- Blood Cancers
- Cancer in Children, Adolescents, and Young Adults
- Liver Cancer
- Lymphoma
- Myeloma
- Neuroblastoma
- Pancreatic Cancer
- Pediatric Brain Tumors

[1] Two program summary sheets were prepared. The following topic areas are discussed on the second program summary sheet: Bladder Cancer, Brain Cancer, Colorectal Cancer, Immunotherapy, Listeria Regimens for Cancer, Melanoma and Other Skin Cancers, Mesothelioma, and Stomach Cancer.

[2] Adrenal cancer was a new topic area for the FY18 PRCRP. Awards for this topic area were not finalized at the time of publication.

Biology/Etiology — **Blood Cancers**



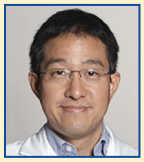
Through her FY12 Visionary Postdoctoral Fellowship Award, **Dr. Michaela Reagan** and her mentor, **Dr. Irene Ghobrial** (shown left to right), developed a novel cell culture model based on a silk-protein scaffold that better mimics tumor growth of multiple myeloma in the bone than traditional culture models. She identified the first microRNA (miR), a short regulatory nucleic acid that is abnormally expressed in bone cancer patients. Targeting this miR could lead to therapeutics that enhance bone healing to fight cancer-induced bone disease and potentially reduce tumor burden.

Dr. Zhiqiang Qin received a FY14 Career Development Award to investigate the role of hepatocyte growth factor (HGF) and its receptor (c-Met) in primary effusion lymphoma (PEL) pathogenesis. Notably, results published in *Blood* demonstrated that targeting the HGF/c-MET pathway induced Kaposi sarcoma herpes virus and PEL cell apoptosis through cell cycle arrest and DNA damage.

Diagnosis/Detection — **Brain Cancer**

Dr. Jason Warram received a FY17 Idea Award with Special Focus to synthesize and test in preclinical models an imaging probe that is both sensitive and specific in distinguishing glioblastoma tissue from healthy tissue. New imaging methods will help surgeons spare healthy cells and remove only malignant cells.

Prevention — **Liver Cancer**



With support from a FY15 Idea Award with Special Focus, **Dr. Yujin Hoshida** is developing a cell culture model that uses oncogenic variants of the hepatitis C virus for fast-track identification of cancer preventive targets and biomarkers, thus identifying molecular changes that persist after viral clearance that could lead to liver cancer.

Prognosis — **Neuroblastoma**

Dr. Clinton Stewart and his Co-Principal Investigator, **Dr. Andras Sablauer** (shown left to right), received a FY13 Idea Award with Special Focus to build a novel pharmacokinetic model with an individualized tumor compartment and 3D transport model to better understand and quantify chemotherapeutic uptake in neuroblastoma tumors. This model more accurately predicted drug effects within the 3D geometry of individual neuroblastoma tumors.

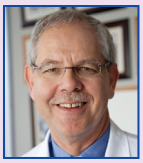
Treatment — **Pancreatic Cancer**

In FY14, **Dr. Michael Curran** received a Career Development Award to test the hypothesis that it was possible to take advantage of the stroma by using immune cell agonists to help, rather than hinder, the immune system. Dr. Curran proposed a combination of T cell stimulation with a Stimulator of Interferon Genes agonist. Through his exhaustive efforts, Dr. Curran's work has resulted in an improved animal model that more closely represents human pancreatic cancer and the development of a novel assay capable of identifying which agonist combinations are optimal.

Treatment — **Pediatric Brain Tumors**

Delivery of oncolytic herpes simplex virotherapy (oHSV) into the spinal fluid offers several advantages for the treatment of medulloblastoma (MB). However, there are toxicity concerns involved with intraventricular delivery of oHSV. **Dr. Gregory Friedman** received a Career Development Award in FY14 to test whether the toxicity is due to an inflammatory immune response to the oHSV and whether it can be prevented by administering an immune regulator. Dr. Friedman characterized the nature of the toxicity and observed that toxicity is dose-dependent. He was then able to build on this observation and show that this lower dose of oHSV is efficacious in a mouse model of MB.

Survivorship — **Liver Cancer**



With a FY15 Translational Team Science Award, **Drs. Scott Friedman, Josep Llovet, Amaia Lujambio, Scott Lowe,** and **Augusto Villanueva** (shown left to right) are investigating the mechanism of sorafenib treatment evasion by primary hepatocellular carcinoma. Determining mechanisms of resistance will improve outcomes, aid in drug development, and impact survivorship.

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