REPORT TO THE U.S. CONGRESS

U.S. ARMY MEDICAL RESEARCH AND MATERIEL COMMAND

CONGRESSIONALLY DIRECTED MEDICAL RESEARCH PROGRAMS

PEER REVIEWED CANCER RESEARCH PROGRAM

5 March 2014

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Peer Reviewed Cancer Research Program
Report to Congress

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BACKGROUND AND PURPOSE OF REPORT

The U.S. Army Medical Research and Materiel Command (USAMRMC) is a major subordinate Command of the U.S. Army Medical Command. The USAMRMC manages biomedical research and development programs that are part of the Department of Defense (DoD), Defense Health Program, and Army Science and Technology Master Plans. The Commanding General (CG), USAMRMC, is assigned authority as the Executive Agent for a number of medical research, development, and acquisition programs. Congressional appropriations totaling over $7 billion for fiscal years 1992 to 2013 (FY92-FY13), assigned to the USAMRMC, are managed by the office of the Congressionally Directed Medical Research Programs (CDMRP), a subordinate organization within the USAMRMC. Biomedical research supported by these funds includes research in autism spectrum disorder; breast, prostate, lung, ovarian, melanoma, and genetic cancers; pediatric brain tumors, pediatric cancers, neurofibromatosis; tuberous sclerosis complex; Gulf War illness; psychological health and traumatic brain injury; and other research.

In additional efforts, the CDMRP provides support to USAMRMC-based Joint Program Committees (JPCs) for program execution and awards management that complements core DoD research and development. The combined approach leverages the CDMRP's expertise in research program administration with the JPCs' expertise in technical areas for the advancement of the mission to expedite the delivery of products and solutions that address challenges related to service members and their families. In FY13, the CDMRP assisted with program execution in the areas of military infectious diseases, psychological health, neurotrauma, vision, neurosensory (pain, hearing, balance, and tinnitus) and neuromusculoskeletal injury research, as well as regenerative medicine.

Tasked for program execution and management, the CDMRP is responsible for planning, coordinating, integrating, programming, budgeting, and executing the research programs. The CDMRP's flexible execution and management cycle includes the receipt of annual congressional appropriations, inaugural stakeholders meeting for new programs, vision setting, release of request for pre-applications or full applications, pre-application screening and invitation to submit full applications, full application receipt and review, recommendation of grants for funding, and oversight of research grants.

Each program's advisory board (Integration Panel, Steering Committee, or JPC) of leading scientists, clinicians, military members, and/or disease survivors (consumers), recommends an investment strategy for the upcoming year that meets the unique needs of the research field, consumer community, and the military. The investment strategy is unique to each program and to each fiscal year cycle. By revisiting the investment strategy yearly, the program is able to explore innovative scientific ideas and research gaps spanning from basic laboratory science to clinical trials. Program announcements requesting research applications through specific award mechanisms are subsequently prepared and released.

The basic programmatic cycle for award recommendation is a two-tiered system. To ensure that each program's research portfolio reflects not only the most meritorious science, but also the most programmatically relevant research, the CDMRP developed this two-tiered model based upon recommendations from a Institute of Medicine (IOM) 1993 report.[1] The IOM

recommended a two-step review procedure for research applications composed of a scientific peer review and a separate programmatic review. The scientific peer review is conducted by an external panel recruited specifically for each peer review session and therefore is not a standing panel. Peer review involves the expertise of scientists, clinicians, military members, and consumers. The peer review process includes evaluation of the applications based on a criterion process as delineated in the program announcements. Each application is judged on its own scientific and technical merit with respect to the described criteria. The second tier of review, programmatic review, is conducted by the program's designated advisory panel, such as the Integration Panel for the Peer Reviewed Cancer Research Program (PRCRP). The advisory panel for each program is charged with reviewing the applications based on the scientific peer review ratings and summaries, a balanced portfolio, programmatic intent, and relevance to the congressional language. Scientifically sound applications that best meet the program's interests and goals are recommended to the CG, USAMRMC, for funding. Once the CG approves the funding recommendations, awards are made in the form of one- to five-year grants, contracts, or cooperative agreements, and assigned to Science Officers (SO) for full-cycle support of research and outcomes. During the management of the lifecycle of an award, the SO continues to monitor the research project for progress and outcomes as well as possible issues or pitfalls. In addition, the Program Office reviews all awards at negotiation and throughout their period of performance for any possible overlap or duplication with other funding agencies, both federal and non-federal. A detailed explanation of this process can be found at the CDMRP website (http://cdmrp.army.mil/funding/researchDup). The programs that comprise the CDMRP are scientifically sound, innovative, and responsive to congressional intent and the needs of the service members, their family and the American public. The USAMRMC and the CDMRP have been praised by the IOM, which issued a report in 1997 stating it was favorably impressed with the processes implemented by the CDMRP and supported its continuation.[2]

The DoD has been directed to submit a report to the congressional defense committees on the status of the PRCRP, and, for each research area, include the funding amount awarded, the progress of research, and the relevance to service members and their families. This report provides an update on the detailed status of the FY09-FY13 PRCRP cycle, research accomplishments, and the relevance of this type of research for U.S. military service members and their families.

FY09-FY13 PEER REVIEWED CANCER RESEARCH PROGRAM

Public Law 110-329 from the Consolidated Security, Disaster Assistance, and Continuing Appropriations Act, 2009, directed that $16M be appropriated for the FY09 PRCRP. The funds and directed research topic areas included $4M for melanoma and other skin cancers as related to deployments of service members to areas of high exposure, $2M for pediatric brain tumors within the field of childhood cancer research, $8M for genetic cancer and its relation to exposure to the various environments that are unique to a military lifestyle, and $2M for noninvasive cancer ablation treatment including selective targeting with nanoparticles. An inaugural stakeholders meeting was held on 23-24 February 2009 that included leading scientists, clinicians, military members, and consumers. The PRCRP Integration Panel was established in April 2009 to conduct vision setting to review the recommendations made at the stakeholders

meeting, to craft a vision and mission of the program, and to develop an investment strategy. Several program announcements were released in June 2009. Following the two levels of review, 38 awards across the four different topic areas were approved by the CG, USAMRMC.

In FY10, Public Law 111-118 from the 2010 Defense Appropriations Act directed funding of $15M for a "peer reviewed cancer research program" that would research cancers not addressed in the breast, prostate, lung, and ovarian cancer research programs currently executed by the DoD and, specifically, the USAMRMC. Specific topics included 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, *Listeria* vaccine for cancer, and radiation protection utilizing nanotechnology. An Integration Panel consisting of members of the FY09 PRCRP Integration Panel and new members to represent the congressional target areas was convened in March 2010. Program announcements were released in May and June 2010. Following the two levels of review, 32 awards across the different topic areas were approved by the CG, USAMRMC.

For FY11, Public Law 112-10 from the Department of Defense and Full Year Continuing Appropriations Act directed $16M for the PRCRP. The Congressional Record of the Senate dated 14 December 2010 specified topics areas of melanoma and other skin cancers, pediatric cancer research, genetic cancer research, kidney cancer, blood cancer, colorectal cancer, pancreatic cancer, mesothelioma, *Listeria* vaccine for infectious disease and cancer, and radiation protection utilizing nanotechnology. This was later revised to remove *Listeria* vaccine for infectious disease. Further clarification acknowledged the requirement for relevance to service members and their families and that the funding would be directed toward research on cancers not addressed in the breast, prostate, lung, and ovarian cancer research programs currently executed by the DoD and, specifically, the USAMRMC. Vision setting was held on 19 April 2011. The FY11 Integration Panel consisting of members of the FY10 PRCRP Integration Panel and new members to represent the congressional target areas was convened to discuss research gaps, community needs, focus areas, and an investment strategy. Program announcements were released in June and September 2011. Full application receipt was in October and November 2011. Following the CDMRP process of review, 43 awards across the different topic areas were approved by the CG, USAMRMC.

For FY12, Public Law 112-74 directed $12.8M for the PRCRP. The committee provided funds directed to be used to conduct research in melanoma and other skin cancers, pediatric brain tumors, genetic cancer, pancreatic cancer, kidney cancer, blood cancer, colorectal cancer, mesothelioma, and *Listeria* vaccine for infectious disease and cancer. This was later revised to remove *Listeria* vaccine for infectious disease. Vision setting for FY12 PRCRP was held in March 2012 with program announcements released in April 2012. Pre-application receipt was in June 2012 with screening completed in July 2012. Following full application receipt in September 2012 and a two-tiered review, 31 awards across the different topic areas were approved by the CG, USAMRMC. Prior to completion of FY12 award negotiations, sequestration affected the total sum available for funding awards. Several awards were withdrawn due to scientific or funding overlap and/or duplication issues, which allowed for all of the remaining awards to be made without decreases in budgets due to sequestration.

For FY13, Public Law 113-6 directed $15M for the PRCRP. The committee provided funds directed to be used to conduct research in melanoma and other skin cancers, pediatric brain tumors, genetic cancer, pancreatic cancer, kidney cancer, blood cancer, colorectal cancer, mesothelioma, and neuroblastoma. Vision setting for FY13 PRCRP was held in January 2013. Program announcements were released in May 2013. In FY13 a military focus targeted program announcement, Idea Award with Special Focus, was released to solicit applications in areas of relevance to military exposures and cancer risks. Additionally, the Career Development Award program announcement also encouraged applications in military-relevant focus areas including as military deployments, environmental exposures, and risk. Pre-application receipt was in July with screening taking place in September 2013. Full application receipt was in October 2013 with peer review in December 2013. Programmatic review was in February 2014 with final award obligation no later than 30 September 2014.

FY14 PEER REVIEWED CANCER RESEARCH PROGRAM

In FY14, the Public Law 113-76, Consolidated Appropriations Act, provided $25M for the PRCRP. As stated in the HR 3547 Joint Explanatory Statement for Defense dated 14 January 2014, the Secretary of the Navy was directed to take all necessary steps to ensure that any health effects resulting from the humanitarian mission efforts during Operation Tomodachi in response to the devastating earthquake and tsunami that hit Japan in March 2011 are fully addressed. It also directed that a portion of the $25M PRCRP funds should be utilized, if necessary, to carry out additional research on the health effects of radiation exposure as it relates to cancer.. The committee directed these funds to be used to conduct research in blood cancer, colorectal cancer, genetic cancer research, kidney cancer, *Listeria* vaccine for cancer, melanoma and other skin cancers, mesothelioma, myeloproliferative disorders, neuroblastoma, pancreatic cancer, pediatric brain tumors, and cancers related to radiation exposure. Vision setting for FY14 PRCRP was held in February 2014. Program announcements will be released before or during May 2014. Pre-application receipt and screening will take place approximately 90 days after release of the program announcements. Full application receipt should be scheduled approximately eight weeks after the invitation to submit is posted to the applicants. Peer review will be scheduled about eight weeks later, with programmatic review approximately 60 days later. Award obligation will be no later than 30 September 2015.

RESEARCH AREA INVESTMENT AND PROGRESS

Research area investment is detailed in Appendix A. Research areas included are blood cancer, colorectal cancer, genetic cancer (and genomic medicine), kidney cancer, *Listeria* vaccine for cancer, melanoma and other skin cancers, non-invasive cancer ablation, and pediatric brain tumor. In FY10, no applications in the research areas of radiation protection utilizing nanotechnology were recommended or selected for funding. Award information for FY13 is pending completion of programmatic cycle for award selection and management.

A tabular summary of the proposed work and progress for each of the awards for FY09 and FY12 is contained in Appendix B. The log number, topic area, last name of principal

investigator, award amount, institution, title, research progress, and military relevance are noted for each award. Both FY12 and FY13 were affected by sequestration where 7%-8% of funds were cut and, therefore, were not available to be used for the program (were not budgeted for PRCRP management).

RELEVANCE TO SERVICE MEMBERS AND THEIR FAMILIES

Members of the military are exposed to hazardous environments and dangerous deployments due to the nature of their service.[3] Hazardous exposures can lead to the development of cancer, many of which present a potential risk for service members and their families. The Veterans Health Administration (VHA) identified malignancies that may be associated with military service (VHA-Directive 2003-34, Attachment B). Exposure to chemical weapons, or storage, ionizing radiation, herbicides, electromagnetic fields, jet fuel, organic materials, etc. have been linked to different malignancies (see Table I).

TABLE I: Malignancies Associated with Military Service[a]

Exposure Type	Cancer Type
Full-body to Nitrogen, Sulfur Mustard or Nitrogen Mustard [b]	Nasopharynx, larynx, lung (except mesothelioma), squamous cell carcinoma of the skin, and acute nonlymphocytic leukemia
Ionizing Radiation [b,c]	Leukemia (except chronic lymphocytic leukemia), thyroid, bone, brain, breast, colon, lung, ovary, pharynx, esophagus, stomach, small intestine, pancreas, bile ducts, gall bladder, salivary gland, urinary tract (kidneys, renal pelvis, ureter, urinary bladder and urethra), lymphomas (except Hodgkin's disease), multiple myeloma, primary liver cancer, and bronchioloalveolar carcinoma (a rare lung cancer)
Certain Herbicide Agents [b-d]	Non-Hodgkin's lymphoma, soft-tissue sarcoma (other than osteosarcoma, chondrosarcoma, Kaposi's sarcoma, or mesothelioma), Hodgkin's disease, multiple myeloma, respiratory cancers (lung, larynx, trachea and bronchus), prostate cancer, chronic lymphocytic leukemia
Specific physical, chemical, or biological factors (electromagnetic fields, jet fuel, volatile organic materials, etc) [b-f]	Melanoma, testicular, thyroid, cervical, vulvar, oral squamous cell, pancreatic, and uterine

[a]VHA-Directive 2003-34.; [b] Crawford RS, Wu J, Park D, and Barbour GL. 2007. A study of cancer in the military beneficiary population. *Military Medicine* 172:1084-1088.; [c]The Selected Cancers Cooperative Study Group. 1990. The association of selected cancers with service in the US military in Vietnam. I. non-Hodgkin's lymphoma. *Arch Intern Med* 150:2473-2483.; [d] Department of Defense Automated Central Tumor Registry; [e] D'Este C, Attia JR, Brown AM, Gibberd R, Tavener M, Guest M, Horsley K, Harrex W, and Ross J. 2008. SHOAMP Study Team. 2008 Cancer incidence and mortality in aircraft maintenance workers. *Am J Ind Med* 51:16-23.;[f] Dalanger NA, Kang HK, and Thomas TL. 1995. Cancer mortality patterns among women who served in the military: The Vietnam Experience. *J Occup Environ Med* 37:298-305.

The possibility of direct or indirect links to cancer development in service members and their families as a result of military service or deployment is still undergoing investigation.

Detailed analysis by The Automated Central Tumor Registry of the DoD published data demonstrated that the incidence of melanoma was higher in the U.S. military population in comparison to the U.S. general population.[4] The Senate Appropriations Committee on Defense for FY14 acknowledged that melanoma diagnoses are increasing in service members and that it is the fifth most common cancer among veterans due to the exposures to areas of high ultraviolet radiation. The Committee has encouraged investments in melanoma research to combat this cancer risk (DoD Senate Appropriations Bill, 2014, S. 1429, page 194). Current studies by the PRCRP include examination of risk factors as well as susceptibility and progression of the disease. Dr. Mohammed Kashani-Sabet and Dr. Sancy Leachman were funded by a FY09 Collaborative Translational Science Award to identify and validate novel determinants of melanoma risk in a U.S. military population (DoD contract number W81XWH-10-2-0185). Studies are still ongoing.

The investigation into multiple cancer risks and military service include the study of specific chemical exposures. A meta-analysis using published epidemiological data on cancer risk in male military pilots, civilian pilots, and flight attendants revealed a higher standardized incidence ratio for melanoma and other skin cancers in those with exposure to specific physical, chemical, or biological factors (electromagnetic fields, jet fuel, volatile organic materials, etc.).[5] In addition, studies of common military exposures, such as aircraft maintenance, have been associated with an increased risk of cancer.[6] A recent study by Fastje et al.[7] and funded by the PRCRP, showed that *in utero* exposure to tungsten and other environmental agents primed the immune system for aberrant responses to infectious agents and could lead to increased carcinogenic risk.

Yamane reported that the most frequent cancers diagnosed in Air Force service members between 1989 and 2002 were different from the general U.S. population, with a higher[8,9] incidence of melanoma, testicular, thyroid, cervical, and vulvar cancers in the Air Force population,[8] particularly cervical and vulvar cancer. Another review demonstrated a higher rate of prostate cancer in the military beneficiary population compared to the general population.[10] Occupational exposures is a frequent risk of military service. Asbestos-related lung diseases such as mesothelioma are a known risk to Naval shipyard work.[11] It is generally accepted that nearly 95% of all mesothelioma cases are due to asbestos exposure.

Hodgkin's disease, a blood cancer, was the most common cancer diagnosis in men who served in the U.S. Navy.[12] The Selected Cancers Cooperative Study Group showed that veterans of the Vietnam War had a 50% increase in risk of Hodgkin's disease as compared to subjects who had not served in Vietnam.[13] Evidence links an increased risk for soft tissue sarcomas, non-Hodgkin's lymphoma, Hodgkin's disease, and chronic lymphocytic leukemia to Vietnam War service and exposure to herbicides such as Agent Orange.[14] Cancer patterns of Vietnam War military women nurses in comparison to non-Vietnam War military women nurses and the general population showed that site-specific cancer patterns were different, with excess deaths from pancreatic and uterine corpus cancers in the Vietnam War military women nurses.[15] As the

configuration of the military population changes to include more women, consideration into research on their risks and exposures is critical.

Chemical agents are not the only hazards service members might encounter during deployments. Many deployments are to developing countries where there may be a higher incidence of infectious vectors. It is estimated that over 18% of cancers may be a result of infections such as gastric adenocarcinoma, cervical carcinoma, and hepatocarcinoma.[16] Service members are increasingly presenting with sero-positive scores for infectious agents such as *Helicobacter pylori.*[17] These service members may be more at risk for chronic inflammation and the development of cancers of the gastrointestinal track.

Indirect causative agents for cancer risk are also under investigation. Two studies funded by the PRCRP recently published results that linked higher stress to increased cancer risk.[18, 19] Chronic stress murine models revealed an important link to attenuation of p53 (a tumor suppressor) and tumorigenesis.[18] Another study demonstrated the potent effect of neuropeptides and other stress mediators on tumor development and progression.[19] Stress and related issues are a concern of the military and the ultimate health and well-being of service members both during and after deployment.

Military families may also be at risk for developing cancers due to environmental exposures as shown by investigations into leukemia clusters near military aviation facilities.[20] Additionally, transgenerational occupational exposures may lead to increased risk of cancer development in progeny. Children of Vietnam War veterans have an increased risk of developing acute myeloid leukemia.[14] As shown by Hicks et al.,[21] children of men in the Air Force had a higher incidence of tumors of the central nervous system (brain and spinal cord) and lymphatic system. The VHA acknowledged the toll of cancer on service members and their families when releasing its National Cancer Strategy in 2003 (VHA-Directive 2003-34). A serious illness in a family member, such as cancer, may have consequences on the warfighter's ability to complete the mission. A healthy family unit, free of serious illnesses, allows the service member to focus on his or her role as a warfighter and facilitates the overarching military mission. There are a total of 355,442 military beneficiaries with a cancer diagnosis, for a prevalence of 4.1%, comprised of over 60 different cancer types.[22] The cost of cancer care within the Military Health System in FY02 was over $1 billion.[22] Funding studies on the detection, diagnosis, treatment, and prevention of these diseases benefits both the warfighter and the American public, ultimately leading to increased survival rates and decreased costs of medical care.

In summary, the CDMRP, USAMRMC, manages the FY09-FY13 PRCRP using its established and highly recognized management process. The FY14 PRCRP directly impacts military welfare by providing research into cancers that may develop due to exposure in various uniquely military environments. The CDMRP will plan, execute, and manage the FY09-FY14 PRCRP with the same rigor and integrity it has demonstrated for other research programs.

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APPENDIX A: TOTAL RESEARCH DOLLARS INVESTED PER TOPIC AREA

TOTAL DOLLARS INVESTED PER TOPIC AREA: FY09-FY12

Topic Area	Total Dollars Recommended for Investment ($) FY12	Total Invested FY09-FY12 ($)
Blood Cancer	3,041,168	6,895,929
Colorectal Cancer	2,146,329	5,445,502
Genetic Cancer[1]	417,501	10,490,884
Kidney Cancer	746,160	3,059,150
Listeria Vaccine for Cancer	0	839,200
Melanoma and Other Skin Cancers[2]	1,218,000	9,914,390
Mesothelioma	636,613	1,805,333
Non-invasive cancer ablation[3]	0[4]	1,753,431
Pancreatic Cancer	1,539,122	5,225,804
Pediatric Cancer	0	770,586
Pediatric Brain Tumor	440,425	4,719,564
Radiation Protection utilizing nanotechnology[5]	0	0
Total Dollars for Investment[6]	**10,185,318**	**50,919,773**

[1]Topic area includes FY09 congressional language: genetic cancer and its relation to exposures to the various environments that are unique to the military lifestyle and the FY10 congressional language: genetic cancer research and genomic medicine.
[2]Topic area includes FY09 congressional language: melanoma and other skin cancers as related to deployments of service members to areas of high exposure and the FY10 congressional language: melanoma and other skin cancers.
[3]Non-invasive cancer ablation treatment including selective targeting with nanoparticles.
[4]No applications met the intention and scope of the program announcement for recommendation for funding.
[5]No full applications were submitted for this topic area.
[6] Total appropriations for FY09-FY12 was $59.8M; total investment in research dollars is less USAMRMC and CDMRP management costs (12.1%) and FY12 sequestration costs ($938,860).

APPENDIX B: FISCAL YEAR 2009 (FY09)-FY12 PEER REVIEWED CANCER RESEARCH PROGRAM RESEARCH LIST AND MILITARY RELEVANCE OF RESEARCH

Log No/ Amount/ Status	Principal Investigator	Institution	Application Title	Research Project (RP) and Military Relevance (MR)
Blood Cancer				
CA100164 $545,036 Open	Trobridge	Washington State University, Pullman	Identification of Biomarkers for Myelodysplastic Syndrome (MDS) and Acute Myeloid Leukemia (AML) Using a Novel High-Throughput Forward Mutagenesis Screen	RP: Mutagenesis screen and drug development study for biomarkers of myelodysplastic syndrome (MDS) and acute myelogenous leukemia (AML). Generated MDS and AML transplanted mice for biomarker screening. Identified a candidate gene that is differentially expressed in AML patients. MR: Military personnel are at risk of exposure to alkylating agents, in the form of chemical weapons, and ionizing radiation, from nuclear and/or radioactive sources, that can cause therapy-related AML (t-AML)/ therapy-related MDS (t-MDS).
CA100254 $443,899 Open	Sarantopoulos	University of North Carolina at Chapel Hill	BAFF-Driven Targeted Immunotherapy for Patients with Leukemia	RP: Study how BAFF (B-cell activating factor) promotes specific anti-leukemia responses to develop novel therapeutic agents for leukemia. Established two murine leukemia models for hematopoietic stem cell transplantation and vaccination treatment. Identified B cell subsets related to chronic graft versus host disease and graft versus leukemia. MR: The environmental exposure to cytotoxins and chemicals during deployment is associated with higher incidence of leukemia.
CA100623 $1,138,820 Open	Lanza: Tomasson	Washington University	Treatment of Multiple Myeloma with VLA4-Targeted Nanoparticles Delivering Novel c-MYC Inhibitor Prodrug	RP: Develop nanoparticle encapsulated prodrug to inhibit Myc and test its efficacy on multiple myeloma (MM). The Myc prodrug markedly improved bioactivity in several myeloma cell types. The prodrug decreased the S-phase of mitosis of myeloma cells and extended the days of survival of mice with metastatic myeloma by 50% compared to controls. Outcomes: Three manuscripts are under review. One National Institutes of Health (NIH) R01 grant has been submitted. MR: Male veterans using Department of Veterans Affairs (VA) hospitals are at 51% increased risk of MM compared to the general public.

Log No/ Amount/ Status	Principal Investigator	Institution	Application Title	Research Project (RP) and Military Relevance (MR)
CA110020 $250,662 Open	Masamha	University of Texas Health Science Center at Houston	Deciphering the Mechanism of Alternative Cleavage and Polyadenylation in Mantle Cell Lymphoma (MCL)	RP: Study of the mechanism of cyclin D1 mRNA alternative cleavage and polyadenylation in aggressive Mantle Cell Lymphoma. Demonstrated that human cleavage factor IM (CFIm25) regulates changes in alternative cleavage and polyadenylation in cyclin D1 and other genes. Found CFIm25 depletion leads to a decrease in cell proliferation. MR: The environmental exposure to cytotoxins and chemicals during deployment is associated with a higher incidence of blood cancers.
CA110081 $376,790 Open	Newman	Stanford University	Genomic Signatures for Integrative Models of Clinical Heterogeneity in Patients with Follicular Lymphoma	RP: Development of a novel method to determine which follicular lymphoma patients will be responsive to treatment. The Principal Investigator (PI) developed a novel computational method to validate therapeutic response. Using this method, the PI found that effector memory T cells and the frequency of CDR1 tyrosines are potential biomarkers for immunotherapeutic responses. http://cdmrp.army.mil/prcrp/research_highlights/13newman_alizadeh_highlight MR: The environmental exposure to cytotoxins and chemicals during deployment is associated with a higher incidence of blood cancers.
CA110096 $378,000 Open	McClellan	Stanford University	Reprogramming of Human Acute Lymphoblastic Leukemia Cells by Myeloid Transdifferentiation	RP: Reprogram human B cell acute lymphoblastic leukemia (B-ALL) cells in vitro to characterize the genes and to determine if it can be triggered in vivo for disease regression. Demonstrated that 8 out of 24 adult B-ALL patients can be induced to transdifferentiate to the myeloid lineage, that the transdifferentiated cells resemble and function as normal human macrophages, and that transdifferentiation of malignant B-ALL cells reduces the disease in immunodeficient mice. MR: The environmental exposure to cytotoxins and chemicals during deployment is associated with a higher incidence of blood cancers.
CA110584 $275,334 Open	Reuther	H. Lee Moffitt Cancer Center & Research Institute at the University of South Florida	Enhancing Targeted Therapy for Myeloproliferative Neoplasms	RP: This study will focus on the molecular targeted therapy for myeloproliferative neoplasms and how it can be enhanced by combination therapy with modulators of lipid biosynthesis. MR: The environmental exposure to cytotoxins and chemicals during deployment is associated with a higher incidence of blood cancers.

Log No/ Amount/ Status	Principal Investigator	Institution	Application Title	Research Project (RP) and Military Relevance (MR)
CA110791 $315,922 Open	Wei	University of Texas M.D. Anderson Cancer Center	Innate Immunity Dysregulation in Myelodysplastic Syndromes	RP: Investigate whether a signaling axis is formed by Toll-like receptor activation of NF-κB, is maintained by the histone demethylase JMJD3, and is central to the pathogenesis of MDS. Completed a systematic gene expression profiling of key components of the TLR2-JMJD3-mediated innate immunity signaling pathway. Established associations between the deregulation of TLR2-JMJD3 innate immunity genes and key prognostic results of patients with MDS. Demonstrated that inhibition of TLR2 and JMJD3 could rescue the differentiation of erythroid lineage in patients with MDS. MR: Military personnel are at risk of exposure to alkylating agents, in the form of chemical weapons, and ionizing radiation, from nuclear and/or radioactive sources, that can cause t-AML/t-MDS.
CA110834 $200,000 Open	FitzGerald	National Cancer Institute	Anti-CDR3 Therapy for B-Cell Malignancies	RP: Devise a proof-of-concept method for rapidly producing B-cell cancer-specific immunotherapy molecules customizable to individual patients. Cloned, sequenced, and engineered the variable region of two surface immunoglobulin molecules. These molecules were detected on the surface of the Mec1 and JVM3 cell lines. MR: The environmental exposure to cytotoxins and chemicals during deployment is associated with a higher incidence of blood cancers.
CA120025 $415,470 New Award	Reagan	Dana-Farber Cancer Institute	Reciprocal Interactions between Multiple Myeloma Cells and Osteoprogenitor Cells Affect Bone Formation and Tumor Growth	RP: Determination of the role of osteoprogenitor cells on the progression of multiple myeloma (MM) and elucidation of mechanisms by which MM cells alter their local bone microenvironment to encourage osteolysis. Research has just been initiated. MR: MM is a disease of particular relevance to our military veterans. Male veterans using VA hospitals are at 51% increased risk of MM compared to the general public.
CA120064 $308,400 New Award	Brander	Duke University	Understanding Drug Resistance to Targeted Therapeutics in Malignant B-Cell Lymphoproliferative Disorders	RP: The study aims to determine mechanisms for drug resistance in chronic lymphocytic leukemia and to define the role of the microenvironment in drug resistance to targeted small molecule inhibitors. Research has just been initiated. MR: This study will potentially advance the care of military patients with leukemia.

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CA120120 $344,007 New Award	Xie	Rutgers, State University of New Jersey	Regulation of Mitochondria Function by TRAF3 in B Lymphocytes and B-Cell Malignancies	RP: Study the role of mitochondria in TRAF3-induced apoptosis in B cells. TRAF3 is novel tumor suppressor in B lymphocytes. TRAF3 deletions and mutations occur in a variety of B cell malignancies. Research has just been initiated. MR: This study seeks to find new avenues for the prevention and treatment of major blood cancers, which impact many military personnel.
CA120128 $399,600 New Award	Halene	Yale University	Assessing the Mechanisms of MDS and Its Transformation to Leukemia in a Novel Humanized Mouse	RP: Development of a humanized mouse model for MDS and study of the kinetics of progression of MDS to leukemia in vivo. Research has just been initiated. MR: Myelodysplasia and leukemia affect military personnel with normal aging or with exposure to genotoxic agents.
CA120184 $420,000 New Award	Lin	Dana-Farber Cancer Institute	Understanding Selective Downregulation of c-Myc Expression through Inhibition of General Transcription Regulators in Multiple Myeloma	RP: Investigation of the selectivity of JQ1 in multiple myeloma (MM). JQ1 is a small molecular bromodomain and extra-terminal inhibitor that serves as a therapeutic target for MM. Research has just been initiated. MR: MM is a disease of particular relevance to military veterans. Male veterans using VA hospitals are at 51% increased risk of MM compared to the general public.
CA120212 $417,600 New Award	Cheloufi	Massachusetts General Hospital	Investigating Epigenetic Parallels between Carcinogenesis and Reprogramming to Pluripotency	RP: Identification of the epigenetic regulators of somatic cell reprogramming to pluripotent stem cells and characterization of the common molecular traits of cancer cells and induced pluripotent stem cells. Research has just been initiated. MR: The study has a broad impact on the understanding of cancer development and identification of novel cancer drug targets, which will lead to a better quality of life for service members and their families.
CA120373 $374,400 New Award	Liu	Indiana University, Indianapolis	Modulating Leukemia-Initiating Cell Quiescence to Improve Leukemia Treatment	RP: Determination of the role of necidin in the initiation of AML and characterization of whether lowering of necidin expression affects the response of leukemia-initiating cells to chemotherapy or radiotherapy. Research has just been initiated. MR: This study seeks to understand how necidin functions in normal and leukemic stem cells, which may lead to innovative clinical applications and benefit those military personnel impacted by the disease.

Log No/ Amount/ Status	Principal Investigator	Institution	Application Title	Research Project (RP) and Military Relevance (MR)
CA120381 $383,998 New Award	Reshef	University of Pennsylvania	Chemokine Receptor Signatures in Allogeneic Stem Cell Transplantation	RP: To determine the role of chemokine receptor expression in regulating the organ distribution of effector T cells after stem cell transplantation and to determine the effect of targeted chemokine receptor blockade on trafficking patterns of T-cell clones. Research has just been initiated. MR: Graft-versus-host disease is a major cause of morbidity and mortality in allogeneic stem cell transplantation in treatment of blood cancers.
Colorectal Cancer (CRC)				
CA100111 $313,725 Open	Jessup	National Cancer Institute	Inhibition of Embryonic Genes to Control Colorectal Cancer Metastasis	RP: Demonstrated NANOGP8 inhibition decreases cell proliferation and induces tumor cell death by targeting MCL-1. Also showed that vector-delivered shRNA to NANOGP8 can inhibit BCL-2 and BCL-XL to kill colorectal cancer cells. Outcome: *Oncogene* (2013) 32:4397-4405. MR: CRC is the second highest cause of cancer-specific mortality in the general public and military population. Approximately 50% of military beneficiaries diagnosed with colon or rectal carcinoma will die of the disease.
CA100512/ CA100512P1 $1,076,301 Combined Open	Eckhardt/ Tan	University of Colorado Denver	Collaborative Model for Acceleration of Individualized Therapy of Colon Cancer	RP: To use predictive biomarkers and novel preclinical models towards the discovery of colorectal cancer treatments. Three novel anti-cancer agents have been identified to develop predictive classifiers using preclinical CRC models. MR: The largest segment of the military, white males, has an incidence rate of 53/100,000, whereas black males have a higher incidence (and mortality) of 63/100,000. Only about 50% of CRC patients are completely cured by surgery; thus, recurrent and metastatic disease is an ongoing problem.
CA100879 $592,307 Open	Ellis	University of Texas M. D. Anderson Cancer Center	Microenvironmental Influence of Endothelial Cells on Colorectal Cancer Stem Cell Phenotype	RP: Study into the interactions of inflammation, endothelial cells, and cancer stem cells and the chemoresistance development. Identified and confirmed that soluble JAG1, a paracrine factor of endothelial cells regulates cancer stem cell phenotype in CRC cells. Outcome: *Cancer Cell* (2013) 23:171-185. MR: The understanding of critical pathways to resistance will support military cancer treatment of service members and their families.

Log No/ Amount/ Status	Principal Investigator	Institution	Application Title	Research Project (RP) and Military Relevance (MR)
CA110130 $364,800 Open	Yue	University of Notre Dame	Proteomic Analysis to Identify Functional Molecules in Drug Resistance Caused by E-Cadherin Knockdown in 3D-Cultured Colorectal Cancer Models	RP: Conduct a proteomic analysis to identify functional molecules in drug resistance caused by E-cadherin knockdown in 3D cultured colorectal cancer models. Established a 3D culture system to study epithelial-to-mesenchymal transition. Outcome: *J Proteome Res* (2013) 12:4176-4186. MR: CRC is the second highest cause of cancer-specific mortality in the general public and military population. Approximately 50% of military beneficiaries diagnosed with colon or rectal carcinoma will die of the disease.
CA110261 $318,000 Open	Potts	University of Texas Southwestern Medical Center at Dallas	Role of Germline MAGE Cancer-Testis Antigens in Colorectal Cancer	RP: To investigate the role of MAGE cancer-testis antigens as oncogenes driving cell transformation and tumorigenesis in CRC. Findings defined the oncogenic potential of the MAGE gene family and identified specific genetic contexts and signaling pathways involved during cell transformation. Outcome: *Cell* (2013) 152:1051-1064. MR: CRC is the second highest cause of cancer-specific mortality in the general public and military population. Approximately 50% of military beneficiaries diagnosed with colon or rectal carcinoma will die of the disease.
CA110495 $341,040 Open	Kufe	Dana-Farber Cancer Institute	Targeting of the MUC1-C Oncoprotein in Colitis-Associated Colorectal Cancer	RP: To explore the mechanisms responsible for the progression of inflammatory bowel disease to colorectal cancer for new strategies for drug development. Preliminary results indicate that MUC1-C is a potential therapeutic target. MR: CRC is the second highest cause of cancer-specific mortality in the general public and military population. Approximately 50% of military beneficiaries diagnosed with colon or rectal carcinoma will die of the disease.

Log No/ Amount/ Status	Principal Investigator	Institution	Application Title	Research Project (RP) and Military Relevance (MR)
CA111002 $293,000 Open	Mohamadzadeh	University of Florida	Reprogramming Intestinal Immunity by Novel L. Acidophilus Strains Results in Protective Immunity against Colon Cancer	RP: To elucidate the regulatory effects of *Lactobacillus acidophilus* surface layer proteins on induced intestinal inflammation and to demonstrate the regulatory effects of *L. acidophilus* SlpA in decreasing cancer-promoting inflammation in colonic polyposis. Results thus far suggest that lipoteichoic acid on the surface of *L. acidophilus* plays a pro-inflammatory role. MR: CRC is the second highest cause of cancer-specific mortality in the general public and military population. Approximately 50% of military beneficiaries diagnosed with colon or rectal carcinoma will die of the disease.
CA120198 $374,403 New Award	Roper	Tufts Medical Center	The Role of Akt Isoforms in Colorectal Cancer	RP: To determine the role of Akt1 and Akt2 in the induction, invasiveness, and metastatic potential of colorectal tumors and to determine the role of Akt isoform-dependent phosphorylation events in CRC growth and metastasis. Research has just been initiated. MR: This study seeks to identify new targets for the development of therapeutics for CRC, which would benefit service members and their families.
CA120206 $238,515 New Award	MacNeill	Wake Forest University Health Sciences	Electrically Conducting Polymer Nanoparticles to Selectively Target and Treat Metastatic Colorectal Cancer	RP: Development of near-infrared phototherapy using electrical conducting polymer nanoparticles to treat colorectal cancer. Research has just been initiated. MR: This new polymer-based nanomaterial holds promise to selectively target and treat CRC and benefit military personnel impacted by CRC.
CA120261 $363,411 New Award	LaBarbera	University of Colorado Denver - Anschutz Medical Campus	Novel Antimetastatic Agents for the Treatment of Drug-Resistant and Metastatic Colon Cancer	RP: Development of new competitive ATPase inhibitor of topoisomerase IIa that blocks t-cell transcription factor (TCF) transcription and inhibits the metastasis of CRC. Research has just been initiated. MR: Active military personnel, veterans, and family members are at considerable risk for CRC. Novel therapies that target TCF-transcription may prevent metastasis and recurrence of CRC.

Log No/ Amount/ Status	Principal Investigator	Institution	Application Title	Research Project (RP) and Military Relevance (MR)
CA120296 $379,200 New Award	Kizhakke Mattada	University of Virginia	Functional Characterization of CENP-A Post-Translational Modifications in Chromosome Segregation	RP: To study the mechanism of centromeric protein A (CENP-A) methylation and its role in chromosome segregation and cancer development. Research has just been initiated. MR: CRC is the second leading cause of cancer death in the U.S. This study could potentially lead to new targets for CRC treatment and reduce cancer burden among military beneficiaries.
CA120342 $417,600 New Award	Sebastian	Massachusetts General Hospital	Role of SIRT6 in Metabolic Reprogramming During Colorectal Carcinoma	RP: To study the role of SIRT6 in regulating glycolytic activity and transformation in CRC cells and determine the role of SIRT6 in CRC development. Research has just been initiated. MR: Understanding the metabolic reprogramming in CRC can offer an alternative way for therapeutic development and benefit the military personnel impacted by CRC.
CA120403 $373,200 New Award	Shah	University of Michigan, Ann Arbor	The Role of the Noncanonical NF-KappaB Pathway in Colon Cancer	RP: To identify the mechanism that activates NF-κB in colon cancer and to characterize this pathway's role in disease progression. Research has just been initiated. MR: This study will identify new targets for the development of therapeutics for CRC, which could benefit military personnel impacted by CRC.
Genetic Cancer				
CA093054 $113,319 Closed	Lantz	University of Arizona, Tucson	The Carcinogenic Potential of JP-8 and Tungsten in C57BL/6 Mice	RP: The study of environmental exposures (JP-8 and tungsten) known to be a health risk for service members. The project included interactions with viral infections, which may lead to long-term health consequences such as cancer development. Found that JP-8 alone did not cause reactivation of Epstein-Barr virus (MHV-68). Yet the combination of tungsten and other environmental agents with in utero exposure was able to prime the immune system for aberrant response to infectious agents. MR: Military personnel encounter environmental exposures related to their service that risk long-term health care issues, e.g., leukemia clusters.

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CA093111 $115,500 Closed	Yennu-Nanda	University of Texas M.D. Anderson Cancer Center	Role of Melanin in Oncogenesis	RP: This study tested the hypothesis that melanin itself can cause melanoma. Results showed the induction of excessive melanin production leads to changes in gene expression profiles dependent on skin type. MR: The prevention and early diagnosis modalities for skin cancers will be of immense benefit to U.S. soldiers on the frontlines, and in theater where high ultraviolet (UV) exposures increases risks.
CA093139 $559,548 Open	Cao	Clemson University	New Protein Modification under Nitrosative Stress	RP: Reactive nitrogen species leads to unstable DNA and carcinogenesis. Treatment of endonuclease V resulted in decreased DNA repair activity. Outcomes: *J Biol Chem* (2011) 285:41483-41490. *Nucleic Acids Res* (2011) 39:536-544. *Cell Mol Life Sci* (2013) 70:3145-3156. MR: Explosions and blasts occurring in battlefield intensify the contacts of military personnel with gaseous reactive nitrogen species and may inflict acute and chronic impact on the health of military personnel.
CA093155 $109,875 Closed	Wallis-Schultz	Texas A&M University	Functional Genomics Screen for Radiation Responsive Genes in Mutant Mouse Embryonic Stem Cells	RP: Identification of candidate genes responsible for cellular response to radiation exposure. This project involved the search for genes that affect the cellular response to radiation exposure and led to the identification and validation of seven differentially expressed candidate genes. MR: Armed forces members are occupationally at higher risk for exposure to carcinogenic radiation sources such as excessive sunlight and depleted uranium. Military exposures and risks include radiation exposures, which have long-term health risk factors and outcomes.
CA093176 $111,301 Closed	Su	Drexel University	Development of a Genetic Urine Test Using a Padlock-Mediated Microarray for Colon Cancer Screening	RP: Development of a colorectal cancer biomarker screening test using urine. Outcomes: *J Mol Diagn* (2012) 14:112-119. One patent. MR: Technological advances supported by the military increase the ability of military medicine to answer the needs of service members and their families and decrease general health care costs to the military.
CA093193 $109,125 Open	Elble	Southern Illinois University	A Novel Therapy for Metastatic Melanoma	RP: Study of the CLCA2 tumor suppressor as a gene therapy candidate for the prevention and treatment of melanoma. Demonstrated that restoration of CLCA2 expression is lethal to melanoma cells. MR: Deployment to areas of high UV exposures puts service members at increased risk for the development of melanoma and other skin cancers.

Log No/ Amount/ Status	Principal Investigator	Institution	Application Title	Research Project (RP) and Military Relevance (MR)
CA093204 $109,399 Closed	Yusuf	University of Alabama at Birmingham	Role of p16/INK4a in Ultraviolet Radiation-Induced Inflammation and Photocarcinogenesis	RP: To study the role of p16 in UVB radiation-induced inflammation and skin tumor development. Results indicate that p16/INK4a deficiency does lead to inflammation and associated cutaneous tumor development. MR: Deployment to areas of high UV exposure puts service members at increased risk for the development of melanoma and other skin cancers.
CA093257 $96,750 Open	Chen	Southern California Institute for Research and Education	Monitor microRNA Expression in Blood and Saliva to Detect Radiation-Induced Cancer Progression	RP: Development of a blood and/or saliva biomarker test for radiation-induced lymphomas. Determined that there is a stable baseline of serum miRNA profiles that can allow for the possible detection of changes associated with radiation induced lymphoma. MR: Military personnel are at higher risk of radiation exposures related to their service and therefore development of long-term health issues such as lymphomas and leukemias.
CA093269 $115,875 Completed	Ongkeko	University of California, San Diego	Tobacco and Nicotine Promote Acquisition of Cancer Stem Cell Properties in Head and Neck Cancer	RP: Study of the impact of nicotine and smoking on cancer stem cells. Determined that long-term nicotine exposure generates cells with cancer stem cell-like properties. Outcome: *PLoS One* (2012) 7, e51967. MR: Military personnel have a higher level of cigarette smoking than the general population. Nicotine and tobacco smoking is a risk factor for head and neck cancer.
CA093337 $114,500 Open	Kitlinska	Georgetown University	Neuropeptide Y: A New Link between Stress and Cancer	RP: Examination of the role of chronic exposure to psychological and physical stress on cancer progression via release of neuropeptide Y. Potent effects of neuropeptide Y and other stress mediators on tumor development and progression has been demonstrated. Outcomes: *J Oncol* (2010) 2010:539706. MR: Understanding the role of post-traumatic stress disorder and chronic stress in potential future cancer development of veterans is an important area of research.
CA093377 $383,315 Completed	Armani	University of Southern California	Real-Time Detection of DNA Methylation	RP: Development of a new tool to detect epigenetic changes in response to environmental factors that the service members encounter. The PI demonstrated sensor design, instrument design, surface chemistry of labeling, and detection of methylated DNA. Outcomes: *Applied Physics Letters* (2012) 100:013305. *Optics Lett* (2012), 37:4068-4070. Several manuscripts are under review. MR: Radiation exposure is of high risk in military populations.

Log No/ Amount/ Status	Principal Investigator	Institution	Application Title	Research Project (RP) and Military Relevance (MR)
CA093395 $560,148 Open	Brooks	Maine Medical Center	UV-Induced Triggering of a Biomechanical Initiation Switch within Collagen Promotes Development of a Melanoma-Permissive Microenvironment in the Skin	RP: Study of the mechanism of UV radiation damage and melanoma and other skin cancers. Found that UV radiation of extracellular matrix proteins altered the adhesion, migration, and proliferation of fibroblast, melanoma cells, and macrophages in vitro. UV exposure of mouse skin induced inflammation and exposure of the HU177 cryptic collagen epitope. MR: Deployment to areas of high UV exposure puts service members at increased risk for the development of melanoma and other skin cancers.
CA093415 $428,999 Open	Hu	University of Medicine and Dentistry of New Jersey, Robert Wood Johnson Medical School	Psychological Stress Promotes Irradiation-Induced Tumorigenesis through Attenuation of p53 Function	RP: Study of the linkage between chronic stress, radiation exposure, and cancer development. Demonstrated that (1) glucocorticoid is elevated during chronic stress and promotes tumorigenesis and (2) a negative regulator of the p53 gene, SGK1, is induced by glucocorticoids during chronic stress and promotes tumorigenesis. Provided a direct link between chronic stress and tumorigenesis in mouse models and revealed the attenuation of p53 function as an important underlying mechanism. Outcomes: *PNAS* (2012) 109:7013-7018. *Genes Cancer* (2012) 3:199-208. MR: Understanding the role of chronic stress and radiation exposure for potential future cancer development in the veteran population is of significant military relevance.
CA093417 $404,299 Open	Yusuf	University of Alabama at Birmingham	Regulation of Ultraviolet Radiation-Induced Cutaneous Photodamage and Nucleotide Excision Repair by Toll-Like Receptor-4	RP: Study of the gene expression and linkages to UV radiation damage. Found that Toll-like Receptor 4 (TLR4) deficiency enhanced DNA repair in mouse skin after UVB exposure; cytokine IL-2 had a significant effect on repairing cyclobutane pytimidine dimmers (CPD) in TLR4 knockout mice. Double knockout mice (TLR/Xpa) were generated. Outcome: *J Invest Dermatol* (2013) (in press). MR: Deployment to areas of high UV exposures puts service members at increased risk for the development of melanoma and other skin cancers.

Log No/ Amount/ Status	Principal Investigator	Institution	Application Title	Research Project (RP) and Military Relevance (MR)
CA093422 $404,849 Open	Jimeno	University of Colorado Denver	The XactMice: A Xenochimaeric Mouse with Tumor and Hematopoietic System Obtained from the Same Patient	RP: Development of mouse model to better understand carcinogenesis and its treatment. Demonstrated the feasibility of engrafting human tumors on humanized mice. The humanized and non-humanized tumor expression profiles will be made available to public. MR: Advancing genetic research has a direct application to active, reserve, and retired U.S. service members and their families, since military lifestyle entails potential exposure to carcinogens known and presumed, chemical and physical/radioactive in nature, both in training and in deployment, and related to equipment utilization and/or combat.
CA093492 $657,517 Open	Testa	Fox Chase Cancer Center	Role of the Inflammasome in Asbestos-Induced Mesothelioma Formation	RP: Study of the role of NALP3 inflammsome and the development of mesothelioma due to asbestos exposure. Demonstrated the genetic link between asbestos-associated inflammation and the development of malignant mesothelioma. Found targeting IL-1β signaling with IL-1R antagonist results in delayed asbestos-induced MM onset and progression. MR: Asbestos exposure was widespread among naval personnel even after the 1980s. Malignant mesothelioma has a long lag time of 20-40 years from the initial exposure to the diagnosis of the disease. Long-term risk of mesothelioma development following asbestos exposures is critical for U.S. veterans and active military.
CA093544 $653,132 Open	Cantor	Children's Hospital, Boston	Runx-1-Centered Transcriptional Pathways as Tools to Discover Novel Genetic Risk Factors for Radiation-Induced Myelodysplastic Syndrome and Leukemia	RP: Characterization of a potential gene target (Runx1) of chemical and radiation exposures that may lead to cancer development. Identified 5'UTR mutations in ANKRD26 gene as a novel cause of leukemia predisposition and thrombocytopenia in humans. Identified a role of 5'UTR in DNA repair and chromosome segregation and connected it to two leukemia factors, Menin and MLL. MR: Advancing genetic research has a direct application to active, reserve, and retired U.S. military personnel and their families as a military lifestyle entails potential exposure to carcinogens known or presumed, chemical and physical/radioactive in nature, both in training and in deployment, and related to equipment utilization and/or combat.

Log No/ Amount/ Status	Principal Investigator	Institution	Application Title	Research Project (RP) and Military Relevance (MR)
CA093566 $423,038 Open	Dai	Oregon Health & Science University	Regulation of c-Myc mRNA by L11 in Response to UV and Gamma Irradiation	RP: Study of the downregulation of key gene (c-myc) due to DNA damage. Indicated that miRNA-mediated c-myc mRNA decay is an important mechanism for ribosomal biogenesis and c-myc activity during stress conditions. Found that L11 destabilizes c-myc mRNA. DNA damage by UV or infrared light and ribosomal stress leads to the reduction of c-myc mRNA; such reduction requires L11. Outcome: *Mol Cell Biol* (2011) 31:4007. MR: Exposure to environmental hazards in military personnel is associated with increased cancer risks. Studies of hazardous exposures that may cause damage to DNA and long-term health care issues such as cancer are beneficial to military personnel.
CA093573 $449,979 Closed	Majeti	Stanford University	Genetic Characterization of Leukemia Stem Cells in Chemical- and Radiation-Induced Acute Myelogenous Leukemia	RP: Identification and molecular characterization of leukemia stem cells from mouse models of t-AML/t-MDS induced by alkylating agents or ionizing radiation. Established a mouse model of radiation-induced t-AML/t-MDS. MR: Military personnel are at risk of exposure to alkylating agents, in the form of chemical weapons, and ionizing radiation, from nuclear and/or radioactive sources, that can cause t-AML)/t-MDS.
CA093588 $631,258 Open	Tsao	Massachusetts General Hospital	Governance of Cutaneous Photocarcinogenesis by Chronic UVA-Exposed Dermal Fibroblasts	RP: Investigation of the impact of UVA in skin cancer development. Created a co-culture system and demonstrated that UVA irradiation increased oxidative stress. Confirmed a bystander transmission of reactive oxygen species from the fibroblast target to neighboring non-irradiated cells. Identified p53 as a potent modulator of bystander defense. MR: Melanoma and other skin cancers represent a significant disease burden to the U.S. military. Military personnel are at risk for higher UV radiation exposures and melanoma development and other skin cancers.

Log No/ Amount/ Status	Principal Investigator	Institution	Application Title	Research Project (RP) and Military Relevance (MR)
CA093616 $659,431 Open	Kemp	Fred Hutchinson Cancer Research Center	Transgenerational Radiation Epigenetics	RP: Study to identify an epigenetic signature of radiation exposure in normal lung tissue and determine if these epigenetic changes are also seen in radiation-induced lung tumors. Showed that in utero irradiation leads to reduced body weight in young adult mice, which is transmitted through the maternal line to a subsequent generation. Also showed that in utero irradiation leads to increased incidence of lung tumors in susceptible mice. MR: Military personnel are at risk for radiation exposures (UV and gamma) and development of cancers.
CA100459/ CA100459P1 $1,204,447 Combined Open	Moritz; Foltz	Institute for Systems Biology; Swedish Health Services	Development of Advanced Technologies for Complete Genomic and Proteomic Characterization of Quantized Human Tumor Cells	RP: Study of three innovative new tools to find relevant biomarkers for novel approaches to the study of all cancers; technical development of whole genome sequencing and quantitative assays. Generated Glioblastoma cell lines from resected human tumor samples to allow for the study of cell type differentiation to define new molecular targets. MR: Technological advances supported by the military increase the ability of military medicine to answer the needs of service members and their families.
CA100545 $571,819 Open	Broome	Medical University of South Carolina	Targeting Cancer Protein Profiles with Split-Enzyme Reporter Fragments to Achieve Chemical Resolution for Molecular Imaging	RP: Study to advance imaging technology toward chemical resolution at the single cell level. A NIRF-EGF peptide probe was synthesized, and genetically engineered rat glioma cell lines with 0, 1, or 2 human cell surface receptors were created. MR: Technological advances supported by the military increase the ability of military medicine to answer the needs of service members and their families.
CA100865/ CA100865P1/ CA100865P2 $1,085,960 Combined Open	Alvarez; Couto; Huang	Research Institute at Nationwide Children's Hospital; Ohio State University	Integrative Lifecourse and Genetic Analysis of Military Working Dogs	RP: Identification of environmental influences with potential to alter gene structure, stability, and expression, thereby altering cancer risk. Identification of specific genetic variations and environmental exposures, resulting in different epigenetic profiles capable of modifying cancer risk. The informatics infrastructure, statistical method for analyzing genetic data, and military dog registry database are now established. MR: The study of military working dogs, environmental exposures, and cancer risk will directly relate to military exposures and cancer risk within the human handlers population.

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CA120215 $417,501 New Award	Gutierrez	Children's Hospital, Boston	Zebrafish Functional Genetics Approach to the Pathogenesis of Well-Differentiated Liposarcoma	RP: Examine oncogenes that contribute to well-differentiated liposarcoma in a zebra fish model. Research has just been initiated. MR: Exposure to herbicidal agents and radiation predispose one to soft-tissue sarcomas. Development of effective therapies for sarcoma will benefit military service members and veterans.
Kidney Cancer				
CA100587 $454,900 Open	Singamaneni	Washington University	Label-Free, Point-of-Service Assay for Noninvasive Detection of Kidney Cancer	RP: Study to develop a urine test for kidney cancer. Demonstrated that a 3D surface enhanced Raman scattering substrate was 2 orders of magnitude more sensitive as compared to planar 2D substrate. Also demonstrated that the detection limit of AQP1, a urinary biomarker for kidney cancer, is 10 ng/ml. Created a novel biosensing platform in the form of bioplasmonic paper with a capability of detecting 20 ng/ml. Outcomes: *Anal Chem* (2012) 84:9928- 9934. *ACS Nano* (2013) 7:4252-4260. Total publications: 15. MR: Successful development of such a test will enable early cancer detection, removal at a curative and kidney-sparing stage, prompt recovery, and earlier return to active duty.
CA100606/ CA100606P1 $1,206,215 Combined Open	Tewari; Pantuck	Fred Hutchinson Cancer Research Center; University of California, Los Angeles	Early Diagnosis of Clear Cell Kidney Cancer via VHL/HIF Pathway-Regulated Circulating microRNA	RP: Development of a serum miRNA-based biomarker for early detection of kidney cancer. Initially optimized the detection method for miR-210. Demonstrated that miR-210 was elevated in renal carcinoma serum samples. Identified seven additional miRNAs as potential serum biomarkers, which will be further examined along with miR-210. Outcome: *Nat Methods* (2013) 10:1003-1005. MR: Successful development of such a test will enable early cancer detection, removal at a curative and kidney-sparing stage, prompt recovery, and earlier return to active duty.

Log No/ Amount/ Status	Principal Investigator	Institution	Application Title	Research Project (RP) and Military Relevance (MR)
CA101070 $115,875 Closed	Wang	University of California, San Francisco	Noninvasive Assessment of Renal Tumor Aggressiveness Using Hyperpolarized 13C MR	RP: Development of imaging tools to discriminate between indolent and aggressive renal cancers (RC). Demonstrated the feasibility of using ^{13}C pyruvate magnetic resonance to differentiate metastatic RC from localized RC. Outcome: *Cancer Res* 73(2):529-538. MR: This work is of potential significant impact on military beneficiaries because of (1) the higher incidence of renal cell carcinoma in men versus women (2:1 ratio), (2) the risk of cigarette smoking (doubles the risk of renal cell carcinoma), and (3) the risk of occupational exposure to heavy metals, chlorinated solvents, and petrochemicals. Successful development of such a test will enable early cancer detection, removal at a curative and kidney-sparing stage, prompt recovery, and earlier return to active duty.
CA110032 $240,000 Open	Sriram	University of California, San Francisco	Hyperpolarized ^{13}C MR Markers of Renal Tumor Aggressiveness	RP: To test a new technique of hyperpolarized carbon-13 magnetic resonance to determine if it can differentiate between benign and aggressive kidney tumors. Established model systems of renal cell carcinoma (RCC) to study metabolism using hyperpolarized carbon magnetic resonance. MR: This work is of potential significant impact on military beneficiaries because of (1) the higher incidence of renal cell carcinoma in men versus women (2:1 ratio), (2) the risk of cigarette smoking (doubles the risk of renal cell carcinoma), and (3) the risk of occupational exposure to heavy metals, chlorinated solvents, and petrochemicals. Successful development of such a test will enable early cancer detection, removal at a curative and kidney-sparing stage, prompt recovery, and earlier return to active duty.
CA110769 $296,000 Open	Frisch	West Virginia University	Role of Grainyhead in Kidney Cancer	RP: To study Grainyhead-like-2 (GRHL2), a transcription factor involved in kidney development, to determine its role as a tumor suppressor for renal cell carcinoma and how it prevents RCC progression. Results so far suggest that GRHL2 expression is highly protective against clear cell RCC. MR: This work is of potential significant impact on military beneficiaries because of (1) the higher incidence of renal cell carcinoma in men versus women (2:1 ratio), (2) the risk of cigarette smoking (doubles the risk of renal cell carcinoma), and (3) the risk of occupational exposure to heavy metals, chlorinated solvents, and petrochemicals. Successful development of such a test will enable early cancer detection, removal at a curative and kidney-sparing stage, prompt recovery, and earlier return to active duty.

Log No/ Amount/ Status	Principal Investigator	Institution	Application Title	Research Project (RP) and Military Relevance (MR)
CA120297 $364,353 New Award	Krishnan	University of North Carolina at Chapel Hill	Reprogramming of the Kinome to Enhance Mammalian Target of Rapamycin (mTOR) Inhibitor Responsiveness in Renal Cell Carcinoma	RP: To identify kinases upregulated by mammalian target of rapamycin (mTOR) inhibitors in renal cancer cell and determine if inhibition to these kinase improves the responsiveness of mTOR inhibitors in renal cell carcinoma. Research has just been initiated. MR: This study could potentially improve the outcomes and survival of military personnel with RCC.
CA120409 $381,807 New Award	Shen	Health Research, Inc., Roswell Park Division	A Novel Tumor Antigen and Foxp3 Dual-Targeting Tumor Cell Vaccine Enhances the Immunotherapy in a Murine Model of Renal Cell Carcinoma	RP: Characterization of the biological activity and therapeutic potential of a novel tumor cell antigen and Foxp3 dual-targeting vaccine as a single treatment or in combination with tasquinimod in a RCC mouse model. Research has just been initiated. MR: Service members have higher risk to develop kidney cancer because of deployment-related exposure to environment hazards.
***Listeria* Vaccine for Cancer**				
CA100463 $543,200 Open	Chung	Memorial Sloan-Kettering Cancer Center	Evaluation of Immune Responses Mediated by *Listeria*-Stimulated Human Dendritic Cells: Implications for Cancer Vaccine Therapy	RP: Development of *Listeria* modulated human dendritic cells (DC) for enhanced immunoresponse for cancer vaccination. The study demonstrated that *Listeria* infection induced DC maturation and activation, leading to T-cell proliferation. These findings confirmed that *Listeria* could stimulate an immune response and potentially serve as a DC vaccine adjuvant. MR: The development of immune-enhanced technology will benefit military medicine from cancer to infectious diseases (a main exposure risk in deployed military populations).
CA110297 $296,000 Open	Bahjat	Providence Portland Medical Center	Synergy of SOCS-1 Inhibition and Microbial-Based Cancer Vaccines	RP: To test that the induction of negative regulators of inflammation and cytokine signaling, such as SOCS-1, limit the potency of the tumor-specific immune response and that the inhibition of SOCS-1 will enhance the anti-tumor efficacy of a *Listeria monocytogenes*-based cancer vaccine. MR: The development of immune enhanced technology will benefit military medicine from cancer to infectious diseases (a main exposure risk in deployed military populations).

Log No/ Amount/ Status	Principal Investigator	Institution	Application Title	Research Project (RP) and Military Relevance (MR)
Melanoma/Skin Cancer				
CA093370 $1,188,381 Open	Kashani-Sabet; Leachman	California Pacific Medical Center; University of Utah	Molecular Determinants of Melanoma Susceptibility and Progression	RP: Development of a melanoma risk prediction model in the U.S. military population. Completed preparation for sample analysis. Obtained permission to access the Department of Defense Automated Central Tumor Registry database. Submitted the query to the database. Sample analysis in progress. MR: Deployment to areas of high UV exposures puts service members at increased risk for the development of melanoma and other skin cancers. Study directly relates to military population and risk.
CA093471 $1,187,984 Open	Hernando: Osman	New York University School of Medicine	Altered microRNAs in Melanoma Brain Metastasis	RP: Characterization of the metastasis potential of melanomas. Identified seven miRNAs that are differentially expressed in brain metastasis. Found that melanoma brain metastasis-associated miRNAs contributed to the adaptation of melanoma cells to the brain parenchyma. Outcomes: *Cancer Cell* (2011) 20(1):104-118. *Cancer* (2011) 117(8):1711-1720. MR: The prevention, detection, and treatment of melanoma are of particular importance to the military population, who are at high risk due to the deployment related exposure to UV radiation.
CA093473 $1,196,001 Open	Halaban: Brash: Bosenberg	Yale University	UVL, ROS, Pigmentation, Genetic Predisposition, and Epigenetic Gene Silencing in Melanoma	RP: Study of the linkage between reactive oxygen species (ROS), genetic and epigenetic changes, and UV radiation leading to melanoma development. Found a "photochemistry in the dark" phenomena: DNA damage by UV light continued after sun exposure. The delayed sunlight damage could be prevented by an identified agent. This finding could lead to a new formulation of sunscreen to protect the delayed skin damage by sun exposure. Outcome: *Pigment Cell Melnanoma Res* (2013) (in press). MR: The prevention, detection, and treatment of melanoma are of particular importance to the military population, who are at high risk due to the deployment-related exposure to UV radiation.

Log No/ Amount/ Status	Principal Investigator	Institution	Application Title	Research Project (RP) and Military Relevance (MR)
CA100039 $561,626 Open	Antony	University of Maryland, Baltimore	Mechanisms of Relapsing Cancer and the Origin of Melanoma-Specific Regulatory T Cells	RP: Study of immunosuppression and melanoma development. Found a more complexed role of T_{reg} cells in melanoma relapse. Showed that T_{reg} cells prevent treatment of relapse and also that T effector cells become exhausted and can be rescued by antibody therapies to chronic inhibitory receptors. Outcome: *J Immunol* (2013) 190:4899-4909. MR: The high exposure to UV radiation to military personnel during deployment is associated with increased risk for melanoma.
CA100311 $581,250 Open	Aplin	Jefferson Medical College	Role and Regulation of FOXD3 in Mutant B-RAF Melanoma	RP: This study aims to understand resistance mechanisms in melanoma for improved targeted therapeutic strategies. Established systems to analyze the response of melanoma xenografts to RAF inhibitors in vivo and showed the downregulation of FOXD3 targets enhances the effects of RAF inhibitors in vivo. Outcome: *J Clin Invest* (2013) 123:2155-2168. MR: The prevention, detection, and treatment of melanoma are of particular importance to the military population, who are at high risk due to the deployment related exposure to UV radiation.
CA101019 $116,250 Completed	Aplin	Jefferson Medical College	Novel Mechanisms of Resistance to B-RAF Inhibitors in Melanoma	RP: Study into the novel mechanisms of chemotherapy resistance to RAF inhibitors and melanoma treatments. Developed a system to quantify changes in ERK1/2 signaling in tumor cells with elevated activity. Outcomes: *J Biol Chem* (2012) 287:41797-41807. One invention disclosure. MR: The rate of new melanoma diagnoses among service members is higher than that of the general population even after correcting for age and ethnicity. Melanoma is strikingly the second most common cancer among males in the U.S. Navy. Military personnel are at risk for UV radiation exposures and development of cancers.

Log No/ Amount/ Status	Principal Investigator	Institution	Application Title	Research Project (RP) and Military Relevance (MR)
CA101118 $114,750 Completed	Serafini	University of Miami School of Medicine	Converting Myeloid-Derived Suppressor Cells into Immunogenic Antigen-Presenting Cells in Melanoma-Bearing Mice	RP: Investigation of the conversion of the tolerogenic myeloid-derived suppressor cells by siRNA into functional immunogenic activated protein C to generate effective tumor immunity. Confirmed genetic modification via shRNA of tumor-educated myeloid cells alters the immune system by creating an anti-tumor immune response able to restrain the growth of melanomas. Developed an IL4-PAMAM dendrimer platform able to target tumor-educated myeloid cells and myeloid-derived suppressor cells in vivo. MR: Service members are deployed to areas of high risk and exposure to UV light. With more and more deployment of troops in countries with high sun exposure and UVA and UVB penetration (e.g., Afghanistan, Iraq, and the Middle East region), melanoma can be the most frequent cancer that military personnel will face during their lives.
CA101202 $130,498 Open	Libermann	Beth Israel Deaconess Medical Center, Boston	Testing New Drugs for Treatment of Melanoma Patients Applying Connectivity Map Database Analysis with Melanoma Gene Signatures	RP: Technology-driven study to map the treatment and disease to exploit the chemotherapeutic properties of drugs. Results provide strong support that transcriptome analysis can prioritize drugs. Identified several drugs that are predicted to reverse the metastatic phenotype of melanoma. MR: Military personnel are at risk for UV radiation exposures and development of cancers.
CA110011 $240,000 Open	Ransom	University of, Colorado, Denver	Determining the Location of DNA Modification and Mutation Caused by UVB Light in Skin Cancer	RP: To map and characterize UVB damaged “hotspots” in the human genome using a novel enzyme and sequencing methodology. Developed a method to study DNA modifications caused by exposure to UV light. MR: Service members are deployed to areas of high risk and exposure to UV light. With more and more deployment of troops in countries with high sun exposure and UVA and UVB penetration (e.g., Afghanistan, Iraq, and the Middle East region), melanoma can be the most frequent cancer that military personnel will face during their lives.

Log No/ Amount/ Status	Principal Investigator	Institution	Application Title	Research Project (RP) and Military Relevance (MR)
CA110017 $368,400 Open	Goding	University of Maryland, Baltimore	Therapeutic Intervention for the Treatment of Relapsing Melanoma	RP: To determine the roles of chronic CD4 T cell exhaustion and the inhibitory pathways involved in melanoma tumor relapse. CD4+T cells from mice with relapsing tumors expressed hallmark indicators of chronic exhaustion, and when the mice were treated for exhaustion, tumors regressed and the markers decreased. Outcome: *J Immunol* (2013) 190:4899-4909. MR: The rate of new melanoma diagnoses among service members is higher than that of the general population even after correcting for age and ethnicity. Melanoma is strikingly the second most common cancer among males in the U.S. Navy. Military personnel are at risk for UV radiation exposures and development of cancers.
CA110094 $322,849 Open	Callahan	Memorial Sloan-Kettering Cancer Center	Evaluation of the Immunologic Impact of RAF Inhibitors to Guide Optimal Combination of RAF Inhibitors and Immunotherapy for the Treatment of Advanced Melanoma	RP: To investigate ways to optimally combine targeted pathway inhibition with checkpoint blockade. Findings suggest a model where BRAF inhibitors are likely to combine with immunotherapies to generate robust, long-lasting anti-tumor T-cell responses while MEK inhibitors may compromise the generation of long-lasting T-cell memory. MR: Service members are deployed to areas of high risk and exposure to UV light. With more and more deployment of troops in countries with high sun exposure and UVA and UVB penetration (e.g., Afghanistan, Iraq, and the Middle East region), melanoma can be the most frequent cancer that military personnel will face during their lives.
CA110107 $259,200 Open	Zhang	Mount Sinai School of Medicine, New York	Insight into Skin Tumorigenesis Highlighting the Function of Epigenetic Regulators in SCC Formation	RP: To dissect the Ezh2 regulatory network that controls skin squamous cell carcinoma (sSCC) formation, focusing on the evaluation of regulatory networks and their mechanisms in control of the early steps of sSCC formation. Observations suggest that Ezh2 may function in multiple ways to form a regulatory network. Outcome: *EMBO J* (2013)32:1990-2000. MR: Service members are deployed to areas of high risk and exposure to UV light. With more and more deployment of troops in countries with high sun exposure and UVA and UVB penetration (e.g., Afghanistan, Iraq, and the Middle East region), melanoma can be the most frequent cancer that military personnel will face during their lives.

Log No/ Amount/ Status	Principal Investigator	Institution	Application Title	Research Project (RP) and Military Relevance (MR)
CA110183 $313,000 Open	Marchetti	Baylor College of Medicine	Heparanase Mechanisms in Melanoma Brain Metastasis	RP: To examine the use of heparanase as a novel therapeutic target for the personalized treatment of melanoma brain metastasis. Could not detect naturally occurring miR-1258 in human melanoma cells, differences in heparanase transcription or protein expression among human melanoma cell lines. MR: The rate of new melanoma diagnoses among service members is higher than that of the general population even after correcting for age and ethnicity. Melanoma is strikingly the second most common cancer among males in the U.S. Navy. Military personnel are at risk for UV radiation exposures and development of cancers.
CA110338 $296,400 Open	Bikle	Northern California Institute for Research and Education	The Tumor Suppressor Actions of the Vitamin D Receptor in Skin	RP: In vivo study of the vitamin D receptor as a tumor suppressor in relation to epidermal tumor formation through the blocking of the beta catenin and hedgehog pathways. Developed mouse models for the expression of the hedgehog and wnt/beta-catenin pathways to determine if they would alter the susceptibility of the VDR null mouse to UVB-induced epidermal cancer. Outcomes: *J Steroid Biochem* Mol Biol (2013) (in press). *Landes Bioscience* (2013) (in press). Three additional publications. MR: The rate of new melanoma diagnoses among service members is higher than that of the general population even after correcting for age and ethnicity. Melanoma is strikingly the second most common cancer among males in the U.S. Navy. Military personnel are at risk for UV radiation exposures and development of cancers.
CA110396 $327,333 Open	Faller	Boston University Medical Campus	Targeting N-Ras as a Therapeutic Approach for Melanoma	RP: To test whether the inhibition or downregulation of PKCδ in human and murine models of melanoma with aberrant activation of N-RAS signaling will cause targeted cytotoxicity in melanoma tumors. Results validate PKCδ as a target in melanoma and provide proof of principle for the use of PKCδ inhibitors. MR: Service members are deployed to areas of high risk and exposure to UV light. With more and more deployment of troops in countries with high sun exposure and UVA and UVB penetration (e.g., Afghanistan, Iraq, and the Middle East region), melanoma can be the most frequent cancer that military personnel will face during their lives.

Log No/ Amount/ Status	Principal Investigator	Institution	Application Title	Research Project (RP) and Military Relevance (MR)
CA110462 $289,871 Open	Zhang	University of Colorado, Denver, Anschutz Medical Campus	Targeting "Dynamic Stemness" of Melanoma by Blocking the NADH-Dependent CtBP Function	RP: To study whether hypoxia, hyperglycemia, and UV irradiation trigger the conversion of melanoma cells by the activation of CtBP-mediated transcription and if blocking its function can be used as a novel therapeutic strategy. Found that CtBP hyperfunction leads to the induction of the H3K4 demethylase JARID1B protein, a key marker for melanoma self-renewal. Outcome: *J Invest Dermatol* (2013) 133:1294-1301. MR: Military personnel are at risk for UV radiation exposures and development of cancers.
CA110602 $284,597 Open	Hernando	New York University School of Medicine	Identification of Glycomic Alterations during Melanoma Metastasis	RP: To define glycomic and functional changes in the tumor microenvironment associated to progression from primary to metastasis, triggered by miRNA-carrying exosomes. Data suggest that alterations in cell surface glycosylation may be an early event in the malignant transformation of melanocytes to melanoma. MR: Deployment to areas of high UV exposures puts service members at increased risk for the development of melanoma and other skin cancers. This study directly relates to military population and risk.
CA110802 $305,000 Open	Morris	University of Minnesota, Twin Cities	A Novel Mechanism for the Pathogenesis of Nonmelanoma Skin Cancer Resulting from Early Exposure to Ultraviolet Light	RP: To determine if keratinocyte stem cells are chemotactic and migrate away from the skin and into the bone marrow. Findings support the hypothesis that skin keratinocytes can leave the cutaneous epithelium and enter the blood and bone marrow. MR: The rate of new melanoma diagnoses among service members is higher than that of the general population even after correcting for age and ethnicity. Melanoma is strikingly the second most common cancer among males in the U.S. Navy. Military is at risk for UV radiation exposures and development of cancers.
CA110823 $308,000 Open	Bullock	University of Virginia	Functional Proteomics to Identify Moderators of CD8+ T-Cell Function in Melanoma	RP: To identify and characterize inhibitory molecules expressed by melanoma tumor infiltrating CD8+ cells through the novel use of functional proteomics incorporating phage display. Progress has been made in defining the conditions necessary for identifying phage specific for tumor infiltrating lymphocytes. Candidate clones have been readied for functional assessment. MR: Military at risk for UV radiation exposures and development of cancers.

Log No/ Amount/ Status	Principal Investigator	Institution	Application Title	Research Project (RP) and Military Relevance (MR)
CA111032 $305,000 Open	Basu	Ohio State University	Role of Catecholamines in the Regulation of Angiogenesis in Preneoplastic Skin Lesions	RP: To investigate the role of dopamine receptors during skin carcinogenesis and to elucidate the molecular mechanisms by which these receptors regulate vascular endothelial growth factor A in skin. Developed a mouse model of skin carcinogenesis and demonstrated that vascular endothelial growth factor-induced angiogenesis is responsible for the initiation and progression of disease in those animals. MR: Service members are deployed to areas of high risk and exposure to UV light. With more and more deployment of troops in countries with high sun exposure and UVA and UVB penetration (e.g., Afghanistan, Iraq, and the Middle East region), melanoma can be the most frequent cancer that military personnel will face during their lives.
CA120099 $400,800 New Award	Ceol	University of Massachusetts Medical School	Uncovering the Role of BMP Signaling in Melanocyte Development and Melanoma Tumorigenesis	RP: Investigation of the bone morphogenetic protein GDF6 in melanocyte development and melanoma tumorigenesis. Research has just been initiated. MR: Melanoma is one of the most common cancers among active-duty personnel. This study could serve as a diagnostic and prognostic marker of melanoma.
CA120161 $417,600 New Award	Wu	Massachusetts General Hospital	Targeting Palmitoyl Acyltransferases in Mutant NRAS-Driven Melanoma	RP: Development of a new class of palmitoyl acyltransferase inhibitors that target N-RAS mutant melanomas. Research has just been initiated. MR: Deployment to areas of high UV exposures puts service members at increased risk for the development of melanoma and other skin cancers. This study will lead to new therapeutics to combat melanoma, which can improve the survival and quality of life of the impacted personnel.
CA120240 $399,600 New Award	Yan	Yale University	Targeting Epigenetic Regulator JARID1B in Malignant Melanoma	RP: Determination of the effects after the loss of an epigenetic regulator, JARID1B, on melanoma formation and progression in the Braf/Cdkn2 mouse melanoma model. Research has just been initiated. MR: The military service members are at increased risk for melanoma and other skin cancers. This study aims to identify novel inhibitors to a drug target for melanoma. The outcome could be translated into novel clinical application for the treatment of melanoma.

Log No/ Amount/ Status	Principal Investigator	Institution	Application Title	Research Project (RP) and Military Relevance (MR)
Mesothelioma				
CA110442 $296,850 Open	Robinson	University of Western Australia	Targeting Immunological Restrainers: Understanding the Immunology behind Combination Chemoimmunotherapy to Improve the Treatment of Malignant Mesothelioma	RP: To determine if the adaptive immune response plays a key role in the early changes associated with mesothelial cell transformation and tumor development and is inhibited by immunological restraints. Observed that the depletion of Treg cells can significantly enhance anti-tumor immunity and delay tumor development. MR: Asbestos exposure was widespread among naval personnel even after the 1980s. Malignant mesothelioma has a long lag time of 20-40 years from the initial exposure to the diagnosis of the disease. Long-term risk of mesothelioma development following asbestos exposures is critical for U.S. veterans and active military.
CA110751 $308,000 Open	Sharma	University of California, Los Angeles, David Geffen School of Medicine	Mesothelioma Snail-Mediated Modulation of Inflammatory Responses	RP: To determine if mesothelioma Snail knockdown will have an impact on tumor growth, invasion, and migration by modulating the activities of immune effectors and suppressors. Generated three different mesothelioma knockdown cell lines and have studied the growth and invasion characteristics of these cells in vitro. MR: Asbestos exposure was widespread among naval personnel even after the 1980s. Malignant mesothelioma has a long lag time of 20-40 years from the initial exposure to the diagnosis of the disease. Long-term risk of mesothelioma development following asbestos exposures is critical for U.S. veterans and active military.
CA110765 $316,000 Open	Salgia	University of Chicago	PI3K as a Therapeutic Target in Malignant Pleural Mesothelioma	RP: To investigate the therapeutic potential of phosphatidyl inositol 3'-kinase (PI3K) in malignant pleural mesothelioma (MPM) and determine the efficacy of some of the PI3K and PI3K/TOR inhibitors in MPM cell culture and mouse models. Results suggest that a combination of drugs is more effective than using each alone in suppressing tumor growth and motility. MR: Asbestos exposure was widespread among naval personnel even after the 1980s. Malignant mesothelioma has a long lag time of 20-40 years from the initial exposure to the diagnosis of the disease. Long-term risk of mesothelioma development following asbestos exposures is critical for U.S. veterans and active military.

Log No/ Amount/ Status	Principal Investigator	Institution	Application Title	Research Project (RP) and Military Relevance (MR)
CA110772 $294,870 Open	Heasley	University of Colorado, Denver, Anschutz Medical Campus	Targeting Fibroblast Growth Factor Receptor Signaling Pathways in Mesothelioma	RP: To test the hypothesis that the co-expression of fibroblast growth factors (FGFs) and FGF receptors create an autocrine growth loop in mesothelioma that promotes cancer growth. Studies support that FGFR1 activation through autocrine FGF2 is a driver of oncogenic growth in a subset of mesothelioma cell lines. MR: Asbestos exposure was widespread among naval personnel even after the 1980s. Malignant mesothelioma has a long lag time of 20-40 years from the initial exposure to the diagnosis of the disease. Long-term risk of mesothelioma development following asbestos exposures is critical for U.S. veterans and active military.
CA120102 $256,613 New Award	Klein	VA Medical Center, Minneapolis, MN	Development of Novel p16INK4a Mimetics as Anticancer Therapy	RP: Determination of the structure-function relationships of overlapping peptides derived from p16INK4a that inhibit the activity of CDK4/6; screening stabilized peptides that inhibit CDK4/6; and preclinical assessment of the stabilized peptides. Research has just been initiated. MR: Mesothelioma is a highly fatal disease that can affect those exposed to asbestos, especially those who have been in Navy ships and shipbuilding.
CA120355 $360,000 New Award	Yang	University of Hawaii	Mesothelioma: Identification of the Key Molecular Events Triggered by BAP1	RP: Study of the impact of BAP1 on the release of HMGB1 and other downstream factors and the effect of BAP1 status on the development of mesothelioma. Research has just been initiated. MR: Veterans from all branches of the armed forces are at high risk for mesothelioma due to the widespread use of asbestos in the construction of military vehicles, air craft, ships, and buildings.
Non-Invasive Ablation Only				
CA093108 $114,836 Open	O'Donnell	University of California, Davis	Immuno-Nanomicelles Targeted Therapy of Non-Hodgkin's Lymphoma	RP: Research into fabrication and development of nanomicelles for the direct delivery of treatment (chemotherapy) to a disease site (non-Hodgkin's lymphoma). Mice treated with encapsulated micelles had a superior anti-tumor response as compared to using vincristine alone. Outcome: *Mol Pharmaceutics* (2012) 9(6):1727-1735. MR: Biomedical development of nanotechnology that is translatable to various treatments for diseases, conditions, and injuries specific to the military deployments and exposure risks, e.g., Agent Orange.

Log No/ Amount/ Status	Principal Investigator	Institution	Application Title	Research Project (RP) and Military Relevance (MR)
CA093166 $134,884 Closed	Gach	Nevada Cancer Institute	Targeted RF Ablation of Tumors Using Monocyte/ Macrophage Carriers of Conductive Nanoparticles	RP: Development of radiofrequency (RF) ablation therapies for specific treatment of tumors. Observed that metallic single-wall carbon nanotubes may have the potential to generate enough heat at biologically relevant concentrations to have an impact in clinical use. Outcomes: *Bioelectromagnetics* (2012) 33(2):134-146. *Bioelectromagnetics* (2010) 31(8):582-588. MR: Development of a new treatment modality for tumor ablation may translate to expansive medical methodologies with military benefit.
CA093180 $117,684 Closed	Berdis	Case Western Reserve University	Gold-Containing Nucleosides as Noninvasive Ablation Agents	RP: Development of gold-containing nucleosides as target agents to potentiate the efficacy of ionizing radiation for maximal tumor ablation. Outcome: *J Med Chem* (2012) 55(5):2437-2451. MR: Technological advances supported by the military increase the ability of military medicine to answer the needs of service members and their families.
CA093210 $117,000 Closed	Pan	University of Chicago	Testing Delivery Platforms for New Anticancer tRNA-Based Drugs	RP: Development of killer tRNA nanoparticles as a potential blood cancer treatment. Obtained proof of concept results in blood cancer cells. MR: The military benefits through the development of drug delivery systems to decrease side effects and increase efficacy. Technology can be broadly employed for various treatments outside cancer.
CA093389 $598,307 Open	Torti	University of Connecticut	Targeted Nanoparticles for Kidney Cancer Therapy	RP: Development of novel optically activated multifunctional nanotubes to target and kill renal cancer cells. Soluble D5-conjugated nanotubes were produced; the toxicity of unconjugated nanotubes to kidney cancer cells was tested. The results demonstrated that the combination of NIR and nanotubes could successfully inhibit both human and mouse kidney cancer cells. MR: Biomedical development of nanotechnology that is translatable to various treatments for diseases, conditions, and injuries specific to the military will benefit military personnel.

Log No/ Amount/ Status	Principal Investigator	Institution	Application Title	Research Project (RP) and Military Relevance (MR)
CA093453 $670,720	Panyam	University of Minnesota, Twin Cities	Targeted Magnetic Hyperthermia for Lung Cancer	RP: Development of super-paramagnetic iron oxide nanoparticles to specifically target lung tumor cells. The study demonstrated that super paramagnetic iron oxide nanoparticles with EGFR targeting ligand enhanced tumor cell uptake and in vivo mouse lung retention. Outcomes: *Drug Delivery Trans Res* (2012) 2:31-44. *Mol Pharm* (2013)10:1432-1441. *Mol Pharm* (2013) 34:5163-5171. MR: Military biomedical development of nanotechnology that is translatable to various treatments for diseases, conditions, and injuries specific to the military will benefit military personnel.
Pancreatic Cancer				
CA110076 $368,400 Open	Lunt	Michigan State University	Understanding the Warburg Effect and the Metabolic Requirements of Cancer Cells	RP: To uncover the metabolic pathways that blood and pancreatic cancers rely on for survival. Studies have focused on understanding the role of pyruvate kinase isoform expression in altered metabolism in pancreatic and blood cancer cells. MR: Higher risk of pancreatic cancer has been shown in populations exposed to pesticides such as Agent Orange. Higher risk of pancreatic cancer in Vietnam nurses has been reported.
CA110164 $296,000 Open	Houchen	University of, Oklahoma Health Sciences Center	Tuft Cell Regulation of miRNAs in Pancreatic Cancer	RP: To test the hypothesis that tuft cells are specialized chemosensing cells in the pancreas and upon appropriate oncogenic signals become the cells of origin for pancreatic cancer. Progress to date includes the successful deletion of DclK1 throughout the pancreatic ducts of a transgenic mouse model. MR: Higher risk of pancreatic cancer has been shown in populations exposed to pesticides such as Agent Orange. Higher risk of pancreatic cancer in Vietnam nurses has been reported.

Log No/ Amount/ Status	Principal Investigator	Institution	Application Title	Research Project (RP) and Military Relevance (MR)
CA110449 $320,000 Open	Beatty	University of Pennsylvania	Listeria Vaccines for Pancreatic Cancer	RP: Examination of whether *Listeria* vaccines can overcome the immune suppression associated with pancreatic ductal adenocarcinoma by stimulating anti-tumor responses able to target both tumor cells and their surrounding microenvironment. Found that *Listeria* vaccines produce little impact on late-stage tumors with an absence of T-cell infiltration into tumor tissue, but do appear to have non-antigen specific anti-stromal effects. Outcomes: *Oncoimmunology* (2013A) (in press). *Oncoimmunology* (2013B) (in press). MR: Higher risk of pancreatic cancer has been shown in populations exposed to pesticides such as Agent Orange. Higher risk of pancreatic cancer in Vietnam nurses has been reported.
CA110530 $241,880 Open	Solomon	National Cancer Institute	Metabolomic Profiles and Pancreatic Cancer Risk	RP: The study of metabolites to identify those associated with pancreatic cancer to define profiles correlating with risk levels. Metabolites have been measured on fasting serum samples, and preliminary analysis has been conducted. MR: Higher risk of pancreatic cancer has been shown in populations exposed to environmental agents and pesticides such as Agent Orange. Higher risk of pancreatic cancer in Vietnam nurses has been reported.
CA110535 $310,000 Open	Yu	Emory University	The Replication Stress Response in Pancreatic Cancer	RP: To identify Replication Stress Response genes and evaluate them as potential biomarkers for pancreatic cancer treatment response. Completed a loss of function genetic screen using a siRNA library of somatically mutated genes. Selected 20 gene candidates for further analysis. MR: Higher risk of pancreatic cancer has been shown in populations exposed to environmental agents and pesticides such as Agent Orange. Higher risk of pancreatic cancer in Vietnam nurses has been reported.
CA110636 $313,690 Open	Fletterick	University of California, San Francisco	Inhibition of Pancreatic Cancer Cell Proliferation by LRH-1 Inhibitors	RP: To find selective and potent compounds that inhibit LRH-1 activity in human pancreatic ductal adenocarcinoma cells and blunt their growth, proliferation, and spread. Performed computational filtering of over 5 million compounds with top ranked hits selected for further analysis. Outcomes: *J Biol Chem* (2013) 288:19830-19844. MR: Higher risk of pancreatic cancer has been shown in populations exposed to environmental agents and pesticides such as Agent Orange.

Log No/ Amount/ Status	Principal Investigator	Institution	Application Title	Research Project (RP) and Military Relevance (MR)
CA110724 $289,988 Open	Phanstiel	University of Central Florida	Development of Novel Cancer Therapies that Target Polyamine Metabolism	RP: To determine if sustained polyamine depletion in human pancreatic cells leads to apoptosis so that a combination therapy can be developed using inhibitors of polyamine biosynthesis and transport. Identified a new gene associated with polyamine transport that could serve as a potential biomarker. MR: Higher risk of pancreatic cancer has been shown in populations exposed to environmental agents and pesticides such as Agent Orange. Higher risk of pancreatic cancer in Vietnam nurses has been reported.
CA110731 $340,894 Open	Corcoran	Massachusetts General Hospital	An in Vivo shRNA-Drug Screen to Identify Novel Targeted Therapy Combinations for KRAS Mutant Cancers	RP: To use a novel in vivo RNAi drug screening approach to rapidly identify genes that when inhibited, allow MEK inhibitors to work against KRAS mutant pancreatic cancer cells. Completed the primary in vitro shRNA drug screen and prioritized the top 100 gene targets for a secondary screen in an orthotopic mouse model of pancreatic cancer. MR: Higher risk of pancreatic cancer has been shown in populations exposed to environmental agents and pesticides such as Agent Orange. Higher risk of pancreatic cancer in Vietnam nurses has been reported.
CA110832 $290,720 Open	Mukherjee	University of North Carolina, Charlotte	A Novel Association and Therapeutic Targeting of Neuropilin-1 and MUC1 in Pancreatic Cancer	RP: Exploration of the hypothesis that MUC1, a marker of aggressive tumors, is driving metastatic spread by increasing Neurophilin 1 levels within pancreatic tumors. Showed that NRP1 may be an excellent target for treating MUC1 positive, but not negative, pancreatic ductal adenocarcinoma. MR: Higher risk of pancreatic cancer has been shown in populations exposed to environmental agents and pesticides such as Agent Orange.
CA110994 $388,633 Open	Sabatini	Whitehead Institute for Biomedical Research	Targeting Pathways that Process Endogenous Toxic Metabolites in Pancreatic Cancers	RP: To identify the pathways that produce and remove endogenous toxic metabolites in pancreatic cancers and to examine how those pathways can be targeted to selectively cause toxicity in pancreatic cancer cells. Results so far suggest that intermediates of tryptophan breakdown may be good targets for therapies based upon toxic metabolites. MR: Higher risk of pancreatic cancer has been shown in populations exposed to environmental agents and pesticides such as Agent Orange. Higher risk of pancreatic cancer in Vietnam nurses has been reported.

Log No/ Amount/ Status	Principal Investigator	Institution	Application Title	Research Project (RP) and Military Relevance (MR)
CA111019 $311,152 Open	Jacks	Massachusetts Institute of Technology	Investigating the Mechanism of K-RAS-Independent Growth of Murine Pancreatic Ductal Adenocarcinoma in Vitro and in Vivo	RP: To use RNAi-based technology to knock down K-RAS mutant cells both in vivo and in vitro to identify the K-RAS-independent growth pathways in pancreatic cancer that can be targeted for drug therapy. Progress includes the identification and characterization of a reversible K-ras-independent state as murine cells, both in vitro and in vivo, can survive and proliferate despite persistent K-ras knockdown. MR: Higher risk of pancreatic cancer has been shown in populations exposed to environmental agents and pesticides such as Agent Orange. Higher risk of pancreatic cancer in Vietnam nurses has been reported.
CA111036 $215,325 Open	Kimmelman	Dana-Farber Cancer Institute	In Vivo Measurement of Oncogenic Kras-Dependent Glucose Metabolism in Mouse Models of Pancreatic Cancer	RP: To develop a novel method to measure the incorporation of glucose into pancreatic tumor models to assess where it is metabolized to develop a list of critical elevated metabolites and their associated pathways. Method development in progress. Data so far support the feasibility of in vivo tumor labeling using ^{13}C glucose. MR: Higher risk of pancreatic cancer has been shown in populations exposed to environmental agents and pesticides such as Agent Orange. Higher risk of pancreatic cancer in Vietnam nurses has been reported.
CA120028 $405,600 New Award	Du	Cornell University, Weill Medical College	RHAMMB Promotes Liver-Specific Metastasis of Pancreatic Neuroendocrine Tumors	RP: To determine the role of EGFR in RHAMMB (receptor for hyaluronan-mediated motility isoform B) induced liver metastasis and the clinical relevance of RHAMMB in human pancreatic neuroendocrine tumors. Research has just been initiated. MR: Military missions benefit when the military families are healthy and well.
CA120057 $410,940 New Award	Ting	Massachusetts General Hospital	Impact of Noncoding Satellite Repeats on Pancreatic Cancer Metastasis	RP: To study the role of RNA satellites in pancreatic cancer genetics, metastasis, and circulating tumor cells. Research has just been initiated. MR: Higher risk of pancreatic cancer has been shown in populations exposed to environmental agents and pesticides such as Agent Orange. Higher risk of pancreatic cancer in Vietnam nurses has been reported

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CA120188 $373,200 New Award	Rhim	University of Michigan	A Novel Mechanism for Post-Transcriptional Regulation in Pancreatic Cancer Progression	RP: To study the RNA-DNA differences (RDD) in pancreatic pre-cancer and tumor cells and determine the genes in which RDD occur during cancer progression. Research has just been initiated. MR: Pancreatic cancer is one of the most lethal forms of cancer that affects service members, veterans, and military beneficiaries and their families.
CA120412 $349,382 New Award	Nagrath	University of Michigan, Ann Arbor	Integrated Microfluidic Magnetic CTC Sorter and Enumerator for Early Diagnosis and Management of Pancreatic Cancer	RP: Development of an integrated microfluid magnetic cell sorter and enumerator to separate circulating tumor cells (CTC) from blood for early diagnosis of pancreatic cancer. Research has just been initiated. MR: Higher risk of pancreatic cancer has been shown in populations exposed to environmental agents and pesticides such as Agent Orange. Higher risk of pancreatic cancer in Vietnam nurses has been reported.
Pediatric Brain Tumor				
CA093469 $1,786,229 Open	Gilbertson; Guy; Ellison; Malkin	St. Jude Children's Research Hospital; Hospital for Sick Children	Molecular-Targeted Therapies of Childhood Choroid Plexus Carcinoma (CPC)	RP: Large throughput screening to study candidate oncogenes and potential drug targets for rare cancers. Validated the overlapping human and mouse genetics and initiated the first whole genome sequencing of CPC. Screened 1.26 million compounds in the primary round and 688 compounds in the secondary round and identified 23 hits. The highest hit was gemcitabine, a Food and Drug Administration-approved drug. Selected five compounds for preclinical study and demonstrated in vivo efficacy and favorable pharmacology of gemcitabine that can be progressed immediately to clinical trial. MR: Development of cost-efficient screening techniques for rare diseases will benefit military medicine.

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CA100157 $465,000 Open	Read	Emory University	Identification and Characterization of Metastatic Cancer Stem Cells in Medulloblastoma	RP: To identify and characterize cells responsible for metastatic disease in medulloblastoma patients, identify genetic markers that predict metastasis, and find novel molecular targets for therapeutics. Found that smo/smo and ptc +/- primary medulloblastoma could be propagated by CD15+/Math1+ cancer stem cells. Identified a unique protein, Math1, as well as markers and drivers of metastasis as therapeutic targets. MR: Epidemiology studies have shown that several forms of cancer including pediatric brain tumors have higher incidence in military populations compared to the general population. Environmental exposure to cytotoxic and chemical carcinogens could be a contributing factor.
CA100335 $450,843 Open	Keating	University of Colorado, Denver, Anschutz Medical Campus	Targeting Pediatric Glioma with Apoptosis and Autophagy Manipulation	RP: This study seeks to understand the molecular signaling mechanisms involved in pediatric glioma cell survival with the goal to manipulate them and develop novel efficacious therapies. Confirmed the upregulation of autophagy by MerTK and Axl shRNA inhibition in several human glioma cell lines. Successful inhibition of Mer and Axl RTK with a commercially available small molecule inhibitor resulted in increased apoptosis, decreased migration, and suppressed tumor growth. MR: The health and welfare of the force is partially determined by the health and welfare of their supportive families. Military missions benefit when the warfighters' families are healthy and well.
CA100469 $531,373 Open	Zong	University of Virginia	Social Behavior in Medulloblastoma: Functional Analysis of Tumor-Supporting Glial Cells	RP: Investigation for understanding the crosstalk between glial cells and medulloblastoma. The study found that glial-ablation treatment resulted in complete remission of tumors. Such treatment was also effective for late-stage tumors. MR: The health and welfare of the force is partially determined by the health and welfare of their supportive families. Military missions benefit when the warfighters' families are healthy and well.

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CA100601 $456,583 Open	Becher	Duke University	Genetically Engineered Mouse Model of Diffuse Intrinsic Pontine Glioma as a Preclinical Tool	RP: Development of valid animal models to promote understanding of tumorigenesis, safety, and toxicities of therapies and identification of novel therapeutic targets and/or resistance mechanisms. Generated several diffuse intrinsic pontine glioma mouse models in which a transcription factor, pax3, was found to be significantly upregulated. Outcomes: *Science* (2013) 340:857-861. MR: The health and welfare of the force is determined by the health and welfare of their supportive families. Military missions benefit when the warfighters' families are healthy and well.
CA100735 $511,136 Open	Paddison	Fred Hutchinson Cancer Research Center	Pediatric Glioblastoma Therapies Based on Patient-Derived Stem Cell Resources	RP: Isolation and characterization of glioma stem cells (GSC) from pediatric patients in orthotopic xenograft mouse models and the assessment of whether they diverge from adult GSC. The PI isolated GCS and developed a protocol for Glioblastoma multiforme tumor classification from RNA-sequencing data. MR: The health and welfare of the force is partially determined by the health and welfare of their supportive families. Military missions benefit when the warfighters' families are healthy and well.
CA101163 $117,975 Closed	Li	Baylor College of Medicine	Harnessing Autopsied DIPG Tumor Tissues for Orthotopic Xenograft Model Development in the Brain Stems of SCID Mice	RP: Development of mouse models to better understand carcinogenesis and its treatment. Created two orthotopic xenograft models for DPIG via the engrafting of autopsy tumor cells into the brains of SCID mice. Demonstrated that xenograft tumors could replicate key histopathological features of the original tumor. MR: Advancing genetic research has a direct application to active, reserve, and retired U.S. military personnel and their families, as a military lifestyle entails potential exposure to carcinogens known and presumed, chemical and physical/radioactive in nature, both in training and in deployment, and related to equipment utilization and/or combat.

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CA120318 $400,425 New Award	Huang	Cornell University, Weill Medical College	Characterizing and Targeting Bone Marrow-Derived Inflammatory Cells in Driving the Malignancy and Progression of Childhood Astrocytic Brain Tumors	RP: To study the functions of bone marrow-derived inflammatory cells (BMDCs) in the progression of pediatric glioma and develop therapeutic strategies to target a specific population of BMDCs to suppress the malignant transformation of gliomas. Research has just been initiated. MR: Military missions benefit when military families are healthy and well.
Pediatric Cancer				
CA110045 $80,401.50 Open (Early Termination)	Garcia	University of North Carolina at Chapel Hill	Aspm, a Key Element in Medulloblastoma Pathogenesis and a Novel Target for Treatment	RP: To test the hypothesis that Aspm, a growth-promoting gene required for cerebellar development, is subsequently drafted into the process of medulloblastoma formation. Found that Aspm becomes co-opted during medulloblastoma formation to support tumor growth by reducing stress to genomic DNA during cell division. MR: The health and welfare of the force is partially determined by the health and welfare of their supportive families. Military missions benefit when the warfighters' families are healthy and well.
CA110089 $381,600 /Open	Shi	University of Texas, Southwestern Medical Center at Dallas	Function of Brg1 Chromatin Remodeling Factor in Sonic Hedgehog-Dependent Medulloblastoma Initiation and Maintenance	RP: To determine the function of Brg1 in Shh signaling-activated medulloblastoma tumor formation and progression. Results so far show that the chromatin remodeler Brg1 is required for medulloblastoma growth in primary culture and that its deletion inhibits progression. MR: The health and welfare of the force is partially determined by the health and welfare of their supportive families. Military missions benefit when the warfighters' families are healthy and well.

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CA110407 $308,584 Open	Jedlicka	University of Colorado, Denver, Anschutz Medical Campus	Hypoxia in Ewing Sarcoma Stem Cell Properties and Drug Resistance	RP: To evaluate the inhibition of hypoxia inducible factor complex using microRNAs to see if they will inhibit the stem cell-like properties of Ewing Sarcoma cells, thus increasing their sensitivity to chemotherapy. Determined that the hypoxia response is mixed with both tumor promotional and tumor inhibitory effects in Ewing Sarcoma. A new, more specific, target downstream of HIF1α has been identified. MR: The health and welfare of the force is partially determined by the health and welfare of their supportive families. Military missions benefit when the warfighters' families are healthy and well.