

Grant Profile Information

Stanley Adoro, PhD

ER Stress Response as Anti-cancer Brake in Hematopoietic Stem Cells

Case Western Reserve University
Department of Pathology
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Cleveland, OH 44106-4979

Grant No. RSG-19-025-01-DDC
Division: North Central
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$792,000
Total ACS Support: \$792,000

Area of Research:	Cancer Initiation: Oncogenes and Tumor Suppressor Genes	50%
	Endogenous Factors in the Origin and Cause of Cancer	50%
Types of Cancer:	Blood Cancer	100%

Project Summary

Acute myelogenous leukemia (AML), a very aggressive blood cancer in children and adults, is the deadliest of all blood cancers. Despite recent advances in understanding the origins and properties of AML cells, the death toll from this disease has remained unchanged in the last twenty years. About seventy-five percent of patients diagnosed with AML will die within 5-years, translating into an annual death toll of more than 10,000 lives in the US alone. Therefore, more potent and effective therapies are urgently needed to reverse these statistics. Our recent research has uncovered a previously unknown and critical function for an enzyme-transcription factor duo IRE1alpha-XBP1 in restraining the emergence of AML in the bone marrow hematopoietic stem cells from which AML arise. In this proposal we are seeking to understand how IRE1alpha-XBP1 signaling controls the unique properties that enable AML initiation, maintenance and chemotherapy resistance. We envision and will test a new paradigm that induction of IRE1alpha-XBP1 signaling in the malignant blood stem cells which go on to establish AML disease will limit their activity and ameliorate disease. These studies will not only advance our understanding of this deadly disease but also has the potential to uncover new therapeutic strategies for durable AML cure. In this regard, a major advantage of our work is that IRE1alpha is an enzyme (with two interdependent catalytic sites) and enzymes often represent the best targets for therapeutic drug development.

Grant Profile Information

Joshua L. Andersen, PhD

Regulation and Oncogenic Mutation within a Novel PDFR-TNK1 Signaling Axis

Brigham Young University
Department of Chemistry and Biochemistry
685 E. University Parkway
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Grant No. RSG-19-006-01-CCG
Division: North
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$778,000
Total ACS Support: \$778,000

Area of Research:	Cancer Initiation: Alterations in Chromosomes	10%		
	Cancer Initiation: Oncogenes and Tumor Suppressor Genes	70%		
	Cancer Progression and Metastasis	20%		
Types of Cancer:	Colon and Rectal Cancer	30%	Leukemia / Leukaemia	30%
	Hodgkin's Disease	30%	Lung Cancer	10%

Project Summary

Targeted cancer therapies, which offer the hope of improving patient survival while minimizing side effects, are aimed at inhibiting the fundamental genetic alterations that drive cancer in a particular individual. While these genetic alterations can be broadly categorized, they often vary between cancer types and individuals. Therefore, the clinical success of targeted therapies hinges on our ability to identify and characterize these genetic alterations—allowing clinicians to customize treatment for a particular patient. Our laboratory recently discovered a novel genetic alteration/mechanism for a gene called TNK1 that we believe underlies a subset of human cancers. This proposal focuses on gaining a fundamental understanding of how TNK1 is regulated in cancer and developing a strategy to block TNK1 in cancer patients. Thus, the work proposed here would be a major step forward as it would identify a potentially novel cancer driver and avenue for targeted therapy that may ultimately alleviate suffering and save lives.

Grant Profile Information

Elizabeth A. Anderson, MSN

Hispanic Cultural Influences on Breast Cancer-related Lymphedema Behaviors

The Curators of the University of Missouri
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Grant No. DSCN-19-053-01-SCN
Division: North
Term of Grant: 07/01/2019-06/30/2021
Total Award: \$30,000
Total ACS Support: \$30,000

Mentor: Jane M. Armer, PhD, RN

Area of Research:	Patient Care and Survivorship Issues	50%
	Population-based Behavioral Factors	50%
Types of Cancer:	Breast Cancer	100%

Project Summary

Breast cancer-related lymphedema (BCRL) is a condition characterized by the escape of protein-rich fluid from the lymphatic system into the surrounding tissues on the side of the body affected by breast cancer. Caused by surgery, chemotherapy, and/or radiation therapy, this condition can profoundly impact the survivorship journey of the over 3.5 million women currently diagnosed with breast cancer who remain at a lifetime risk for developing this condition. Understanding this condition and taking steps to prevent and manage complications are important to sustaining a functional quality of life for the survivor. Many research studies have sought to identify and define factors that impact BCRL prevention and management behaviors. These include skin care, wearing compression garments, infection and injury prevention, weight management, physical function, and psychosocial support. Research efforts have also attempted to discover culturally-specific concepts to provide health care professionals, community advocates, and caregivers with information that tailors care activities to the needs of the individual survivor. Little of this work has explored these factors and concepts in the Hispanic population. As members of a growing ethnic population in the United States (second largest at 18.1%, 2017 Census Data), Hispanic women face significant challenges in living with BCRL including higher obesity risk, decreased engagement in physical activity, and health care system navigation difficulties. This research project will add to the understanding of Hispanic cultural influences on health behaviors needed to minimize risk of BCRL. This work has the potential to contribute foundational information for developing evidence-based interventions for the lifelong support of Hispanic survivors as well as other ethnic populations.

Breast cancer facts and figures, 2017-2018. American Cancer Society. Retrieved on September 28, 2018 from <https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/breast-cancer-facts-and-figures/breast-cancer-facts-and-figures-2017-2018.pdf>
United States Census Bureau. QuickFacts. Retrieved on September 27, 2018 from <https://www.census.gov/quickfacts/fact/table/US/IPE120217>

Grant Profile Information

Scott Atwood, PhD

GLI Activation in Basal Cell Carcinoma

University of California, Irvine
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Grant No. RSG-19-089-01-DDC
Division: West
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$792,000
Total ACS Support: \$792,000

Area of Research:	Cancer Initiation: Oncogenes and Tumor Suppressor Genes	75%
	Systemic Therapies - Discovery and Development	25%
Types of Cancer:	Skin Cancer (non-melanoma)	100%

Project Summary

Drug resistance to current therapies designed to treat Hedgehog-driven cancers is a growing and unmet problem. Drugs that target the Hedgehog pathway were first approved for advanced basal cell carcinoma, the most common form of skin cancer, but are currently used to treat a variety of Hedgehog-driven cancers such as medulloblastoma and ameloblastoma. Although these drugs result in robust tumor regression in many cases, they are effective in only 40% of advanced basal cell carcinoma tumors with 20% of patients that do respond to therapy developing drug resistance each year. This unmet problem illustrates an urgent need to identify new therapeutic targets to suppress the Hedgehog pathway. The consequence of not meeting this need will likely be the inability to treat patients who are resistant to current approved therapies, leading to an increase in mortality for patients with advanced basal cell carcinoma and other Hedgehog-dependent cancers.

The long-term goals of this proposal are to identify and develop targeted therapeutics to treat drug-resistant Hedgehog-driven cancers. To do this, we will define how GLI, the transcription factor responsible for Hedgehog target gene expression, is activated in drug-resistant basal cell carcinoma. We have performed a large screen of GLI mutations found in patient tumor samples and have found that GLI is activated in several distinct ways. We hypothesize that these GLI activation states drive drug resistance, and that targeting the signaling pathways that activate GLI will suppress tumor growth. The goals of Aim 1 and 2 are to define how specific mutations in GLI promote its activity, how the activation pathways are affected by these GLI mutations, and how they contribute to drug resistance. Additionally, we aim to pharmacologically target these activation pathways during tumor growth to demonstrate their ability to suppress drug-resistant cancer.

Grant Profile Information

Gleneara E. Bates-Pappas, MS

Telemedicine to Improve QOL and Cognitive Function in Cancer Survivors

City College of the City University of New York
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Grant No. DSW-19-065-01-SW
Division: Northeast
Term of Grant: 07/01/2019-06/30/2021
Total Award: \$40,000
Total ACS Support: \$40,000

Area of Research:	Patient Care and Survivorship Issues	100%
Types of Cancer:	Breast Cancer	50%
	Lung Cancer	50%

Project Summary

Title: Telemedicine to Improve Quality-of-Life and Cognitive Function in Post-Treatment Cancer Survivors

The proposed study will provide valuable support in defining how oncology social workers are an integral part of interdisciplinary care teams for cancer patients and how telemedicine can be used as a complementary platform to provide psychosocial care, while simultaneously working towards understanding the barriers to accessing psychosocial treatment beyond health literacy for racial/ethnic minorities. The study aims to 1) Analyze existing telehealth platforms for psychosocial support. 2) Analyze telehealth policies including reimbursement, coverage, and approved providers. 3) Explore how telemedicine can help address racial disparities in accessing psychosocial support.

Grant Profile Information

Claudia Benavente, PhD

Role of UHRF1 in Osteosarcoma

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Grant No. RSG-19-031-01-DMC
Division: West
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$763,000
Total ACS Support: \$763,000

Area of Research:	Cancer Initiation: Oncogenes and Tumor Suppressor Genes	10%
	Cancer Progression and Metastasis	90%
Types of Cancer:	Bone Cancer	100%

Project Summary

Osteosarcoma is the most common primary cancer of bone and typically occurs in children and young adults. As a highly metastatic cancer, 15-20% of osteosarcoma patients are diagnosed after the cancer has already metastasized (typically to the lungs), which translates to 5-year survival rates of less than 40%. In comparison, patients without metastases have survival rates of 65-75%. Unfortunately, pulmonary metastases occur in nearly half of all osteosarcoma patients. Thus, there is a pressing clinical need to determine the factors responsible for metastasis in osteosarcoma to facilitate development of new therapeutic strategies. Loss of the tumor suppressor gene RB1 is associated with increased mortality, metastasis and poor therapeutic outcome in patients with osteosarcoma. However, the mechanism(s) through which RB1 loss leads to poor prognosis remains to be elucidated. This proposal will test a model for how loss of RB1 worsens clinical outcome that has the potential of becoming an alternative therapeutic approach to prevent metastasis in osteosarcoma patients. We found that UHRF1 protein is accumulated in osteosarcoma tumors. UHRF1 is a multifunctional protein involved in epigenetic regulation. We created a novel mouse model to study the role of UHRF1 in osteosarcoma and have tested the effects of high UHRF1 protein levels in human osteosarcoma cells and have results that suggest that the accumulation of UHRF1 protein in osteosarcoma contributes to tumorigenesis, migration, invasion, and potentially metastasis. UHRF1 has interesting connections with RB: the RB pathway in lowering the UHRF1 protein levels in normal cells and further, RB can interact with the UHRF1 protein – potentially controlling its activity. This makes UHRF1 an especially important protein to evaluate its role in the poor prognosis associated with loss of RB1. The main goal of our study is to determine the mechanism(s) through which UHRF1 overexpression in osteosarcoma contributes to tumor progression and determine how RB influences its activity. Overall, this research proposal will broaden our understanding of the function of UHRF1 in osteosarcoma formation and metastasis and further investigate its potential as a therapeutic target. Since UHRF1 is overexpressed in multiple types of cancers, including breast, prostate, and lung cancer, this research proposal has the potential to impact human health beyond osteosarcoma.

Grant Profile Information

Slobodan Beronja, PhD

Oncogene-induced Differentiation Inhibits Tumorigenesis in Oral Epithelium

Fred Hutchinson Cancer Research Center
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Grant No. RSG-19-074-01-TBE
Division: West
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$792,000
Total ACS Support: \$792,000

Area of Research:	Normal Functioning	10%
	Cancer Initiation: Oncogenes and Tumor Suppressor Genes	90%
Types of Cancer:	Head and Neck Cancer	95%
	Skin Cancer (non-melanoma)	5%

Project Summary

Head and neck cancer affects 50,000 new patients in the United States every year, with majority of them classified as squamous cell carcinoma (HNSCC). Its 5-year survival rate is ~62%, up from ~54% in 1975. In addition, the current standard of care of surgery followed by chemotherapy leaves many survivors with painful and disfiguring existence. Such small improvement in therapeutic outcome and significant reduction in quality of life for patients highlight the importance of investing in development of innovative approaches to treat HNSCC.

Tumors, including HNSCC, are composed of cells with unequal potential to sustain long-term growth. Cancer stem or progenitor cells, which make up a small fraction of the tumor tissue, are critical for tumor growth and maintenance. On the other hand, the bulk of the tumor is composed of cells with either limited or no potential to proliferate. They arise from cancer progenitor cells, through a process of differentiation. This natural dynamic of transition from a proliferative to a non-proliferative state, which also occurs in normal oral tissue, suggests a therapeutic intervention that would attempt to eliminate cancer by forcing proliferative cancer progenitors to differentiate. Such approach would be radically different from current chemo and radiotherapy approaches to kill them. Significant block to designing such an innovative therapy is that we still have a poor understanding of molecular mechanisms that regulate differentiation.

Recent advances in DNA sequencing technologies have allowed us to begin to explore cancer in an unprecedented way. Studies have now catalogued thousands of genetic mutations in tumors, and identified *Pik3ca* as the third most commonly mutated gene in HNSCC. Our research is focused on the role of *Pik3ca* in HNSCC initiation and maintenance. We began our investigation in the oral epithelium, the tissue of origin for majority of HNSCC, using a genetic mouse model. We observed that activating mutations in *Pik3ca* drive cell proliferation, yet do not promote cancer and have no effect of overall tissue growth. This suggested a striking hypothesis that, in the oral epithelium, *Pik3ca* also promotes some other cellular process to counterbalance its effect on proliferation.

Using a novel quantitative assay we discovered that mutant *Pik3ca* also promotes differentiation. We decided to use our observation and mutant *Pik3ca*-expressing mice as a springboard to uncover molecular mechanisms that increase differentiation. We tested over 700 genes, some commonly mutated in HNSCC and others known targets of *Pik3ca* signaling, and identified three that mediate loss of progenitor cells through differentiation. We propose to focus on these and perform in depth analysis of how they contribute to initiation and maintenance of HNSCC. We expect this to be a first step in a continuum of research that will explore their suitability as targets for development of new therapies to treat HNSCC.

Grant Profile Information

Christine F. Brainson, PhD

Methionine Metabolism and Lung Cancer Lineage Fate

University of Kentucky Research Foundation
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HSRB 456
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Grant No. RSG-19-081-01-TBG
Division: North Central
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$792,000
Total ACS Support: \$792,000

Area of Research:	Cancer Progression and Metastasis	50%
	Interactions of Genes and/or Genetic Polymorphisms with Exogenous and/or Endogenous Factors	50%
Types of Cancer:	Lung Cancer	100%

Project Summary

Lung cancer is a devastating disease with high mortality even when diagnosed at an early stage, and it has several distinct subtypes. The two major diagnoses within non-small cell lung cancer, adenocarcinoma (ADC) and squamous cell carcinoma (SCC), are historically treated as separate diseases. However, mounting evidence shows that reprogramming from ADC to a more SCC fate allows lung cancers to evade therapies. The proposed studies aim to understand how cellular metabolism influences this cellular reprogramming by using mouse models and human lung cancer cells. This research is important for understanding how to influence lung cancer subtype through modulation of metabolism to improve treatment outcomes.

Grant Profile Information

Yuri Bunimovich, MD, PhD

Novel Treatment of Melanoma Through Sensory Nerve Targeting

University of Pittsburgh
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Grant No. RSG-19-088-01-CSM
Division: Northeast
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$792,000
Total ACS Support: \$792,000

Area of Research:	Cancer Progression and Metastasis	90%		
	Combinations of Localized and Systemic Therapies	5%		
	Complementary and Alternative Treatment Approaches	5%		
Types of Cancer:	Melanoma	95%	Skin Cancer (non-melanoma)	5%

Project Summary

Cancerous cells must meet several conditions to facilitate their growth and invasion. Some of these conditions are cell-dependent: they immortalize tumor cells and allow them to grow indefinitely. Other conditions optimize the environment around tumor, minimizing body's natural resistance against expanding cancer. Cancer relies on presence of various cells within the surrounding environment to support its invasion. For example, blood vessels, immune cells and other components of the tumor microenvironment may assist in cancer progression. Understanding which non-malignant cells support tumor growth is important because new medications may be developed to target these cells.

Nerves are also present in the tumor microenvironment, but their role in supporting tumor progression remains unclear. We recently provided the first evidence that sensory neurons and neuroglia promote melanoma growth. Further work elucidating the mechanism of sensory nerve interaction with tumor is needed. Schwann cells, primary neuroglial cells of the peripheral nervous system, are intimately associated with nerves, functioning in nerve maintenance and repair. However, despite their abundance in most tissues, especially the skin, almost nothing is known about role of Schwann cells in cancer progression. Melanoma cells interact with Schwann cells and sensory nerves, but this interaction is poorly understood. Our preliminary data strongly suggest that interaction between melanoma cells, sensory nerves and Schwann cells facilitates melanoma growth and metastasis, and plays a particularly important role during early melanoma development. Proposed study will uncover how melanoma-associated sensory nerves and Schwann cells support melanoma growth, invasion, and metastasis.

Melanoma and non-melanoma skin cancers, such as squamous cell carcinoma, are significant burden on our society, arising primarily from long and frequent exposures to ultraviolet radiation. Incidence of melanoma is increasing every year, and in advanced forms these types of skin cancer are often fatal. Improving our understanding of factors which influence melanoma metastasis is critical to patient care. The main significance of the proposed study is the discovery of a new important mechanism of melanoma progression, and the identification of new targets for the development of advanced therapy against melanoma and other skin cancers. Uncovering and understanding complex interactions between melanoma cells, nerves Schwann cells and the immune system will open new opportunities for melanoma treatment, and will be invaluable to investigations and treatments of other malignancies.

Grant Profile Information

Lisa Capparella, MSW

Master's Training Grant in Clinical Oncology Social Work

Thomas Jefferson University
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Sidney Kimmel Cancer Center
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Grant No. MSW-19-070-01-SW
Division: Northeast
Term of Grant: 07/01/2019-06/30/2021
Total Award: \$24,000
Total ACS Support: \$24,000

Project Summary

Patient Support Services at the NCI-Designated Sidney Kimmel Cancer Center (SKCC) is a comprehensive program designed to provide our patients, their caregivers and the community at large with support and educational resources throughout the trajectory of cancer care. Our team consists of 10 Masters prepared Social Workers, 2 Clinical Dietitians, 3 Financial Counselors/Advocates, 2 research assistants, a psychiatrist and an American Cancer Society Navigator. We also provide educational and internship/field placement opportunities for Social Work, Public Health and Medicine trainees. Our team members have taught, presented and published at local and national levels and are actively engaged in numerous research projects looking at (selected projects): health and digital literacy, supportive care for behaviorally challenging patients, lung cancer screening for diverse underserved populations, medicinal cannabis, addressing the unique needs of geriatric cancer patients.

Within Patient support Services the following programs are also available:

The SKCC Support and Welcome Center: Freestanding facility which houses all of our educational and support programs as well as a repository of patient facing evidence-based educational materials curated by the center director (Clinical Social Worker-PI) and disease team leads throughout the institution.

The Neu Center for Supportive Medicine and Cancer Survivorship: Comprehensive palliative care/cancer survivorship program driven by a biopsychosocial screening program to ensure patients and caregivers are connected with appropriate supportive care resources throughout their care into survivorship or end-of-life.

Psychiatric-Oncology and Supportive Counseling: A need-blind philanthropy funded program which provides psychiatric consultation and treatment as well as short-term supportive counseling (Clinical Social Worker led) for our patients who require or request these services.

Colameco Medical Transportation Program: Provides transportation to appointments for any patient who experiences this as a barrier. This program has essentially eliminated transportation as an access barrier at the SKCC.

Grant Profile Information

Rumela Chakrabarti, PhD

DLL1 Mediated Notch Signaling in Tamoxifen Resistance of Breast Cancer

The Trustees of the University of Pennsylvania
Department of Biomedical Sciences
411 Hill Pavilion
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Philadelphia, PA 19104

Grant No. RSG-19-026-01-DDC
Division: Northeast
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$792,000
Total ACS Support: \$792,000

Area of Research:	Cancer Initiation: Oncogenes and Tumor Suppressor Genes	50%
	Cancer Progression and Metastasis	50%
Types of Cancer:	Breast Cancer	100%

Project Summary

Breast cancer is a leading cause of death in women. Determining the best way to treat individual breast cancer patients is complicated by the differential response of breast cancer subtypes and the resistance that can develop to known therapies. Since breast cancer in the majority of patients (~75%) depends on signaling through the estrogen receptor (ER), many patients are initially treated with Tamoxifen, a drug that inhibits this process. The initial response of most patients to Tamoxifen treatment is favorable, but approximately 50% of patients eventually acquire resistance to this drug. Unfortunately the survival rate of tamoxifen resistant patients is only 20% at 5 years, highlighting the critical need to advance additional therapies for these patients.

Abnormal activation of Notch signaling is frequently observed in breast cancer patients and we have recently found that tamoxifen resistant ER+ cells express higher levels of Delta like 1 (DLL1), a ligand of the Notch signaling pathway. Interestingly, our recently published studies demonstrated that DLL1 maintains normal mammary gland development by inducing Notch signaling in macrophages, an event that is important for maintenance of mammary stem cells. Moreover, new data from our lab show that DLL1 is specifically overexpressed in ER+ luminal breast cancer and is associated with increased metastasis, suggesting a subtype specific function for this ligand. Notably, the tumor and metastasis promoting function of DLL1 is also associated with increased numbers of cancer stem cells (CSCs), cells that are capable of promoting tumorigenesis and are thought to promote tamoxifen-resistance in ER+ luminal breast cancer cells. Finally, publicly available patient datasets also indicate that tamoxifen treated patients expressing high DLL1 have a worse clinical outcome than do patients expression low levels of DLL1, supporting our hypothesis that DLL1 influences outcome in this group of patients.

This study will benefit a large population of patients with ER+ breast cancer who have developed resistance to tamoxifen. We will determine why some ER expressing tumor cells gain resistance to current therapies and how can we replace the current drug therapy with a new combinational therapy which will improve the prognosis for these patients. Specifically, we predict that therapeutic targeting of DLL1 will be highly beneficial for treatment of tamoxifen resistant patients. DLL1 blocking antibodies are available commercially and are being currently tested in preclinical mouse models in our laboratory to efficiently block endogenous DLL1. Our studies will support the potential translation of a combinatorial treatment combining DLL1 blocking antibodies with tamoxifen to treat ER+ breast cancer. Thus this study has potential to revolutionize the current therapy and reduce the chances of risk and reduce the breast cancer associated mortality rate.

Grant Profile Information

Avonne Connor, PhD

Evaluation of Novel Approaches to Address Breast Cancer Disparities

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E6144
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Grant No. MRS-19-010-01-CPHPS
Division: Northeast
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$583,000
Total ACS Support: \$583,000

Area of Research:	Patient Care and Survivorship Issues	34%
	Surveillance	33%
	Population-based Behavioral Factors	33%
Types of Cancer:	Breast Cancer	100%

Project Summary

Breast cancer (BC) mortality rates in the United States have been declining over the past several decades due to the improvement in BC treatment and early detection. Unfortunately, the same decline in BC mortality rates has not been observed across all races, particularly among African American and Hispanic women. We believe the reason for these differences in mortality is likely due to a combination of factors related to their cancer, overall health status, and their socioeconomic status. Only a few studies have considered the effects of these factors on health outcomes in African American and Hispanic BC survivors. The goal of this research is to identify African American and Hispanic BC survivors at high risk of dying due to poor health status and/or socioeconomic disadvantages. We propose to conduct three studies to address our research goal. First, we will evaluate a novel approach to recruit 100 African American BC survivors to a research study in Baltimore City and Prince Georges County, Maryland. This study will compare church-based recruitment strategies to respondent-driven sampling. Respondent-driven sampling relies on social ties, an important aspect of African American culture. Using this recruitment method, BC patients will help recruit other BC patients to the study. This novel approach has been successfully used among other hard-to reach populations in Maryland. For our second study, we will combine data from the Maryland Cancer Registry and the 2010 Census for BC patients diagnosed between 2004-2015 throughout the state of Maryland to determine the relationship between chronic diseases, socioeconomic status and BC mortality. Based on preliminary data, we expect to have data on 49,500 women, of which 27% are African American and 3% are Hispanic. Lastly, we will examine the relationship between two blood markers of inflammation (soluble tumor necrosis factor receptor-2 and visfatin), and mortality in 498 Hispanic and non-Hispanic white BC patients from the New Mexico site of the Health Eating Activity and Lifestyle cohort study. These blood markers have been found to be linked with cancer and other chronic diseases, including obesity, diabetes, and hypertension. Our three studies will inform the design and conduct of a future intervention study to improve the survival of African American and Hispanic BC patients in Maryland.

Grant Profile Information

Adele D. Crouch

Doctoral Scholarship in Cancer Nursing Renewal

Indiana University, Indianapolis
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600 Barnhill Drive
Indianapolis, IN 46202-5107

Grant No. DSCNR-19-055-03-SCN
Division: North Central
Term of Grant: 07/01/2019-06/30/2021
Total Award: \$30,000
Total ACS Support: \$60,000

Mentor: Diane Von Ah, PhD, RN

Area of Research:	Patient Care and Survivorship Issues	100%
Types of Cancer:	Breast Cancer	100%

Project Summary

Up to 75% of the more than 3.5 million breast cancer survivors living in the United States, report persistent cognitive dysfunction, or "chemo-brain," including problems such as feeling more forgetful, having difficulty concentrating, and problems with processing information or multi-tasking after cancer treatment has been completed. Of those 3.5 million breast cancer survivors, approximately 60% are 65 years of age and older and that number is expected to grow as our society continues to age. Older breast cancer survivors may be at an increased risk for cognitive dysfunction due to a number of factors including the normal aging process, cancer-related factors, and the effects of chemotherapy treatments. Cognitive dysfunction is receiving more attention, yet the focus remains on all aged breast cancer survivors prior to and immediately after chemotherapy treatment. Less is known about the incidence and associated factors of cognitive dysfunction in older (greater than or equal to 65 years of age) long-term (3-8 years post-treatment without recurrence) breast cancer survivors. This study will add to our knowledge, thoroughly investigate cognitive dysfunction in long-term, older breast cancer survivors, and ultimately work to improve the lives of breast cancer survivors.

Grant Profile Information

Monika A. Davare, PhD

Oncogenic Impact and Targetability of Novel ROS1 Aberrations in Cancer

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Grant No. RSG-19-082-01-TBG
Division: West
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$791,000
Total ACS Support: \$791,000

Area of Research:	Cancer Initiation: Oncogenes and Tumor Suppressor Genes	70%		
	Cancer Progression and Metastasis	10%		
	Systemic Therapies - Discovery and Development	20%		
Types of Cancer:	Brain Tumor	50%	Liver Cancer	15%
	Breast Cancer	15%	Lung Cancer	20%

Project Summary

We work on understanding how abnormalities in a gene called ROS1 contribute to cancer growth. The ROS1 gene encodes an enzyme called a kinase; others" and our previous work showed that when ROS1 activity is turned on, it operates as an 'oncogenic driver", meaning that it provokes uncontrolled growth, and metastatic spread of cells. One way that ROS1 activity increases in human cancer is via a process called chromosomal rearrangement; this event of breaking and repairing genes generates a new type of protein, a chimera, referred to in this case as a ROS1-fusion protein. Of significance is that ROS1-fusion proteins are excellent drug targets; clinical trials show robust responses after administration of ROS1-targeted oral drugs in ROS1+ve cancer patients. Interestingly, ROS1-fusion proteins are found in several different tumor types, including in brain, lung, liver, ovarian, thyroid, and blood vessel, and across all age groups, from pediatric to geriatric cancer patients.

The scientific premise of our proposed research is that there are additional, previously unrecognized ways in which the ROS1 activity is increased, and may be driving cancer. These include mistakes in DNA called mutations, or just making more of the protein, referred to as overexpression. Substantial amounts of tumor genome sequencing data has been generated by academic research groups, and is now in the public domain for research use. Analyzing these data, we find that ROS1 is frequently mutated in various cancers. However, the impact of a given mutation on ROS1 function is unknown (i.e., does the mutation activate ROS1?).

Without experimentation, it is essentially impossible to 'guess" which, if any, of these mutations are relevant. We hypothesize that testing the impact of cancer-associated ROS1 mutations in the laboratory is a mandatory step to ensure that all patients who could benefit from targeted ROS1 therapy are included in clinical trials. Further, even 'negative" experimental finding, i.e., these mutations are inactivating (stop kinase activity) or neutral (no change in kinase activity), is equally important as it enables the oncologist to make an informed treatment plan.

In terms of making more ROS1, we hypothesize that about 10% of glioblastoma patients have tumors whose growth and spread may in part be driven by ROS1; glioblastoma is a particularly lethal form of brain cancer. In two of three aims of this grant, we hope to establish whether ROS1 presence in glioblastoma is a biomarker for potential therapeutic benefit of ROS1-targeted drugs. In summary, without experimental testing of these hypotheses, ROS1 genomic data have limited to no translational utility. The results from our proposed experiments will facilitate the translation of cancer genomic data into new diagnostic tests and therapeutic modalities for ROS1-positive cancer patients in the future, and holds the potential to improve their outcomes.

Grant Profile Information

Ann DeLaForest, PhD

The Role of GATA4 During Gastric Epithelial Cell Homeostasis and Metaplasia

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Grant No. PF-19-023-01-DDC
Division: North
Term of Grant: 07/01/2019-06/30/2021
Total Award: \$111,500
Total ACS Support: \$111,500

Mentor: Michele A. Battle, PhD

Area of Research:	Normal Functioning	50%
	Cancer Initiation: Oncogenes and Tumor Suppressor Genes	50%
Types of Cancer:	Stomach Cancer	100%

Project Summary

Gastric cancer is the third leading cause of cancer related deaths worldwide. Predispositions to gastric cancer include infection with helicobacter pylori, tobacco use, stomach lymphoma and obesity, to name a few. Although it is clear what environmental factors increase gastric cancer risk and the transition of normal stomach to gastric cancer has been defined histologically, the molecular drivers of gastric cancer have been ill defined. Several studies have shown that GATA4, a protein present in the normal stomach, is lost in several cases of stomach cancer. This work provides evidence that GATA4 acts as a tumor suppressor in the stomach, however, the role that GATA4 plays during normal stomach function is vastly understudied. The studies we proposed here will elucidate the role GATA4 plays during normal stomach development and also investigate what happens to the stomach upon loss of GATA4. By better understanding normal gastric epithelial cell homeostasis, we expect to gain new insights into disease pathogenesis that will ultimately be applicable to therapies to treat gastric diseases including gastritis, metaplasia, and cancer. Our studies will specifically elucidate the GATA4-dependent molecular mechanisms guiding normal cell differentiation and function of gastric epithelial cell homeostasis. Our studies will also define a novel set of gastric epithelial cell lineage specific markers, including potential new biomarkers of metaplasia, that will advance our field's ability to study normal gastric development, function and gastric diseases.

Grant Profile Information

Rafael Diaz, BA

Graduate Scholarship in Cancer Nursing Practice

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Grant No. GSCNP-19-062-01-SCN
Division: West
Term of Grant: 07/01/2019-06/30/2021
Total Award: \$20,000
Total ACS Support: \$20,000

Mentor: Carol Viele, RN, MS

Area of Research:	Patient Care and Survivorship Issues	40%
	Education and Communication Research	60%
Types of Cancer:	Not Site-Specific Cancer	100%

Project Summary

A personal experience lead me on the path to becoming a Clinical Nurse Specialist in Oncology. While a senior in high school, a close relative was diagnosed with breast cancer. We understood that cancer was bad, but we did not know how it would affect her. We did not know what medications she was taking, side effects to expect, cost of treatment, or life expectancy. After two years, she passed away. I was angry at how the healthcare system failed to educate us. At the time, I worked as a caregiver and art tutor for an adult with autism. Being a caregiver proved itself to be rewarding, fueling my desire to educate and leading me towards a career in healthcare.

I spent the next ten years working as an home caregiver for physically and mentally disabled people, the elderly and people diagnosed with cancer. I noticed health disparities in these populations. Many had low health literacy. Emergency department admittance was frequent, medication adherence was low, and unhealthy lifestyles were prevalent. I worked hard to educate these individuals about disease prevention and healthy lifestyles. As a caregiver, I recognized the limitations I had due to my lack of education and clinical skills. I wanted to continue providing compassionate care, accompanied with clinical practice and expertise. My goal was to become a Clinical Nurse Specialist in Oncology.

I was accepted to the UCSF Masters Entry-level Program in Nursing, Adult Gerontology Clinical Nurse Specialist in Oncology. I obtained my nursing degree after a year and began working as an infusion nurse in an oncology infusion center. As a nurse, I continued witnessing low health literacy and knowledge deficits. I attributed this to the complexity of the disease and the difficulty of treatment. I have attempted to remedy this by using simplified written data about the disease and review it with the patient, emphasizing teach-back methods. I use the same approach with medication, where I explain each medication and side effects, then have the patient explain it. We prioritize new treatment starts in the morning to give more one-on-one time to educate patients. Nurse burnout also contributes to patient education. I have addressed this problem by working with scheduling staff to set a recovery time during clinic hours that helps to alleviate the demanding work schedule, create time where nurses can take breaks for themselves to focus on clearing their mind. Although I have attempted to create change as a nurse, I understand that knowledge deficits among cancer patients is a system wide problem. My goal once I complete my graduate study is to place myself in a position where I can continue to manage the care of people diagnosed with cancer, by providing education and support to patients and their families, committing to effective communication among the interdisciplinary staff, and facilitate change by using evidence based data to implement policy, emphasizing patient outcomes and safety.

Grant Profile Information

Diana M. Dunn, PhD

Elucidating the Role AMPK Plays in Human Cytomegalovirus Infection

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Grant No. PF-19-038-01-MPC
Division: Northeast
Term of Grant: 07/01/2019-06/30/2022
Total Award: \$163,500
Total ACS Support: \$163,500

Mentor: Joshua Munger, PhD

Area of Research:	Normal Functioning	30%		
	Cancer Initiation: Alterations in Chromosomes	10%		
	Cancer Initiation: Oncogenes and Tumor Suppressor Genes	20%		
	Exogenous Factors in the Origin and Cause of Cancer	10%		
	Patient Care and Survivorship Issues	30%		
Types of Cancer:	Hodgkin's Disease	25%	Myeloma	25%
	Leukemia / Leukaemia	25%	Non-Hodgkin's Lymphoma	25%

Project Summary

Human Cytomegalovirus (HCMV) infection is associated with increased death in cancer patients undergoing immunosuppressive therapies for diseases such as, leukemia and lymphoma. The virus is an opportunistic pathogen, which means it takes advantage of a person's weak immune system in order to hijack cellular function and promote its own replication. HCMV infection is also associated with cancerous phenotypes through manipulation of cellular processes involved in oncogenesis. Viral infection is often a contributor to metabolic reprogramming in the host cell, most notably through the upregulation of energy production needed for viral growth. Our lab has identified a protein, AMP-activated protein kinase (AMPK), as a major facilitator of this HCMV-mediated energy production. AMPK is a tumor suppressor and an energy sensing kinase, which responds to low levels of ATP (energy) in the cell, thus upregulating processes involved in ATP production, and shutting down processes involved in ATP consumption. Identification of this metabolic process has uncovered a new avenue in understanding HCMV infection and replication. Currently, HCMV treatment options are ineffective due to high toxicities and the development of drug resistance. Therefore, we seek to identify novel mechanisms through which HCMV infection can be inhibited. By targeting HCMV-mediated metabolic reprogramming through AMPK regulation, we can develop new anti-HCMV targeting therapies that with fewer side effects in cancer patients. The major questions we are trying to answer are aimed towards understanding the underlying mechanisms behind AMPK regulation by HCMV infection and the subsequent changes in cellular metabolism. We also aim to uncover the causes of AMPK activation during infection. These studies will inform us about the mechanisms behind AMPK regulation and HCMV infection, which will contribute not only to a better understanding of HCMV infection, but also of HCMV-associated cancerous processes. The proposed studies will also help to reach our long-term goal which is to uncover novel targets for anti-HCMV therapies for the treatment of cancer patients. Novel anti-HCMV drugs will alleviate the current issues with HCMV treatment and improve the lives of not only cancer patients, but of individuals with other HCMV-associated diseases such as diabetes and cardiovascular disease.

Grant Profile Information

Alex J. Fauer, BSN

Care for Hematologic Cancers: Patient Experiences and Adverse Events

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Systems, Populations, and Leadership
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Grant No. DSCN-19-048-01-SCN
Division: North Central
Term of Grant: 07/01/2019-06/30/2021
Total Award: \$30,000
Total ACS Support: \$30,000

Mentor: Christopher R. Friese, PhD, RN,
AOCN, FAAN

Area of Research:	Patient Care and Survivorship Issues	40%
	Surveillance	15%
	Resources and Infrastructure Related to Cancer Control/ Survivorship/ and Outcomes Research	5%
	Health Services/ Economic and Health Policy Analyses	40%
Types of Cancer:	Hodgkin's Disease	20%
	Leukemia / Leukaemia	35%
	Non-Hodgkin's Lymphoma	45%

Project Summary

The cancer care system in the United States is markedly complex, and measuring quality of care is challenging. Older adults receiving treatment for cancer are at high risks for adverse health events due to potentially-harmful chemotherapy and presence of other chronic illnesses. Patient experience is one approach to study quality of care because it includes aspects of care coordination, timely access to needed care, and communication with providers. Populations with hematologic (i.e. blood and lymphatic) cancers are rarely the focus of quality of care research.

To date, research focusing on improving care coordination have studied patient navigation, community-based cancer education, and tools to enhance patient-provider communication. Evidence shows that there are rising numbers of cancer survivors who fill prescriptions for psychotropic medications, suggesting persistent needs for psychosocial care throughout survivorship. Quality of care research in breast and colorectal cancer populations is routinely studied, but rarely studied in hematologic cancer populations. Few studies from the literature surveyed patients on the quality of care that was delivered during active treatment and survivorship care. Further research is needed to understand patient experiences of care for hematologic cancers among older adult populations with leukemia and lymphoma diagnoses.

This secondary data analysis will measure patient experiences in terms of care coordination, communication with providers, and the prevalence of emergency department use among diverse Medicare enrollees receiving care for leukemia and lymphoma diagnoses. We will obtain patient experience data from the Surveillance, Epidemiology, and End Results linked Consumer Assessment of Healthcare Providers and Systems dataset (SEER-CAHPS®), in addition to health care utilization data from Medicare claims. We will analyze data from 1,284 participants in the SEER-CAHPS® database who were diagnosed with leukemia or lymphoma from 2000-2015, and have completed at least one CAHPS® survey within the twelve months after diagnosis. We will build statistical models to find associations in patient experience outcomes with racial and ethnic identity, urban/rural variables, and income-level variables. We will conduct statistical analyses on emergency department utilization for anemia, neutropenic fevers, bleeding, and blood product administration.

This study will fill an important gap in oncology literature by measuring patient experiences in terms of care coordination, communication with providers, and the prevalence of emergency department use in older adults with leukemia and lymphoma diagnoses. The results of this study have the potential to influence health care delivery by informing future evidence-based practice and policy improvements towards enhanced health outcomes in this vulnerable patient population.

Grant Profile Information

Christina Ferrer, PhD

Role of Lin28b in Metastatic Outgrowth and Self-renewal in PDA

Massachusetts General Hospital
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Grant No. PF-19-018-01-CSM
Division: Northeast
Term of Grant: 07/01/2019-06/30/2022
Total Award: \$163,500
Total ACS Support: \$163,500

Mentor: Raul Mostoslavsky, MD, PhD

Area of Research:	Cancer Progression and Metastasis	100%
Types of Cancer:	Pancreatic Cancer	100%

Project Summary

Pancreatic ductal adenocarcinoma (PDA) is a grave public health problem with dismal outcomes and a rise in incidence over the past several decades. It is projected to become the second leading cause of cancer-related deaths in the US by 2020. One of the major hurdles to effectively treating pancreatic cancer patients is the high incidence of extra-pancreatic metastasis upon diagnosis, which is the root cause of patient mortality. While the genetic mutations that cause pancreatic cancer have been extensively studied, there has been little work done to explain the mechanisms behind metastatic tumor growth. Our lab has previously identified a subset of pancreatic cancer containing abnormal levels of the embryonic protein Lin28b. Importantly, we determined that Lin28b is required for growth of these highly aggressive tumors and that high levels of Lin28b is associated with poor outcomes in pancreatic cancer patients. More recently, we have demonstrated that Lin28b remains increased in metastatic tumor cells derived from mice with pancreatic cancer. However, the role Lin28b plays in promoting metastatic tumor growth has yet to be explored and will be addressed in this proposal. Since the presence of Lin28b is completely restricted to cancer cells in adults, this information will provide us with a potential target to treat pancreatic cancer metastasis.

Grant Profile Information

Scott R. Floyd, MD, PhD

Role of BRD4 in the Cancer Cell Replication Stress Response

Duke University
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Grant No. RSG-19-030-01-DMC
Division: Southeast
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$789,000
Total ACS Support: \$789,000

Area of Research:	Cancer Initiation: Alterations in Chromosomes	40%		
	Systemic Therapies - Discovery and Development	60%		
Types of Cancer:	Blood Cancer	20%	Lung Cancer	20%
	Brain Tumor	20%	Not Site-Specific Cancer	20%
	Breast Cancer	20%		

Project Summary

All dividing cells must copy their DNA through a process known as DNA replication in order to pass on genetic information to their cellular descendants. DNA is also the template used to make RNA (through a process called transcription) as well as proteins that then carry out all of the functions of the cell. DNA replication in rapidly dividing cells, such as cancer cells, represents a special case. These cells are under stress because the DNA replication process must happen continually to maintain rapid cell growth. Also, cancer cells frequently have abnormally elevated transcription, causing conflicts with the replication of DNA. As a result, conflicts between DNA replication and transcription can damage the DNA, and lead to cell death. Cancer cells have developed mechanisms to tolerate this damage and continue to grow despite replication stress and replication-transcription conflicts. We have identified a new component, the protein BRD4, that we believe cancer cells use to tolerate replication stress and replication-transcription conflicts. BRD4 is particularly important because there are new drugs that can specifically target BRD4 function. In this proposal, we will explore the function of BRD4 in cancer cells, and test ways to manipulate its function. The knowledge gained from this work will help us understand how cancer cells survive stress and conflicts in the DNA and continue growing. This information can be used to target this cancer cell survival process in order to create new cancer therapies specifically using new BRD4-inhibitor drugs.

Grant Profile Information

Kristin Foster, MSN

GSCNP Focusing on Emotional & Mental Health in Pediatric & AYA Cancer

University of Iowa Hospitals and Clinics
College of Nursing
203-ICNB
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Iowa City, IA 52242

Grant No. GSCNP-19-061-01-SCN
Division: North
Term of Grant: 07/01/2019-06/30/2020
Total Award: \$20,000
Total ACS Support: \$20,000

Mentor: Daniel Wesemann, DNP, MSN

Area of Research: Patient Care and Survivorship Issues 100%

Types of Cancer: Not Site-Specific Cancer 100%

Project Summary

Despite significant increases in treatment effectiveness, the diagnosis and treatment of cancer remains one of the most emotionally distressing events in medical care. Distress may extend along the continuum of the cancer experience, ranging from common normal feelings of vulnerability, sadness and fears to problems that can become disabling, such as depression, anxiety, panic, social isolation, and existential and spiritual crisis. During my time working with the pediatric and adolescent and young adult (AYA) cancer populations, it has become clear to me that our patients have a need for emotional and mental health support throughout the cancer trajectory, beginning at diagnosis and continuing throughout survivorship. In the past 2-3 years, our team has conducted gap analyses for development of a variety of programs as well as focus groups for patient insight. Throughout these initiatives, specific gaps in psychosocial care delivery were identified. It was also recognized that our institution, like so many others, has a reactive model for psychosocial aspects of care. Most commonly, those patients receiving support from members of our team were identified after they had entered a crisis and independently began to seek assistance.

Following this startling realization, I took special interest in this problem. I began to conceptualize strategies to convert our practice in this area of care from reactive to proactive. As ideas began to take shape and my passion grew, I began to envision a shift in my own career path to focus on the psychiatric and mental health aspect of cancer care. While we have a constellation of incredible psychosocial health care providers including a psychologist, social workers, child life specialists, and others with specific skill sets to offer, we do not have an individual dedicated to formal assessment of distress at multiple time points throughout the cancer experience, nor do we have a provider dedicated to pharmacological interventions for clinical levels of distress. My decision to return to graduate school to obtain my Doctorate of Nursing Practice (DNP) along the Psychiatric and Mental Health Nurse Practitioner (PMHNP) track was specifically made to gain skill sets in both psychotherapy and psycho-pharmacology to better serve the pediatric and AYA cancer populations in the emotional and mental health aspect of care. This new training coupled with my years of experience as a nurse practitioner dedicated to the care of pediatric and AYA oncology patients should allow me to provide unique, well-rounded care to this patient population.

Following completion of my PMHNP DNP, I plan to continue to collaborate with colleagues to build a robust psycho-oncology program at our institution. Ultimately, we hope to provide proactive, comprehensive psychosocial care to pediatric and AYA oncology patients as well as their family members. This educational pathway is a major step toward accomplishing this goal.

Grant Profile Information

Katherine C. Fuh, MD, PhD

Tumor-stromal DDR2 Promotes Metastasis in Ovarian Cancer

Washington University, St. Louis
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Grant No. RSG-19-080-01-TBG
Division: North
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$792,000
Total ACS Support: \$792,000

Area of Research:	Cancer Progression and Metastasis	100%
Types of Cancer:	Ovarian Cancer	100%

Project Summary

Although ovarian cancer is the 11th most common cancer among women, it is the 5th leading cause of cancer-related death among women. This is largely because most patients first learn they have ovarian cancer after it has already spread to other locations in their bodies. After undergoing surgery to remove the tumors, patients are given chemotherapy, which aims to stop tumor cells from growing. However, no current ovarian cancer drugs inhibit tumor cell spread, so the ovarian cancer often spreads to new locations in the body. Eventually, the cancer blocks the bowels and causes the patient to die. Indeed, the original tumor does not kill the patient; the cancer spread kills the patient. Thus, our long-term goals are to learn how ovarian cancer spreads and to develop drugs that can prevent the steps of cancer spread. In our search for proteins to target with drugs, we found that up to 80% of ovarian cancer tumors make a protein called Discoidin Domain Receptor 2 (DDR2). Additionally, we found that the supporting, non-tumor cells close to the tumor also make DDR2. Moreover, we found that DDR2, working in both the tumor cells and the non-tumor cells, helps promote tumor cell spread. Here, we will determine how DDR2 in the tumor and the surrounding non-tumor cells promotes cancer spread. Additionally, we will test the ability of a new DDR2 inhibitor to prevent cancer spread. This work will make use of patient ovarian cancer cells in a dish as well as in mice, thus mimicking ovarian cancer spread in a patient. This work will have several important outcomes. First, we will learn how non-tumor cells help tumor cells spread. Second, we will learn how DDR2 helps ovarian tumor cells spread. Finally, if the drug we are testing is successful in the lab, researchers will be able to test it, or versions of it, in patients. Long term, we envision that this drug, which only inhibits DDR2, will be combined with drugs that inhibit other important cancer-promoting proteins to reduce ovarian cancer spread. Moreover, several other cancers, such as colon, stomach, and pancreas cancer, all spread to similar places in the body as ovarian cancer. Thus, the lessons we learn in this study of ovarian cancer may, in the long term, help us understand and treat spread of other cancer types.

Grant Profile Information

Allie Grossmann, MD, PhD

The Small GTPase ARF6 in Melanoma Progression & Metastasis

University of Utah
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2000 Circle of Hope Drive
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Grant No. RSG-19-019-01-CSM
Division: North
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$792,000
Total ACS Support: \$792,000

Area of Research:	Cancer Progression and Metastasis	100%
Types of Cancer:	Melanoma	100%

Project Summary

We study melanoma because it is common, it affects all age groups and both sexes, and because it is one of the most aggressive cancers. It spreads early in the course of the disease and once it has spread, melanoma is extremely difficult to treat. Melanoma is a useful cancer to study because the genetic causes are similar to many other cancer types. If we can understand how to successfully treat metastatic melanoma, we may be able to help eradicate other cancer types as well.

Within cancer cells there is a command central from which most orders for growth and cell movement originate. Genetic driver mutations create the equivalent of a commander-in-chief protein within cancer cells. In many cancers, including melanoma, the initial signal for growth emanates from either RAF or RAS commanders. Their orders are executed by a hierarchy of subordinate proteins. Similar to successful military operations, cancer cells must have a reliable and efficient means of transporting commanders and their subordinates to strategic rendezvous sites. ARF6 is a protein that coordinates such transportation within the cell. The role of ARF6 is similar to that of a train conductor, ensuring trafficking of key proteins and lipid messengers to the appropriate destination within the cell. Without this transport step, cells cannot function properly. Because intracellular trafficking is essential for cancer cells, it is our goal to discover ways to cripple tumor cells by blocking ARF6. We have identified ARF6 as a potential therapeutic target for melanoma and propose to elaborate on this by pairing mechanistic studies with pre-clinical development of ARF6-targeted therapy. With a combination of genetic and pharmacologic tools we provide powerful complementary approaches that not only address fundamental mechanistic questions about melanoma disease progression, we also investigate potential solutions.

Grant Profile Information

Colleen Hannon, PhD

Nuclear Dynamics and Interactions of Intrinsically Disordered Proteins

University of California, Berkeley
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Grant No. PF-19-004-01-CCG
Division: West
Term of Grant: 07/01/2019-06/30/2022
Total Award: \$163,500
Total ACS Support: \$163,500

Mentor: Michael B. Eisen, PhD

Area of Research:	Normal Functioning	70%
	Interactions of Genes and/or Genetic Polymorphisms with Exogenous and/or Endogenous Factors	30%
Types of Cancer:	Not Site-Specific Cancer	100%

Project Summary

Transcription factors (TFs) are proteins that bind to DNA and determine where and when genes are expressed. TFs play a role in nearly all cellular functions, including development, growth, and response to environmental stimuli. Predictably, they have also been implicated in a vast number of diseases, including many cancers, as misregulation of gene expression can have catastrophic consequences. At the structural level, TF proteins consist of a sequence-specific DNA binding domain and a transcriptional activation or repression domain. Many eukaryotic TFs are highly enriched for low complexity amino acid sequences outside of their DNA binding domains, which can give rise to proteins with intrinsically disordered regions (IDRs). The unstructured nature of IDRs has made them difficult to study, and their roles in TF function remain largely unexplored. The proposed project is a broad study of multiple maternally provided TFs that are functional in early embryonic development. Using CRISPR, I will fluorescently tag multiple TFs and assess their nuclear localization and dynamics by live imaging in *Drosophila* embryos. In parallel to the imaging study, I will perform a structure-function analysis to test the importance of the IDRs for normal TF localization and function. Finally, I plan to identify and analyze any interactions between IDR-containing TFs with an aim to determine the sequence features necessary for these interactions. In order to effectively target TFs as a cancer treatment, it is essential to understand their normal functions. Studies such as the one proposed here therefore provide a crucial foundation for developing therapeutic approaches.

Grant Profile Information

Leighanne Hartman, BS

Graduate Scholarship in Cancer Nursing Practice

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Grant No. GSCNP-19-058-01-SCN
Division: Southeast
Term of Grant: 07/01/2019-06/30/2021
Total Award: \$20,000
Total ACS Support: \$20,000

Mentor: Susan M. Schneider, PhD, RN, AOCN,
FAAN

Area of Research:	Exogenous Factors in the Origin and Cause of Cancer	10%		
	Interventions to Prevent Cancer: Personal Behaviors (Non-Dietary) that Affect Cancer Risk	20%		
	Patient Care and Survivorship Issues	50%		
	End-of-Life Care	20%		
Types of Cancer:	Blood Cancer	10%	Lung Cancer	10%
	Breast Cancer	20%	Not Site-Specific Cancer	50%
	Colon and Rectal Cancer	10%		

Project Summary

My acceptance into the Adult-Gerontology Nurse Practitioner program at the Duke University School of Nursing will provide me with the knowledge and skills required to provide exceptional, compassionate care across a variety of age groups and settings. The opportunity to further specialize in oncology, incorporating my current oncology research experience, is a bonus. The oncology specialty will provide me with a curriculum that follows the Oncology Nursing Society Scope and Standards which is tailored from the latest evidence-based knowledge. This experience will allow me to become a skilled clinician, providing holistic care for individuals with cancer. Upon graduation, my goal is to obtain my certification as an Advanced Oncology Certified Nurse Practitioner (AOCNP).

My current experience as a GI Oncology research nurse provides me with a strong foundation in the oncology specialty. This position enables me to see the progress of what research can do for cancer patients. My collaboration in a research trial utilizing immunotherapy in MSI-high metastatic colorectal cancer allowed me to witness cancer patients become survivors. As an AOCNP, my goal is to continue to work in my areas of scholarly interest such as oral chemotherapeutic medication compliance, management of sequelae in cancer survivors treated with immunotherapies and dealing with coping interventions for cancer patients and their families.

As a future Advanced Practice Nurse in oncology, I vow to treat the whole patient, not just the cancer. I will advocate for my patients by offering them specifically tailored evidence-based treatment. I will incorporate individual-based and population-wide approaches to cancer screening and prevention interventions. I will provide treatment and survivorship care for my patients as new treatments emerge from research. Until that time, I will provide supportive and symptom care during end-of-life. Receiving the Graduate Scholarship in Cancer Nursing Practice from the American Cancer Society will allow me to progress towards my degree in preparation for a career as an AOCNP.

Together with my nursing background, research experience, and critical skills acquired through the AGNP program, I can make a positive contribution in filling the growing need of nurse practitioners in oncology. Moreover, I can have a positive impact on patients who are living with and surviving cancer.

Grant Profile Information

Taro Hitosugi, PhD

Role of Mitochondrial Creatine Kinase 1 in Breast and Ovarian Cancers

Mayo Clinic Cancer Center
Department of Oncology
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Grant No. RSG-19-076-01-TBE
Division: North
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$775,000
Total ACS Support: \$775,000

Area of Research:	Cancer Initiation: Oncogenes and Tumor Suppressor Genes	75%		
	Systemic Therapies - Discovery and Development	25%		
Types of Cancer:	Breast Cancer	50%	Ovarian Cancer	50%

Project Summary

The mutational activation of growth-promoting oncogenes drives cancer development and growth. In the case of breast cancer, the HER2 receptor tyrosine kinase is a key driver of the disease. HER2-targeted therapies such as trastuzumab and lapatinib, have activity in the disease, but patients often relapse. To improve the efficacy of such therapies, we propose to study the interaction between two common cancer hallmarks: HER2 signaling and HER2-dependent alterations in tumor metabolism that promote tumor growth by favoring the synthesis of proteins, nucleotides, and lipids.

From our preliminary data from mitochondrial phospho-proteomic analysis of HER2+ breast cancer cells, we found that mitochondrial creatine kinase 1 (MtCK1), a mitochondrial protein that facilitates creatine energy shuttle, is tyrosine phosphorylated and activated by HER2 signaling. Furthermore, we have detected MtCK1 phosphorylation in ovarian cancer cells in addition breast cancer cells. We thus propose to assess how this MtCK1 phosphorylation impacts breast and ovarian cancer metabolism and growth. To address this, in addition to in vitro culture cell breast cancer model, we will use in vivo (HER2+ PDX) breast cancer and (MtCK1 phosphorylation+ PDX) ovarian cancer models that accurately reflect the in vivo setting. Importantly, we will also assess how disabling MtCK1 (using cyclocreatine, a small molecule inhibitor) affects ovarian tumor growth. Because cyclocreatine has been used as a dietary supplement and our preliminary data showed that oral administration of 0.3% CCr in drinking water significantly inhibited growth of the trastuzumab-resistant BT474-R and breast PDX tumor models in mice, cyclocreatine might be able to inhibit ovarian tumors with much less toxicity in vivo as compared to conventional anticancer drugs.

We have contributed substantively to current understanding of the direct link between tyrosine kinase signaling and cancer metabolism and demonstrated that targeting a metabolic enzyme has therapeutic benefit in mouse xenografts. As such, we are in a unique position to push this field forward through the proposed studies that 1) will yield insights into the basic mechanisms by which tyrosine kinases programs tumor metabolism by regulating MtCK1 and 2) may help develop novel therapeutic approach targeting creatine metabolism in ovarian cancer, a disease that urgently needs new therapeutic approaches.

Grant Profile Information

Dirk Hockemeyer, PhD

The Role of Cancer Associated TERT Promoter Mutations in Melanoma

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Grant No. RSG-19-029-01-DMC
Division: West
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$792,000
Total ACS Support: \$792,000

Area of Research:	Cancer Initiation: Alterations in Chromosomes	40%		
	Cancer Initiation: Oncogenes and Tumor Suppressor Genes	20%		
	Cancer Progression and Metastasis	20%		
	Technology Development and/or Marker Discovery	20%		
Types of Cancer:	Melanoma	80%	Not Site-Specific Cancer	20%

Project Summary

The proposed studies will determine the molecular events that lead to cancer cell immortality, the ability of cancer cells to divide indefinitely. In 90% of cancer cases, this fundamental feature is dependent on an enzyme called telomerase, which counteracts DNA loss and DNA damage at the telomere, the sequences at end of human chromosomes. One of the long-standing questions in cancer biology is how cancer cells activate the telomerase enzyme. The recent discovery that cancer cells have, with very high frequency, mutations in the genomic regions that regulate the key component of the telomerase gene provides a starting point to address this question. These mutations are found in 10-15% of all cancers and are therefore among the most frequent mutations in cancer. However, as they were only recently discovered little is known about the molecular mechanisms by which they promote cancer progression. Understanding these mechanisms will be of key importance to develop drug interventions that target telomerase and cancer cell immortality. The experiments in this proposal will address how these mutations function in the context of melanoma, where they occur in more than 70% of the cases. We will elucidate the mechanism by which the mutations in the telomerase gene result in cancer cell immortality and to what extent these mutations are driving melanoma progression and genomic instability.

Grant Profile Information

Liam Holt, PhD

Genetic and Physical Mechanisms of Adaptation to Compressive Stress

New York University School of Medicine
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Pharmacology
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Grant No. RSG-19-073-01-TBE
Division: Northeast
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$792,000
Total ACS Support: \$792,000

Project Summary

Physical pressure is fundamentally important for cancer biology, but its effects remain poorly understood. When solid tumors grow confined within surrounding tissue, they build up compressive stress. Given that cells evolved to function in a stable mechanical environment, even slight changes in pressure perturb physiology. Normal cells and early stage cancer cells stop growing when pressure builds up. In contrast, in advanced cancer, compression can change cellular behavior to drive migration of cancer cells to other organs or confer resistance to chemotherapy. This difference implies that cancer cells somehow adapt to physical pressure. A lack of tools has slowed progress in understanding the relationships between compression, the physical properties of cells, and cancer behavior. We developed two new technologies to overcome this limitation: First, we created a gene that enables cells to produce a steady supply of fluorescent nanoparticles that act as tell-tales for shifts in intracellular physical properties. Second, we developed microfluidic devices to control compressive stress, either quickly or slowly, while maintaining a constant chemical environment. We will combine these innovations to test the overarching hypothesis that mutations that confer resistance to mechanical compression enable pancreatic cancer cells to adapt to their high-pressure environment and drive their oncogenic evolution. Aim 1: We will determine how compression differentially impacts wildtype and mutant pancreatic cells. We will use GEM nanoparticles to quantify the physical response to pressure and test the hypothesis that oncogenic mutations alter both the physical and physiological response to pressure. Aim 2: We will determine the effects of compression on phase separation. We will investigate the hypothesis that decreased cell volume under pressure leads to increased phase separation of stress granules. We will evaluate molecular crowding as a mechanism for these effects. We will determine the importance of stress granule formation for mechanical adaptation and drug resistance. Aim 3: We will determine genetic mechanisms of pressure adaptation. We will follow up on preliminary mutants that confer resistance to compression, using a CRISPR modifier screen to determine mechanisms of adaptation. We will overexpress known oncogenes to find further adaptation pathways.

Our innovative combination of genetic nanoparticles and microfluidic approaches, and our expertise that bridges biophysics, mechanobiology and cell biology make us uniquely qualified to connect compression, the physicochemical properties of cells, and cancer physiology. Our studies promise to reveal key network perturbations essential to cancer cell growth and survival under pressure. Understanding these adaptive mechanisms promises to suggest treatments that exploit the aberrant mechanical properties of tumors caused by high compressive stress.

Grant Profile Information

Neil M. Iyengar, MD

Targeting the Dysregulated Microenvironment in Obesity and Breast Cancer

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Grant No. RSG-19-013-01-CPPB
Division: Northeast
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$792,000
Total ACS Support: \$792,000

Area of Research:	Systemic Therapies - Discovery and Development	20%
	Systemic Therapies - Clinical Applications	80%
Types of Cancer:	Breast Cancer	100%

Project Summary

Overweight and obesity affect more than two-thirds of Americans, and are now leading modifiable lifestyle factors that increase the risk of cancer and cancer relapse. Several studies have established that diet and exercise programs for patients with breast cancer are safe, tolerable, and can improve obesity-related blood factors. While long follow-up times are needed to determine whether these interventions prevent relapse and improve survival, a major knowledge gap is whether such interventions impact biology within the breast. Understanding the effects of an intervention on the target tissue is critical to the development of therapies that successfully prevent cancer recurrence and prolong life. The major goal of this proposal is to directly address this gap in knowledge by investigating the impact of a tailored diet and precision exercise intervention on key biologic pathways within the breast. Our group has made the following relevant discoveries: 1) 90% of obese breast cancer patients have inflamed fat in the breast, which is a strong predictor of recurrence in patients with early-stage breast cancer (independent of BMI); 2) breast fat inflammation is associated with increased expression of aromatase, the key enzyme in estrogen production which can stimulate breast tumor growth; 3) breast fat inflammation is associated with reprogramming of hundreds of genes within the breast microenvironment that can promote tumor growth; and 4) breast fat inflammation is also associated with systemic reprogramming including altered blood levels of several metabolic and inflammatory factors. Collectively, our work to date provides new insights into how obesity transforms the breast microenvironment to drive breast cancer progression. Whether diet and/or exercise interventions can reverse obesity-related disturbances in the breast has not been investigated. Accordingly, we will conduct a phase II randomized control trial to determine whether a tailored diet and precision exercise intervention can improve the obesity-related disturbances in the breast that can promote tumor growth. In this trial, we will use the following new approaches: 1) a unique selection strategy in which patients with breast fat inflammation, who are at high risk for relapse, are targeted; 2) an American Cancer Society (ACS) diet tailored to be protein-enriched and energy restricted (ACS-PEER diet) combined with structured exercise training designed to reduce body fat while maintaining muscle; and 3) pre- and post-intervention biopsies of the breast. This study builds upon our prior work, which provided a biologic understanding of how obesity promotes breast tumor growth, and will be the first intervention study that aims to reverse the cancer-promoting disturbances induced by breast fat inflammation. Directly modifying breast tissue biology through specialized diet and exercise is a new and promising strategy to reduce the risk of recurrence for many patients with breast cancer.

Grant Profile Information

Ranee Kang, MSW

Master's Training Grant in Clinical Oncology Social Work

Beckman Research Institute of the City of
Hope
Supportive Care Medicine
Office of Sponsored Research
1500 East Duarte Road
Duarte, CA 91010-3000

Grant No. MSW-19-066-05-SW
Division: West
Term of Grant: 07/01/2019-06/30/2021
Total Award: \$24,000
Total ACS Support: \$72,000

Project Summary

The Master of Social Work Internship Program at City of Hope Medical Center (COHMC) is aimed at teaching master's level 2nd year social work interns to provide clinical social work services to the adult oncology population. Interns build on 1st year clinical skills by honing the skill of completing in-depth bio-psychosocial-spiritual assessments to both the inpatient and outpatient populations. Interns are trained to work in a medical setting with an Interdisciplinary team, which includes physicians, nurses, case managers, chaplains, and physical/occupational therapists, child life specialists and other members of the health care team. Interns are expected to actively participate in patient rounds and family meetings with the Interdisciplinary team. Interns learn to provide Psychosocial support, counseling, and resources to promote healthy adjustment to diagnosis and treatment throughout the continuum of care including end-of-life and bereavement. The expectation is that the interns will develop the clinical skills and confidence needed to provide effective clinical social work services in an oncology setting by the end of their 2nd year of internship.

Also included in the COHMC internship training program is the ability to build and promote program skills by participating in leadership opportunities to build programs for both patients and caregivers. Interns will actively participate in the promotion and implementation of the Advance Directive initiative at COHMC. Interns will also learn how to navigate national, institutional, and departmental policies which directly affect patient care. The social work staff at COHMC has a high degree of experience in the oncology field and are dedicated to providing the best possible training to interns. The Department of Supportive Care Medicine at COHMC is welcoming of interns and provides an excellent environment to hone the skills needed to develop and pursue a career in the oncology/healthcare setting. Social Work interns trained at COHMC have a unique opportunity to be part of a dynamic and innovative institution focused on building supportive care programs across the nation.

Grant Profile Information

Grace Kanzawa-Lee, BSN

Exercise to Reduce Chemotherapy-Induced Peripheral Neuropathy: A Pilot RCT

University of Michigan
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Ann Arbor, MI 48109

Grant No. DSCNR-19-056-03-SCN
Division: North Central
Term of Grant: 07/01/2019-06/30/2021
Total Award: \$30,000
Total ACS Support: \$60,000

Mentor: Ellen L. Smith, FAAN, PhD

Area of Research:	Patient Care and Survivorship Issues	100%
Types of Cancer:	Colon and Rectal Cancer	50%
	Pancreatic Cancer	30%
	Esophageal / Oesophageal Cancer	5%
	Stomach Cancer	10%
	Gastrointestinal Tract	5%

Project Summary

The number of gastrointestinal (GI) cancer survivors is increasing, leading to more people who experience cancer treatment side effects. Most patients with GI cancer receive oxaliplatin – a drug that can also damage peripheral nerves and cause oxaliplatin-induced peripheral neuropathy (OIPN). Patients often describe OIPN as uncomfortable, and painful numbness and tingling that interferes with physical function, balance, and quality of life (QOL). Currently, no good treatments exist for OIPN. Therefore, it is the primary reason for reductions in oxaliplatin-based cancer treatment.

The results of studies in patients with other types of peripheral neuropathy suggest that exercise may help to prevent or minimize peripheral neuropathy by increasing blood flow to vulnerable nerves. But, no studies have investigated the effects of aerobic exercise on OIPN. Therefore, our study aims to evaluate the impact of an 8-week home-based aerobic walking intervention on a) OIPN severity, and b) total oxaliplatin dose received and QOL, compared to health education. Additionally, we will measure feasibility outcomes, including adverse effects, adherence, and perceptions about the walking intervention. We hypothesize that participants who receive the walking intervention will have less OIPN, higher QOL, and have received higher doses of oxaliplatin at the 8-week time point than participants who receive health education.

We will recruit 60 colorectal cancer patients from two comprehensive cancer centers. Patients will be recruited shortly after beginning oxaliplatin-based cancer treatment. Half of the patients will receive the “MI-Walk intervention:” an 8-week home-based aerobic walking intervention. These patients will receive a Fitbit, tailored guidance from research staff, and materials for setting and monitoring exercise goals before practicing the intervention at home for 8 weeks. Participants will also be added to a private email group where they can engage with other participants and receive motivational messages and information about weekly group-walking events. A final progress summary will be given to each participant. All 60 participants will receive an exercise information and tips pamphlet. To equalize attention, both groups will receive regular telephone assessments of symptoms and adverse events. The outcome variables will be measured before and immediately after the 8-week intervention.

This study will be the first to provide preliminary data on the effect and feasibility of an 8-week home-based aerobic walking intervention to reduce OIPN. The potential impact of this research is significant, because we may discover a new non-opioid intervention for OIPN - a problem for which there is no effective treatment.

Grant Profile Information

Max Kates, MD

Intravesical Cisplatin Chemotherapy and Mechanisms of Resistance for NMIBC

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Grant No. CSDG-19-001-01-CCE
Division: Northeast
Term of Grant: 07/01/2019-06/30/2024
Total Award: \$729,000
Total ACS Support: \$729,000

Area of Research:	Technology Development and/or Marker Discovery	25%
	Technology and/or Marker Testing in a Clinical Setting	25%
	Localized Therapies - Discovery and Development	25%
	Localized Therapies - Clinical Applications	25%
Types of Cancer:	Bladder Cancer	100%

Project Summary

Title of Project: Intravesical cisplatin chemotherapy and mechanisms of resistance for Non-Muscle Invasive Bladder Cancer

Bladder cancer is the 7th most common malignancy worldwide, with a 5-year global prevalence of ~1.3 million people. Approximately 70% of patients present with non-muscle invasive bladder cancer (NMIBC), which is managed primarily by trans-urethral (endoscopic) resection of the bladder tumor (TURBT) followed by intravesical instillation of BCG. When 40-60% of patients go onto recur after BCG within 2 years, there are limited options other than major complete bladder removal, which is associated with complications and high morbidity. Treatment for patients with BCG unresponsive disease thus represents a major unmet need in bladder cancer. Cisplatin chemotherapy is the gold standard treatment for advanced bladder cancer, and has recently been evaluated for intravesical use in BCG unresponsive NMIBC patients.

The purpose of this research is to assess whether known biomarkers of systemic cisplatin response for advanced bladder cancer also predict response to intravesical cisplatin in NMIBC. To accomplish this, we will use two large tissue cohorts of paired samples (pre and post-treatment) from patients treated with BCG. We will assess whether known biomarkers of platinum response for advanced bladder cancer, including DNA damage repair mutations, basal molecular subtype membership, and effector T cell signatures are present in the BCG unresponsive population. We will then directly evaluate whether these biomarkers predict response in the only clinical trials to evaluate intravesical cisplatin in the modern era. Finally, in a preclinical animal model of bladder cancer, we will assess whether these biomarkers have increased sensitivity to our novel cisplatin bladder enhanced absorption nanoparticle (BEAN) formulation compared to conventional cisplatin therapy. Taken together, this project has the potential to encourage the urologic oncology community to adopt the principles of precision medicine in NMIBC by enhancing current intravesical chemotherapy and identifying biomarkers that predict response.

Grant Profile Information

Deogwoon Kim, BSN

Reducing Global Cancer Disparities: HPV Vaccination in Sub-Saharan Africa

University of Massachusetts, Boston
College of Nursing and Health Science
100 Morrissey Boulevard
Boston, MA 02125-3393

Grant No. DSCN-19-047-01-SCN
Division: Northeast
Term of Grant: 07/01/2019-06/30/2021
Total Award: \$30,000
Total ACS Support: \$30,000

Mentor: Haeok Lee, RN, FAAN, PhD

Area of Research:	Vaccines	33%
	Resources and Infrastructure Related to Prevention	33%
	Health Services/ Economic and Health Policy Analyses	34%
Types of Cancer:	Cervical Cancer	100%

Project Summary

Cervical cancer is a matter of global health inequities as 85% of cervical cancer cases occur in low- and middle-income countries. Especially, among those countries, Sub-Saharan African countries report more than twice as many cervical cancer cases and more than three times as many cervical cancer deaths than the worldwide average. Moreover, Sub-Saharan Africa (SSA) reports the highest infection rate of human papillomavirus (HPV), a significant cause of cervical cancer. Therefore, cervical cancer is a more serious public health threat in SSA than in any other regions.

To decrease cervical cancer burden, regular cervical cancer screening is important to detect abnormal cervical changes before they progress to cancer. However, the Pap smear uptake rate is extremely low in SSA (ranging from 1.0% to 23.2%) because of limited medical infrastructure, and lack of awareness and knowledge about cervical cancer and the Pap smear among the public and health care providers. Therefore, preventing HPV infection by vaccinating against HPV is important to Sub-Saharan Africans for reducing cervical cancer inequities.

In order to prevent cervical cancer, the World Health Organization recommends HPV vaccination primarily to female adolescents at ages nine to 13. The Global Alliance for Vaccines and Immunization (Gavi), an international organization, has supported HPV vaccination for low-resource countries, including Malawi which is a sub-Saharan country, since 2012 to increase HPV vaccination coverage. The HPV vaccine is provided at US \$4.50 per dose to Gavi-eligible countries, which drastically reduces the cost burden of HPV vaccination.

However, the cost of the HPV vaccine per se is not the only factor that causes the cost burden of HPV vaccination administration: delivery strategies to the target population can yield a cost burden. Targeting only schools for HPV vaccination delivery might not be the most cost-effective strategy because of the high out-of-school rate in SSA. Moreover, females, who are the main target for the HPV vaccination, are more likely to be out-of-school than males. In SSA, which has limited resources, choosing an HPV vaccination delivery option that can maximize the HPV vaccination coverage with the least possible cost is important for the sustainability of HPV vaccination administration programs. A comprehensive cost-effectiveness evaluation model of Malawi will be developed from this proposed project and will be simulated with different HPV vaccination distribution strategies to test the model. This will capture the potential economic benefit of each delivery option that are considered in the decision-making processes and will assist decision-making regarding the most effective and efficient HPV vaccination administration strategy. The model can be expanded later to other sub-Saharan African countries with revision and will contribute to the American Cancer Society's shared vision of an HPV cancer-free world.

Grant Profile Information

Isaac Klein, MD, PhD

Targeting Transcriptional Regulation in Ovarian Cancer

Dana-Farber Cancer Institute
Department of Medical Oncology
450 Brookline Avenue
Milton, MA 02186

Grant No. PF-19-090-01-DMC
Division: Northeast
Term of Grant: 07/01/2019-06/30/2022
Total Award: \$163,500
Total ACS Support: \$163,500

Mentor: Richard A. Young, PhD

Area of Research:	Endogenous Factors in the Origin and Cause of Cancer	50%
	Technology Development and/or Marker Discovery	20%
	Systemic Therapies - Discovery and Development	30%
Types of Cancer:	Ovarian Cancer	100%

Project Summary

Ovarian cancer is the leading cause of gynecologic cancer death in the United States, responsible for over 22,000 cases per year and over 14,000 deaths. The most common type of ovarian cancer is High Grade Serous Ovarian Cancer (HGSOC). Unfortunately, few therapeutic advances for HGSOC have been forthcoming, and the cornerstone of treatment remains chemotherapy and surgery. Identifying therapeutic targets for this disease represents an urgent medical need.

The genomics revolution has yielded personalized treatments for many cancers which are driven by mutated proteins. But HGSOC seems to lack mutations in DNA regions that code for cancer-promoting genes, and so is not amenable to this scientific or therapeutic approach. Rather, HGSOC seems to be driven by dysfunctional gene expression. In cancer, incorrect gene expression is often mediated by regulatory genetic elements called super-enhancers, which we can detect with novel whole genome technologies.

In collaboration with the Dana-Farber Cancer Institute, I aim to map the super-enhancer landscape in human HGSOC tissue samples, and well as normal cells-of-origin, and tumor cell line models. This approach will yield fundamental insights into the mechanisms by which normal cells transform into ovarian cancer cells, and reveal the genes that maintain the oncogenic state in this disease.

Genetic dependencies are genes required for survival or growth of tumor cells, and represent attractive targets for cancer drug development. Super-enhancers are known to mark genes that are dependencies in several tumors. In cancers such as ependymoma and medulloblastoma, super-enhancer analysis has already pointed to novel therapeutic opportunities. Thus, by mapping the super-enhancer landscape of HGSOC, I will uncover putative therapeutic targets, which can rapidly feed clinical trial development for patients.

Grant Profile Information

Nancy R. Kressin, PhD

Dense Breast Notifications: Optimizing Outcomes and Equity with Evidence

Boston Medical Center
Department of Medicine
801 Massachusetts Avenue
Boston, MA 02118

Grant No. RSG-19-085-01-CPHPS
Division: Northeast
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$1,433,250
Total ACS Support: \$1,433,250

Area of Research:	Health Services/ Economic and Health Policy Analyses	25%
	Education and Communication Research	75%
Types of Cancer:	Breast Cancer	100%

Project Summary

Breast cancer causes significant illness and death in the U.S., especially for racial/ethnic minority women. Breast cancer deaths have dropped due to earlier detection via mammograms, yet not all women receive them, due to disparities in levels of awareness, knowledge, perceived risk, and health literacy. Doctors now recommend personalized, risk-based breast cancer screening, but women need clear and understandable cancer risk health communications which encourage discussions with physicians, to determine what is best for them as individuals.

Breast density (amount of non-fatty breast tissue) is a risk factor that should now also be considered in screening decision making, as it affects mammograms' ability to find cancers. Dense breast notification (DBN) legislation in 35 states aims to raise women's awareness of their own cancer risk, but is controversial among doctors, given little evidence for the benefit of additional screening. We do not know whether DBNs have achieved their goals of raising awareness, improving knowledge or motivating women to engage in informed decision making with their doctors, or affected their planned or actual use of supplemental screening, or whether DBNs affect women differently, depending on the DBN's literacy level, or women's social or demographic characteristics. The proposed study will obtain information about women's reactions to DBNs, how they differ by the literacy level of the DBN or by women's characteristics.

We propose a national telephone survey (in English and Spanish) of a diverse sample of approximately 3,500 women from the general population in states with and without DBNs. We will recruit women who are age-eligible for mammography (40-74), received a mammogram in the prior two years, excluding those with a history of breast cancer. We will examine outcomes of women's awareness, knowledge, and future plans regarding breast density (BD) care (to speak with one's physician or to undergo supplemental screening) and reactions to BD information (anxiety, confusion, feeling informed), in states with and without DBNs; in states with DBNs, we will compare these outcomes by the literacy level (high vs. low) of DBN language, and by women's race/ethnicity. We will interview a subgroup of women to gain a deeper understanding of the effects of dense breast notifications, and their preferences for receiving such information. Information from this study will provide needed evidence on DBN outcomes for all women, to support the ultimate goal of improving equity in breast cancer outcomes.

Grant Profile Information

Ashish A. Kulkarni, PhD

Nanoscale Combination Immunotherapy for Bladder Carcinoma

University of Massachusetts, Amherst
Department of Chemical Engineering
N565 Life Sciences Laboratories
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Grant No. RSG-19-009-01-CDD
Division: Northeast
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$792,000
Total ACS Support: \$792,000

Area of Research: Systemic Therapies - Discovery and Development 100%

Types of Cancer: Bladder Cancer 100%

Project Summary

Urothelial bladder cancer (UBC) is the sixth most common cancer in the United States, with an estimated 79,030 new cases and 16,870 deaths in the year 2017. There have been limited major advances in the treatment of urothelial bladder cancer in the past three decades. Chemotherapy is still the standard of care, and patient outcomes remain poor, especially in those who cannot tolerate chemotherapy. Furthermore, despite increasing excitement about immunotherapy in bladder cancer, lower response rates have been observed. The major reason for this lower response rate is because in majority of UBC patients, cancer progresses by creating an environment that suppresses the host immune system. Thus, there is a need to augment the immunogenicity of the tumor and overcome immunosuppression to maximize the effects of immunotherapy. We rationalized that this could be achieved by biology-inspired engineering of a novel nanotherapeutics that can drive the intratumoral immunosuppressive cells to immune-responsive mode, and augment a T cell response. We propose to develop a precise combination of these immunomodulatory nanotherapeutics that can synergistically activate innate and adaptive immunity thereby allowing the focal manipulation of the tumor immune contexture. This translational proposal thus brings together latest advances in cancer immunotherapy with novel biomaterials to engineer nanotherapeutics platform to activate innate and adaptive immunity that can result in a dramatic increase in survival in bladder cancer.

Grant Profile Information

Virginia LeBaron, PhD

Using mHealth to Support Patients and Caregivers in Managing Cancer Pain

The Rector and Visitors of the University of
Virginia
Department of Acute & Specialty Care
P.O. Box 400195
Charlottesville, VA 22904-4195

Grant No. PEP-19-042-01-PCSM
Division: Southeast
Term of Grant: 07/01/2019-06/30/2021
Total Award: \$144,000
Total ACS Support: \$144,000

Area of Research:	Patient Care and Survivorship Issues	50%
	End-of-Life Care	50%
Types of Cancer:	Not Site-Specific Cancer	100%

Project Summary

Despite significant effort, pain remains a common and serious problem for patients with cancer and their family caregivers. In fact, many patients with cancer do not fear dying as much as they fear the possibility of dying in pain; likewise, family members fear watching a loved one suffer. When patients become seriously ill, family caregivers often assume primary responsibility for managing symptoms, such as pain. However, managing difficult symptoms at home is not easy, and patients and caregivers can experience significant stress. Sometimes pain becomes so distressing that patients and caregivers go to the emergency room out of desperation, even if the patient prefers to be at home. Another challenge is that a key class of medications used to treat serious cancer pain – opioids – are highly effective, but can be problematic if used incorrectly. Given concerns about the national 'opioid epidemic' it is especially critical that patients and caregivers have the support they need to safely and effectively manage pain at home. This study proposes a solution to this problem by exploring how we can best use mobile technology (such as wearable devices, like a FitBit, and wireless sensors, like remote thermostats that continually adjust a room's temperature) to help patients and family caregivers monitor, predict, anticipate and manage pain in the home setting. The proposed home-based system is known as the Behavioral and Environmental Sensing Intervention for Cancer (BESI-C) and consists of a package of mobile health technology set up in a patient's home. BESI-C collects a range of information from individuals, as well as the home environment. For example, BESI-C can monitor activity levels, sleep, ambient noise, as well as note events such as when a pain episode occurs or when a patient takes medication; the system can also ask brief questions to assess mood and stress levels. All of this information is put together to paint a picture of the behavior and health of an individual. For example, we begin to see patterns of when a patient may experience pain, or when a caregiver is likely to become the most distressed. A unique aspect of this study is that it focuses not only on patients, but also on family caregivers – in other words it views the patient and caregiver as one unit. This is important because we know there is a strong, reciprocal effect between the experience of the patient and the experience of the caregiver. The goal of this first study is to test BESI-C with patients and caregivers who are seen in an outpatient oncology palliative care clinic. We want to understand if BESI-C can reliably collect the required data, and if patients and caregivers find the system acceptable. If successful, BESI-C offers a powerful approach to help support patients and family caregivers to manage all types of difficult symptoms in the home setting by intervening early and offering personalized management strategies.

Grant Profile Information

Matthew LeBlanc, BA, BSN

Symptom Burden and Quality of Life in Multiple Myeloma Patients

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School of Nursing
DUMC 3322
307 Trent Drive
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Grant No. DSCN-19-045-01-SCN
Division: Southeast
Term of Grant: 07/01/2019-06/30/2021
Total Award: \$30,000
Total ACS Support: \$30,000

Mentor: Sophia K. Smith, MSW, PhD

Area of Research:	Patient Care and Survivorship Issues	100%
Types of Cancer:	Myeloma	100%

Project Summary

While multiple myeloma (i.e., myeloma) is an incurable cancer, new treatments within the last 15 years have led to impressive survival gains for patients living with the disease. Improved treatments have contributed to an overall median survival of 5 years with extended survival greater than 10 years for some groups of myeloma patients. While myeloma is becoming a chronic condition, this extended survival comes at a cost; patients are on perpetual treatment as they consistently transition to new medications when previous therapies stop working. Symptoms caused by myeloma and its treatment have been shown to negatively impact patients' lives. Research indicates that symptom burden, functional status, and quality of life (QoL) outcomes for individuals diagnosed with myeloma are near the worst among all cancer patients. In this new era of constant and variable treatment, more needs to be understood about how longer-term survival (i.e. chronic disease) and treatment side effects affect myeloma patients so that resources can be allocated and interventions developed to address their needs.

The objective of this project is to describe patients outcomes of symptom burden, functional status and QoL and their relationship with personal and disease characteristics among myeloma patients. More specifically, this project will: 1) establish one of the first US-based cohorts of myeloma patients; 2) characterize symptom burden, functional status, and QoL in myeloma patients; and 3) identify personal and disease characteristics that are associated with symptom burden, functional status, and QoL in myeloma patients. Data will be collected through questionnaires mailed to myeloma patients who are receiving care at the Duke Cancer Institute. Advanced statistical methods (e.g., symptom clustering) will be employed to identify personal and disease characteristics that are associated with poor QoL related outcomes.

Identifying patient needs is a necessary first step in improving clinical care as it will likely lead to better allocation of resources and the design and development of nurse-led interventions. By generating knowledge of symptoms in persons with advanced and/or chronic cancers, this study would also further the mission and strategic goals of the American Cancer Society and the National Institute of Nursing Research and align with the National Cancer Institute Moonshot recommendations. It is expected that these findings will have implications for future research, intervention development, and clinical practice. In addition, the established cohort would facilitate future explorations and collaborations and lay the foundation for this applicant's program of research in improving care for patients with advanced cancer.

Grant Profile Information

Fang Lei, MPH

Cross-cultural Refinement and Validation of the LCS Health Belief Scales

University of California, Los Angeles
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Grant No. DSCN-19-052-01-SCN
Division: West
Term of Grant: 07/01/2019-06/30/2021
Total Award: \$30,000
Total ACS Support: \$30,000

Mentor: Eunice Lee, PhD

Area of Research: Interventions to Prevent Cancer: Personal Behaviors (Non-Dietary) that Affect Cancer Risk 100%

Types of Cancer: Lung Cancer 100%

Project Summary

Lung cancer is the third prevalent disease among Chinese Americans (CAs). It is also the leading cause of cancer deaths among CAs. Compared to X-ray, lung cancer screening (LCS) with low-dose computed tomography can significantly decrease the death rate of lung cancer by 20% in the high-risk population. However, the uptake rate of LCS is quite low in the US and there are few studies on LCS among CAs. Previous studies showed people's LCS behaviors were significantly associated with the health belief of LCS. However, no culturally appropriate tool is available to measure the health belief of LCS among CAs.

The purpose of this study is to refine and validate the LCS Health Belief Scales (HBS) to be used with CAs. For doing this, there are two steps. First, the LCS HBS, which was developed for general population in the US, will be refined to be culturally appropriate for CAs. This will include the committee translation process, participant interviews by cognitive interviewing method, and expert review. The translation process will follow the Harkness's translation model. A translation committee will be formed including the primary investigator, a physician, a researcher who has expertise in cross-cultural studies, and two translators. All the committee members are fluent in both English and Chinese. The translated version of LCS HBS will be reviewed among 10 participants using the cognitive individual interview method. The eligibility criteria for the participants are CAs who were born in mainland China but presently living in the US, aged 55 to 74 years old, current smokers or quit smoking in the past 15 years, and smoked at least 1 package of cigarettes for 30 years. The refined scales will be given to a panel of 5 experts to review. The experts include cancer nursing experts, instrument refinement experts, and cancer research experts who know Chinese culture well. Combining each reviewer's suggestions, the translated Chinese version of scales will be refined and finalized. Then It will be tested with 120 CAs for validity and reliability. The eligibility criteria are the same as those for recruiting the 10 participants in the cognitive interviews. Participants will be recruited by flyers distributed in senior centers, supermarkets, churches, and a popular Chinese website. The participants can choose to finish the survey online or using a paper-and-pencil method. We will use SPSS software to analyze data. Construct validity will be evaluated by exploratory and confirmatory factor analysis as well as the known group comparison approach. Content validity will be evaluated by expert review scores. Internal consistency reliability will be evaluated by Cronbach's alpha coefficient using the cut off criteria of 0.7. This study will provide a tool to evaluate CAs' health belief about LCS, contribute to the design of culturally appropriate LCS programs, and help to increase the uptake rates of LCS.

Grant Profile Information

Renfeng Li, PhD

The Role of PIAS1 in Epstein-Barr Virus Lytic Replication

Virginia Commonwealth University
Department of Oral and Craniofacial Molecular
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PO Box 980568
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Grant No. RSG-19-039-01-MPC
Division: Southeast
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$792,000
Total ACS Support: \$792,000

Area of Research:	Exogenous Factors in the Origin and Cause of Cancer	50%		
	Endogenous Factors in the Origin and Cause of Cancer	50%		
Types of Cancer:	Blood Cancer	20%	Hodgkin's Disease	5%
	Head and Neck Cancer	35%	Stomach Cancer	40%

Project Summary

Epstein-Barr virus (EBV) infections contribute to 200,000 new cases of cancer with more than 140,000 deaths worldwide per year. EBV-associated cancers include nasopharyngeal cancer (a type of head-neck cancer), stomach cancer, Burkitt's lymphoma and Hodgkin's lymphoma. Despite the unique presence of EBV in cancer cells, there are no virus-specific therapies available to treat EBV-associated cancers. EBV has two distinct phases in its life cycle, latency (dormant or quiescent phase) and lytic replication (active virus replication phase). EBV in tumor cells is in a latent/dormant phase and very few viral genes are expressed, which provides very few druggable targets for treating EBV cancer. Upon waking up the virus from latency, many viral proteins are expressed, which provides a unique opportunity to target viral proteins for anti-cancer therapy. Therefore the development of successful anti-EBV cancer strategies depends on a deeper understanding of how EBV lytic cycle is regulated by key host factors. Towards this aim, we have begun to analyze a novel PIAS1-centered pathway that controls EBV active replication. We discovered that PIAS1 is a cell protein that blocks EBV active replication. While caspases, cell enzymes important for apoptosis or programmed cell death, functions like "molecular scissors" to cut PIAS1 and therefore facilitates EBV active replication. In addition, we discovered that EBV encodes a protein kinase to phosphorylate and inactivate PIAS1 during virus replication. In this proposal, we will investigate the ways in which PIAS1 suppresses EBV active replication and the mechanisms by which PIAS1 is negatively regulated by caspases and an EBV-encoded protein kinase to favor virus replication. Ultimately, we expect that the knowledge obtained will be translated into new strategies for eradicating EBV-associated cancers.

Grant Profile Information

Hongjin Li, MS

Predictors of the Sickness Behavior Symptom Cluster With Endocrine Therapy

University of Pittsburgh
Department of Health and Community Systems
415 Victoria Building
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Grant No. DSCN-19-046-01-SCN
Division: Northeast
Term of Grant: 07/01/2019-06/30/2020
Total Award: \$15,000
Total ACS Support: \$15,000

Mentor: Catherine M. Bender, FAAN, RN, PhD

Area of Research:	Patient Care and Survivorship Issues	100%
Types of Cancer:	Breast Cancer	100%

Project Summary

Breast cancer is the most common cancer among women in the United States. It is estimated that 266,120 women will be diagnosed with invasive breast cancer in 2018. About 75% to 80% of women with breast cancer are postmenopausal at the time of diagnosis. Aromatase inhibitors (AI) are the mainstay of endocrine therapy for postmenopausal women with hormone receptor positive disease.

During AI therapy, most women with breast cancer experience multiple co-occurring symptoms or symptom clusters that may have a detrimental impact on their functional status and quality of life (QOL). One of the most common symptom clusters experienced by women with breast cancer is "sickness behavior", which may be comprised of fatigue, depression, anxiety and sleep disturbances. This symptom cluster has been reported during multiple phases of treatment and can persist years after completion of therapy among women with breast cancer. In addition to joint pain and hot flashes, a review shows that the sickness behavior symptoms are highly prevalent among women with breast cancer during endocrine therapy. The applicant's pilot work evaluated the prevalence and composition of the sickness behavior symptom cluster among women with breast cancer during AI therapy. However, there have been a few research studies that have identified who are at greater risk for higher intensity of the sickness behavior symptom cluster during AI therapy and what are the demographic, clinical or genotypic factors associated with the subgroup membership of the sickness behavior symptom cluster during AI therapy.

Therefore, the primary aim of this proposed study is to identify distinct subgroups of women with breast cancer based on their experience of the sickness behavior symptom cluster during AI therapy, and assess whether demographic, clinical, and genetic factors are associated with subgroup membership.

Results of this study will directly help nurses and healthcare providers to better assess the sickness behavior symptoms and identify and screen for women with breast cancer who are at higher risk of greater burden associated with the sickness behavior symptom cluster.

Grant Profile Information

Ling Li, PhD

PRMT1 Mediated Regulation of Acute Myeloid Leukemia Maintenance

Beckman Research Institute of the City of
Hope
Department of Hematological Malignancies
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Grant No. RSG-19-036-01-LIB
Division: West
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$792,000
Total ACS Support: \$792,000

Area of Research:	Endogenous Factors in the Origin and Cause of Cancer	25%
	Technology Development and/or Marker Discovery	25%
	Systemic Therapies - Discovery and Development	25%
	Complementary and Alternative Treatment Approaches	25%
Types of Cancer:	Leukemia / Leukaemia	100%

Project Summary

AML outcomes remain poor, with only 25% of patients achieving five-year survival. This proposal addresses a great challenge in leukemia and cancer research overall: how to kill residual cancer cells with stem cell properties to improve patient outcomes. In the leukemia field, researchers propose that these cells, called leukemia stem cells (LSCs), emerge when healthy blood stem cells (called hematopoietic stem cells [HSCs]) acquire mutations that transform them into cancerous LSCs. LSCs then divide, acquire survival properties that make them resistant to all current chemotherapies (such as cell cycle or "tyrosine kinase" inhibitors), and then give rise to an entire population of leukemic cells. Thus LSCs are likely responsible for relapse after treatment. HSC transplantation in some cases eradicates LSCs, but can be toxic or promote potentially lethal graft-vs-host disease. Therefore, effective approaches to kill LSCs are needed to cure AML. We have recently focused on understanding how LSCs differ from normal stem cell counterparts. We found that one remarkable difference is that in most AML patients, LSCs either hyperactivate a cancer-causing gene called FLT3 or exhibit mutant forms of overactive FLT3. This increase in FLT3 signaling enhances LSC survival, even after treatment, leading to poor outcomes. Researchers previously knew that FLT3 protein in LSCs becomes activated when it is chemically modified by small molecules called phosphate groups. However, we have shown that FLT3 protein is also modified in an entirely different manner, by addition of methyl groups, and that this activity also promotes leukemia cell growth and survival. How protein methylation changes protein activity in cancer cells is a very new field. Our lab has generated a new tool to study this modification, namely, an antibody that allows us to detect methylated FLT3. Using it, we discovered that an enzyme called PRMT1 is responsible for methylating FLT3 in AML cells. In fact, we found that PRMT1 protein levels significantly increase in LSCs, linking PRMT1 activity with LSC emergence. More importantly, we showed that co-treatment of LSCs with a drug that blocks PRMT1 methylation activity plus a tyrosine kinase inhibitor has a synergistic effect and potentiates anti-cancer effects of the latter. Here, we will determine experimentally whether PRMT1 inhibition, either by drug treatment or genetic engineering, in combination with currently used anti-leukemia drugs, antagonizes LSC activity in a mouse model of AML. We will also ask whether FLT3 methylation catalyzed by PRMT1 boosts LSC survival, as our model suggests. Our goal is to determine whether targeting PRMT1 could provide AML treatment and whether this strategy could be used in combination with conventional treatments to avert relapse and provide durable therapy. Our preclinical studies, if successful, could lead to clinical testing of this combination therapy for AML in the near future.

Grant Profile Information

Chun-Jung Lin, PhD

The Prognostic and Therapeutic Potential of SPARC in RCC Metastasis

University of Texas Southwestern Medical
Center, Dallas
Department of Urology
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Dallas, TX 75390-9110

Grant No. PF-19-087-01-CSM
Division: South
Term of Grant: 07/01/2019-06/30/2020
Total Award: \$57,500
Total ACS Support: \$57,500

Mentor: Jer-Tsong Hsieh, PhD

Area of Research:	Cancer Progression and Metastasis	25%
	Technology Development and/or Marker Discovery	35%
	Systemic Therapies - Discovery and Development	40%
Types of Cancer:	Kidney Cancer	100%

Project Summary

Renal cell carcinoma (RCC) is one of the most common cancers worldwide and the most lethal urologic malignancy. More than 35% of patients dying with RCC have skeletal metastases. These skeletal metastases cause devastating complications including intractable bone pain, pathological fractures, and hypercalcemia. RCC bone metastases are also relatively resistant to radio- and chemotherapy. Thus, it is critical to identify early prognostic marker(s) associated with RCC metastasis, and discover new agent(s) of preventing RCC metastasis.

In order to understand the molecular mechanisms associated with RCC metastasis, a unique bone metastatic pre-clinical model, and several sublines derived from bone metastatic site were established to profile master gene driver. A significant induction of Secreted protein acidic and rich in cysteine (SPARC) was identified in metastatic subline, as well as high-grade RCC specimens. In this study, I demonstrated that RCC invasiveness is highly correlated with the presence of SPARC by using gene knockdown and recombinant protein approaches. Moreover, by profiling proteomic expression in RCC tumor-derived exosome (TDE) (an extracellular vehicle produced by mammalian cells, which carries different signaling molecules), SPARC were also found. I believe SPARC in TDE functions as initiation factor for metastatic RCC. Therefore, I hypothesize that the presence of SPARC in TDE from RCC patient can be a predictive marker for the onset of distant metastases. I have established the quantitation assay, and successfully detect SPARC expression in TDE purified from the mice model. Importantly, the content of SPARC in exosome is correlated with the tumor growth in mice model. Therefore, I will use clinical bio-fluid to confirm this predicting model. Additionally, I have identified a potent anti-SPARC antibody, I proposed to unveil its therapeutic effect in preventing RCC metastasis. I anticipate that these experimental therapeutic regimens will have a better outcome than current regimen and the detection of SPARC levels in TDE will also provide a specific selection of individual patient subjected to the precision medicine treatment.

Overall, I will unveil the mechanism leading to RCC metastasis, establish a new liquid biopsy assay to determine SPARC levels for predicting the risk of metastatic potential, and develop specific targeted therapeutic strategy. The outcome of this study will provide a foreseeable clinical translation of personalized medicine for incurable and lethal RCC. I expect to write several papers resulting from this work, and start seeking an independent research position after paper published.

Grant Profile Information

Meixiao Long, MD, PhD

Ibrutinib as Immunomodulatory Reagent to Enhance Anti-tumor T cell response

Ohio State University
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Grant No. MRSO-19-033-01-LIB
Division: North Central
Term of Grant: 07/01/2019-06/30/2024
Total Award: \$729,000
Total ACS Support: \$729,000

Area of Research:	Technology and/or Marker Evaluation With Respect to Fundamental Parameters of Method	50%
	Systemic Therapies - Discovery and Development	50%
Types of Cancer:	Leukemia / Leukaemia	70%
	Melanoma	30%

Project Summary

Ibrutinib is a highly effective agent for B cell malignancies such chronic lymphocytic leukemia (CLL). Developed to inhibit Bruton's tyrosine kinase (BTK), Ibrutinib also has alternative targets such as ITK. Our group has reported that Ibrutinib enhances T cell immunity by targeting ITK. Moreover, my preliminary data demonstrated that Ibrutinib significantly enhances the expansion/persistence of T cells in CLL patients without the aforementioned drawbacks. However, our group has also reported that ibrutinib can ameliorate T cell immunity in mouse model under certain autoimmune circumstances. We also found that ibrutinib can increase the expression of checkpoint molecules, which in turn inhibit T cell function. We have reported that in animal models, while Ibrutinib strongly increased the number and function of activated bacteria specific T cells, it does not affect the resting T cells. We hypothesize that Ibrutinib increases the expansion/persistence of activated antigen-specific T cells, but not resting T cells. We also hypothesize that ibrutinib's direct impact on activated T cells (but not resting T cells) is to increase the checkpoint molecules and addition of checkpoint blockade will synergistically enhance ibrutinib's immunomodulatory effect.

Here we propose to investigate how ibrutinib differently affects activated T cell (in response to viral/bacterial pathogen or tumor) versus resting T cells using: 1) mouse models of leukemia. 2) Correlative studies accompanying our phase-2 clinical trial where CLL patients are to receive pneumococcus/influenza vaccine while receiving Ibrutinib (experimental arm) or before starting ibrutinib (control arm). We will also investigate if checkpoint blockade can synergistically enhance ibrutinib's immunomodulatory effect. Furthermore, we will investigate if ibrutinib can enhance the efficacy of an existing immunotherapy drug, blinatumomab, to achieve complete remission and long term survival.

Studies proposed here will lead to better understanding of the underlying mechanisms and unique features of ibrutinib's immunomodulatory effect, which is crucial for designing clinical trials utilizing this drug for cancer immunotherapy.

Grant Profile Information

Margaret Longacre, PhD

The Systematic Integration of Family Caregivers in Cancer Palliative Care

Arcadia University
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Grant No. PEP-19-041-01-PCSM
Division: Northeast
Term of Grant: 07/01/2019-06/30/2021
Total Award: \$144,000
Total ACS Support: \$144,000

Area of Research:	Resources and Infrastructure	60%
	Patient Care and Survivorship Issues	40%
Types of Cancer:	Not Site-Specific Cancer	100%

Project Summary

Palliative care is recommended for cancer patients with advanced disease or high symptom burden, and to benefit family caregivers (“caregivers”) who commonly provide logistical, emotional, and nursing-related assistance to patients. Many caregivers experience high emotional strain and are in need of information and support services. The National Cancer Institute and other experts in health care recommend that caregivers be involved as team members to improve the quality of patient care and to benefit caregivers. Yet, we currently lack an understanding of how to best include and support caregivers. In other words, interest in patient- and family-centered care is increasing, but the processes to achieve this standard of care in a systematic and reproducible way across institutions is lacking.

This research is guided by several frameworks to enhance the delivery of patient- and family-centered care, including the Roadmap for Patient and Family Engagement in Health Care. Highlights of these frameworks include (1) consideration of patient preferences or autonomy; (2) recognizing that the experiences of all who interact within a system must guide changes in the delivery of care; (3) the use of technology to enhance involvement; and (4) consideration of clinical benefit. The study lead along with collaborators in cancer prevention and control, palliative care, and web technologies from Fox Chase Cancer Center (FCCC) have worked together to develop a proposed method, the “I-CARE system” (Integrated-caregiver portal system) to systematically integrate and support caregivers in palliative cancer care. The I-CARE system (1) allows the patient to designate, in their online patient portal system, a primary caregiver and their preferences for care management and communication with that caregiver; (2) allows the designated caregiver, via a unique and secure caregiver page in the patient portal system, to indicate their needs as a caregiver; and (3) informs clinicians of patient/ caregiver responses by electronically notifying the clinical team that the responses are available to view on a staff-specific page in the patient portal system. The goal of this project is to gain feedback on a test version of the I-CARE system from patients, caregivers and providers in palliative care and then explore use of the refined I-CARE system (referred to as feasibility testing) as well as gain providers' perceptions of clinical benefit. These understandings will enable future studies to expand the I-CARE system, including (1) developing and delivering information and support to caregivers through the portal, and (2) assessing the system on caregiver, patient, and system outcomes compared to current standards of care.

Grant Profile Information

Clare Malone, PhD

Targeting the Nuclear Export Factor NXT1 in Neuroblastoma

Dana-Farber Cancer Institute
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450 Brookline Avenue
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Grant No. PF-19-078-01-TBG
Division: Northeast
Term of Grant: 07/01/2019-06/30/2020
Total Award: \$57,500
Total ACS Support: \$57,500

Mentor: Kimberly Stegmaier, MD

Area of Research: Systemic Therapies - Discovery and Development 100%

Types of Cancer: Neuroblastoma 100%

Project Summary

Neuroblastoma, a cancer that arises on the developing nervous system, is the most common tumor of infancy, and causes a disproportionate number of pediatric deaths due to cancer. Despite intensive therapy, including chemotherapy, radiation, stem cell transplants, immunotherapy, and differentiation therapy, the survival rate for children with high-risk neuroblastoma remains unacceptably low, at about 50%. New therapies are needed, but identifying targets for drug discovery efforts has been a challenge in this disease. Neuroblastoma, like most pediatric cancers, has relatively few mutations, so genomic sequencing efforts have not been very successful in identifying new therapeutic targets. In contrast to adult cancers, where therapies targeted to the specific mutations in a cancer have been quite successful, pediatric cancer has not benefited from this approach to the same degree. Indeed, current estimates suggest that only 25% of children have an actionable clinical mutation. Further compounding this problem, many of the established drivers of cancer are transcription factors, which are currently considered undruggable. As new therapies are needed, and identifying targets is a challenge, we have taken a new approach to target discovery by performing large-scale screens using CRISPR/Cas9 gene editing technology to identify genes that are not mutated but are nonetheless essential for the survival of neuroblastoma cell lines. Our screening efforts have identified a gene called NXT1, which seems to be critical for the survival of neuroblastoma cells, but not other cancers. NXT1 encodes for a protein that controls the export of transcribed RNAs from the nucleus to the cytoplasm where they can be translated into proteins. Excitingly, another protein with a similar role in nuclear export has been the target of a successful drug discovery effort, suggesting that drugs that block NXT1's activity could be developed. Here we propose to understand the impact of NXT1 loss on neuroblastoma cell lines, as well as in a mouse model of neuroblastoma, in order to determine whether NXT1 is indeed a good target for therapeutic development in neuroblastoma. Additionally, our preliminary data suggests that cancer cells with low levels of NXT2, a closely related gene to NXT1, appear to be more sensitive to NXT1 loss. This suggests that low expression of NXT2 could be used as a biomarker to identify cancers that would respond to NXT1 inhibition. Therefore, we also propose to investigate this relationship to determine if low NXT2 expression is indeed a biomarker of sensitivity, and if there is any functional redundancy between NXT1 and NXT2 in neuroblastoma cells that could explain this apparent relationship. Our results will help us understand the role of NXT1 in neuroblastoma and could lead to a new drug discovery effort around this target, and ultimately a new treatment option for children with this disease.

Grant Profile Information

Kyle D. Mansfield, PhD

Role of N6-Methyladenosine mRNA Modification in Breast Cancer Progression

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Biology
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Grant No. RSG-19-044-01-RMC
Division: Southeast
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$792,000
Total ACS Support: \$792,000

Area of Research:	Cancer Progression and Metastasis	100%
Types of Cancer:	Breast Cancer	100%

Project Summary

While detection of breast cancer has improved over the last few decades, advanced cases of breast cancer still claim the lives many women each year. Despite intense efforts, the underlying causes of breast cancer progression and metastasis are not completely understood. It is well established that genetic mutations in the DNA of cells can alter the expression of important proteins and often lead to decreases in important checkpoint proteins or the overexpression of regulatory proteins that gives the cancer cell characteristics that promote uncontrolled growth and eventually tumor formation. While DNA is very important, genes must first be converted to messenger RNA, which is actually the template that is used for protein production. In fact, the conversion of DNA to RNA to protein is known as the central dogma of biology and underlies all gene expression in cells of our body. Interestingly, there are many processing steps that must occur to faithfully convert the DNA sequence to a messenger RNA and finally into the proper protein and many regulatory events that control the protein expression to ensure everything works normally. In the last decade, the importance of these intervening steps (termed post-transcriptional) has been recognized and is a growing field of research in many areas of medicine, including cancer, where it is now recognized that alterations in these intervening steps can have effects similar to that of DNA mutations.

Recently, it was discovered that modifications of messenger RNA, driven by cellular enzymes termed methylases, can alter their normal processing and regulation. This can change the type and amount of protein that is produced from a gene. Our lab has discovered that during the progression of breast cancer from normal to malignant cells, there is a dramatic decrease in one particular modification of messenger RNA known as N6-methyladenosine. N6-methyladenosine modification of messenger RNA has been shown to affect many of the post-transcriptional processing and regulatory steps required for normal protein production and the maintenance of stem cells. Because of this, we hypothesize that changes in RNA N6-methyladenosine may play a key role in the progression of breast cancer cells from normal to malignant. In addition to investigating N6-methyladenosine in human tumor samples, we also propose to use a novel well-defined model of breast cancer progression to study the role of N6-methyladenosine in transforming normal human mammary epithelial cells and their response to low oxygen environments (hypoxia). By altering N6-methyladenosine levels in both normal and transformed breast epithelial cells and identifying the affected messenger RNAs we hope to better understand the role this RNA modification plays in cancer progression. Our ultimate goal is to develop novel therapeutics to target the N6-methyladenosine pathway in the hopes of providing new and possibly more effective treatments for breast cancer.

Grant Profile Information

Maura McCall, MSN

Trajectories and Predictors of Aromatase Inhibitor Adherence and Symptoms

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Grant No. DSCN-19-049-01-SCN
Division: Northeast
Term of Grant: 07/01/2019-06/30/2021
Total Award: \$30,000
Total ACS Support: \$30,000

Mentor: Catherine M. Bender, FAAN, RN, PhD

Area of Research:	Technology Development and/or Marker Discovery	25%
	Patient Care and Survivorship Issues	75%
Types of Cancer:	Breast Cancer	100%

Project Summary

Breast cancer is the most frequently occurring cancer worldwide. The U.S. 5-year survival rate is high for most types of breast cancer, with survivors totaling more than 3 million. To prevent tumor recurrence, postmenopausal women with estrogen receptor positive (ER+) breast cancer are prescribed a 5-year treatment with an aromatase inhibitor (AI). To reap its benefits, the entire AI treatment must be completed; yet, as few as 48% of women regularly take the daily dose in the first year. For each additional year (years 2-5), treatment adherence numbers further decrease. Most women will not finish this treatment, leaving them at greater risk of recurrence and cancer progression.

Adherence is the extent to which a person carries out the agreed upon plan of treatment. Chronic disorders research demonstrates that patients only successfully carry out the medication regimen about 50% of the time, regardless of the disorder. Cancer is no different. Unlike chemotherapy given in a controlled hospital setting, oral delivery of cancer treatments is in the hands of the patient at home, making it similar to chronic disease treatment. Ensuring patients correctly and completely carry out the cancer treatment is a major public health concern.

Why would women with ER+ breast cancer not take the AI? Though AIs provide benefit by improving outcomes, they often cause bothersome symptoms. While symptom severity varies, most woman taking an AI report one or more symptoms. Knowing patterns of symptoms and adherence over time will help providers identify when and how to help manage them.

The range in severity of AI symptoms experienced by women may have biological underpinnings. Pharmacogenomics is the study of how traits inherited from our parents affect the way our bodies break down (metabolize) and react to medication. Simply put, our genes affect how quickly and completely a medication is used in our bodies. For instance, if slow, we may experience more symptoms, and if quick, we may not have any symptoms or vice versa. Genes, which help women break down, use, and react to AIs, may play a role in the number and severity of the symptoms they develop. These symptoms are often the reason women stop taking AIs. If providers know gene variations related to AI symptoms, they can offer a more appropriate treatment choice for the women who have them.

The purpose of my dissertation research is to examine patterns of changes over time (trajectories) of AI adherence and symptoms, as well as explore the role of genes involved in AI metabolism, adherence, and symptoms. This study will: 1) identify AI adherence and symptom patterns over time; 2) develop an in-depth understanding of the role of AI adherence and genetic variation on symptoms; 3) guide future research for proactive, precision health care strategies to maximize AI adherence and minimize AI symptoms, ultimately improving the quality of life and long-term outcomes in postmenopausal women with ER+ breast cancer.

Grant Profile Information

Andrew McDonald, MD

Neurocognitive Sequelae of Radiation Therapy for Head and Neck Cancer

The University of Alabama at Birmingham
Department of Radiation Oncology
AB 1170
1720 2nd Avenue South
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Grant No. MRSB-19-012-01-CPPB
Division: South
Term of Grant: 07/01/2019-06/30/2024
Total Award: \$729,000
Total ACS Support: \$729,000

Area of Research: Patient Care and Survivorship Issues 100%

Types of Cancer: Head and Neck Cancer 100%

Project Summary

More than 50,000 cases of head and neck cancer are diagnosed in the United States each year and cure rates are increasing. As a result, the number of head and neck cancer survivors who experience the long-term side effects of their cancer treatment is also increasing. Since most patients who are treated for head and neck cancer receive radiation therapy, the side effects of radiation therapy are particularly important. The long-term side effects of head and neck radiation include dry mouth, difficulty swallowing, jaw problems, and damage to the blood vessels in the neck. Limiting high dose radiation to patients' brains has always been a priority, but many patients with more advanced head and neck cancer will incidentally receive some low and moderate brain radiation exposure. The negative effects of brain radiation on cognition – the ability to think and remember – have been extensively studied in children and patients with brain tumors, but not among patients with head and neck cancer. Since the doses and locations of brain radiation exposure in patients with head and neck cancer are very different from other groups of patients, we believe that patients with head and neck cancer should be studied separately.

This study is divided into three parts, or aims. In the first aim, we will ask head and neck cancer survivors to complete to complete questionnaires about their cognitive function and their overall quality of life. We will use these results to gain a sense of how common cognitive problems are after head and neck radiation and how they are related to quality of life. We will also examine the radiation plans for each patient to explore how these patient outcomes may be related to the radiation dose to different areas of the brain. In the second aim we will ask patients to complete formal testing of their cognition and to provide a saliva sample for genetic testing. We will compare patients' responses about their cognition to their testing results and we will also investigate whether any genetic differences were associated with worse cognitive scores. In the third aim, we will ask participants to undergo a special MRI brain scan that also assesses brain activity (functional MRI). We will compare the MRI scans between patients who have cognitive problems and those who do not. We will also develop new software that will allow us to calculate radiation doses to specific brain areas identified on the functional MRI.

Overall, this study will help us to learn more about the burden of cognitive problems after head and neck radiation, which factors are associated with worse cognitive function, and how the brain structure and activity change. Our long-term goal is to use the results of this study to develop new approaches to reduce the rate and severity of cognitive problems after head and neck radiation so that cancer survivors can live better in addition to living longer.

Grant Profile Information

Geeta Mehta, PhD

Ovarian Cancer Tumoroids to Study Heterogeneity and Chemoresistance

University of Michigan
Department of Materials Science and
Engineering
North Campus Research Complex (NCRC)
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3044W
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Grant No. RSG-19-003-01-CCE
Division: North Central
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$786,000
Total ACS Support: \$786,000

Area of Research:	Cancer Progression and Metastasis	30%
	Technology Development and/or Marker Discovery	40%
	Resources and Infrastructure Related to Treatment and the Prevention of Recurrence	30%
Types of Cancer:	Ovarian Cancer	100%

Project Summary

Most ovarian cancer patients develop malignant ascites, which resist chemotherapies, and are enriched in chemoresistant cancer stem cells. These stem cells are maintained through interactions with cells in ascitic microenvironment and under shear stress. However, little is known about the cellular interactions of cancer cells in ascites or the impact of fluid shear stress on cancer cell biology. In this proposal, we will define and recreate ex-vivo the ovarian cancer ascites microenvironment, to investigate the impact of the ascites TME on cancer stem like cells, and chemoresistance, thereby creating effective platform for identifying novel therapeutic targets.

Grant Profile Information

Emma Michl, BSN

Graduate Scholarship in Cancer Nursing Practice

Duke University
1204 Stone Gate Drive
Raeford, NC 28376

Grant No. GSCNP-19-057-01-SCN
Division: Southeast
Term of Grant: 07/01/2019-06/30/2021
Total Award: \$20,000
Total ACS Support: \$20,000

Mentor: Mary Lou Affronti, DNP, RN, MHSc,
ANP

Area of Research:	Interventions to Prevent Cancer: Personal Behaviors (Non-Dietary) that Affect Cancer Risk	20%		
	Patient Care and Survivorship Issues	60%		
	Population-based Behavioral Factors	20%		
Types of Cancer:	Blood Cancer	25%	Lung Cancer	10%
	Breast Cancer	10%	Not Site-Specific Cancer	50%
	Colon and Rectal Cancer	5%		

Project Summary

I am honored to be a student at Duke University School of Nursing in the Family Nurse Practitioner Program. In addition to the required courses for my general major, I will be participating in the oncology specialty. The oncology specialty consists of multiple didactic classes as well as clinical hours that will prepare me to diagnose, treat, and manage the care of oncology patients as a nurse practitioner.

Throughout my years as a nurse, I have experienced many of the facets of oncology care. I have worked as a nurse in the inpatient hospital setting on a medical and surgical oncology unit, an intensive care oncology unit, and a bone marrow transplant unit. My work experience also includes outpatient clinic nursing in both medical and radiation oncology. In addition to these traditional work opportunities, I have the privilege of being an oncology nurse in the United States Navy. Last year, I became certified as an Oncology Certified Nurse (OCN) through the Oncology Nursing Certification Corporation to validate my knowledge and competency in care of cancer patients.

My goal in life is to build upon my nursing education and become an Advanced Oncology Certified Nurse Practitioner in both civilian and military settings. I plan to apply to the Veteran Affairs Nursing Academic Partnership for Graduate Education in order to complete a post-graduate residency in veteran centered care. I aspire to help veterans, military members, and their families through all stages of cancer care. I intend to be involved in research and clinical trials, always working towards better outcomes and the best quality of life for my patients. I want to partner with my patients in their cancer journey and provide them the same support that my family received while my mother and grandmother were experiencing their own cancer treatment. In my role as a nurse practitioner, I will focus on educating my patients so they are able to make informed decisions regarding their treatment options. It is important to me to be a reliable and trustworthy resource for my patients as they go through one of the most delicate times in their lives. I want to maximize the quality of life of my patients and minimize the stress and anxiety that comes with a cancer diagnosis. I also aim to bring more awareness and preventative services to service members and improve survivorship within this unique population. My goal is to provide evidence-base care and improve the global oncology care of veterans and their families. The Graduate Nursing Scholarship in Cancer Nursing Practice from the American Cancer Society will help me gain the advanced education that will allow me to provide skilled advance practice nursing care to individuals with a cancer diagnosis.

Grant Profile Information

Julie Monda, PhD

Determining Mechanisms of Orphan Protein Degradation

University of California, San Diego
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Grant No. PF-19-072-01-TBE
Division: West
Term of Grant: 07/01/2019-06/30/2022
Total Award: \$163,500
Total ACS Support: \$163,500

Mentor: Eric Bennett, PhD

Area of Research: Cancer Initiation: Alterations in Chromosomes 100%
Types of Cancer: Not Site-Specific Cancer 100%

Project Summary

Proteins play critical roles in all aspects of cellular function. The information required to make each protein is encoded within the DNA. During tumor formation, mutations accumulate within the DNA and ultimately effect the faithful production of the proteins. For example, the sequence of the protein can be changed, potentially resulting in a non-functional product. Alternatively, the amount of protein produced can be either increased or decreased. Frequently, proteins function as part of a multi-protein complex. In these cases, uncoordinated changes in the amounts of each subunit produced will result in excess proteins that are unable to assemble into full complexes. It then becomes critically important for the cell to recognize these excess proteins and selectively target them for degradation to prevent toxic effects. It is clear that cells have a surveillance mechanism in place to remove these unwanted proteins. Additionally, this quality control mechanism must act during the transition from a normal cell to a cancerous cell. However, little is known about the components of the quality control mechanism. The goal of the work I'm proposing here is to identify the molecular mechanisms that govern protein quality control. Toward this goal, preliminary work from the Bennett Lab has identified a critical enzyme that selectively recognizes proteins that fail to assemble into larger functional complexes, also known as "orphan" proteins, and targets them for destruction. Research accomplished within this proposal will lead to a precise molecular understanding of how this enzyme differentiates unassembled proteins from assembled proteins and targets only the unassembled protein pool for degradation. I will directly test if cells that contain losses or gains in chromosome number, a near universal feature of cancer cells, depend upon this enzyme that oversees orphan protein destruction for survival. Lastly, I will screen for new cellular factors that are required for orphan protein degradation. Ultimately, I aim to determine if directly targeting this critical protein quality control pathway will selectively impair cancer cell growth. Because nearly all cancers contain extensive genetic mutations, I anticipate that my findings will be broadly applicable across human cancer subtypes.

Grant Profile Information

R. S. Morrison, MD

Enhancing Quality of Life in Cancer Care

Icahn School of Medicine at Mount Sinai
Department of Geriatrics and Palliative
Medicine
One Gustave L. Levy Place
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Grant No. CRP-19-094-06-COUN
Division: Northeast
Term of Grant: 07/01/2019-06/30/2024
Total Award: \$400,000
Total ACS Support: \$800,000

Area of Research:	Patient Care and Survivorship Issues	80%
	End-of-Life Care	20%
Types of Cancer:	Not Site-Specific Cancer	100%

Project Summary

In the U.S., approximately 14 million people have had cancer and more than 1.6 million new cases are diagnosed each year. By 2022, it is projected that there will be 18 million cancer survivors and by 2030, cancer incidence is expected to rise to 2.3 million new diagnoses/year. While medical advances have transformed previously fatal conditions such as cancer into illnesses that people can live with for many years, they have not been accompanied by corresponding improvements in quality of life for patients and their families – particularly in late stage disease. The National Academy of Medicine 20151 report detailed extensive national data from multiple settings of a high prevalence of physical, psychosocial, and financial suffering associated with cancer and other serious illness; mismatches between patients' goals for care and treatments received; and a healthcare system that fails to deliver appropriate care to persons with serious illness and their caregivers. Living with cancer should not equate to such suffering yet the evidence base that would improve quality of life for seriously ill cancer patients is inadequate.

Palliative care has emerged to meet the needs of seriously ill patients and their families. Palliative care, delivered by teams of doctors, nurses, social workers, chaplains, focuses on achieving the best possible quality of life for patients and their caregivers. It is appropriate at the point of diagnosis of a serious illness like cancer and goes beyond hospice to offer patients and their families treatments that focus on improving quality of life while receiving life-prolonging and curative treatments. It encompasses symptom assessment and treatment; aid with decision making and establishing goals of care; practical support; mobilization of community resources to assure secure and safe living environments; and collaborative care models (hospital, home, and hospice). Palliative care allows seriously ill patients and their families to live as normal a life as possible in the setting of their illness, and to ensure that the quality of that life is the best that can be possibly achieved.

National Palliative Care Research Center (NCPRC) is a unique national organization whose mission is to strengthen the evidence-based foundation needed for health policy and clinical practice in palliative care. Since 2006, NPCRC has partnered with ACS and ACS-CAN to accomplish this by supporting research scientists, stimulating research and innovation, and creating a community of researchers focused on the needs of persons with serious illness like cancer and their families. NPCRC has worked for the past fourteen years to establish priorities for palliative care research, develop a new generation of palliative care clinician promote the development of the research infrastructure, and create a network and community of scientists dedicated to improving quality of life for persons and families living with serious illness like cancer. Renewal of this Clinical Research Professor Award will help further develop new NPCRC programs

Grant Profile Information

Taru Muranen, PhD

Matrix Microenvironment Mediated Drug Resistance in Pancreatic Cancer

Beth Israel Deaconess Medical Center
Department of Medicine
E/BR 264
330 Brookline Avenue
Boston, MA 02215

Grant No. RSG-19-020-01-CSM
Division: Northeast
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$791,000
Total ACS Support: \$791,000

Area of Research:	Cancer Initiation: Oncogenes and Tumor Suppressor Genes	5%
	Cancer Progression and Metastasis	95%
Types of Cancer:	Pancreatic Cancer	100%

Project Summary

Matrix proteins are a key part of the tissue microenvironment that surrounds all organs. This microenvironment consists of several elements including normal epithelial cells that form organs (such as lungs, intestine, and skin), immune cells, and stromal cells. Stromal cells secrete matrix proteins such as collagens that provide structural support for all tissues. Both the stromal cells and the matrix proteins they secrete are important in normal physiology, suppressing growth of pre-cancerous cells and protecting normal cells which must attach to matrix proteins to survive. In cancer, however, this microenvironment changes, and instead of suppressing tumor growth, it can instead protect tumor cells from drug treatments and other stresses, contributing to drug resistance.

One of the most lethal types of cancer is pancreatic cancer, which is often accompanied by a massive increase in the amount of matrix protein surrounding the tumor. During pancreatic cancer development the normal pancreatic stromal cells become overly active, dividing uncontrollably and secreting excess amounts of matrix proteins. Is this abundance of matrix proteins partially responsible for making this cancer so difficult to treat? And how does the matrix protect the tumor? The matrix may form a physical barrier that prevents drugs from penetrating the tumor. Moreover, the matrix also contains other secreted factors that can aid cancer cells and activates survival signaling in the cancer cells, which may also contribute to the poor prognosis in pancreatic cancer.

This proposal aims to understand how the matrix proteins protect tumor cells and promote drug resistance. Our preliminary data suggest that pancreatic stellate cells, the primary matrix-secreting cell type in pancreas, protect pancreatic cancer cells from chemotherapy. This protection is linked to secreted molecules, either the matrix molecules themselves, or other proteins attached to the matrix. Our data has identified candidate proteins and we will study in detail: i) how do these secreted proteins protect the tumor cells, ii) how do the tumor cells respond to these secreted factors, and iii) how we can target these proteins to develop more effective therapies for the treatment of pancreatic cancer.

Our background is in cancer and matrix biology, and this proposal takes advantage of the unique research environment we are working in. One of the goals of our proposal is to utilize patient-derived pancreatic cancer organoids (so-called as they are considered mini-organs) together with stromal cells to identify effective drug combinations that would enhance the effectiveness of current therapies. These studies will form the basis of establishing a framework for future studies whereby patient-derived pancreatic cancer organoids and stellate cells can be used to screen for effective drug combinations, tailored for individual patients' responses.

Grant Profile Information

Kim-Anh Nguyen, BS

Graduate Scholarship in Cancer Nursing Practice

Yale University
School of Nursing
400 West Campus Drive
Orange, CT 06477

Grant No. GSCNP-19-059-01-SCN
Division: Northeast
Term of Grant: 07/01/2019-06/30/2021
Total Award: \$20,000
Total ACS Support: \$20,000

Mentor: Marianne Davies, MSN

Area of Research:	Exogenous Factors in the Origin and Cause of Cancer	30%
	Resources and Infrastructure Related to Detection/ Diagnosis/ or Prognosis	70%
Types of Cancer:	Lung Cancer	100%

Project Summary

Before starting my nursing education, I was a clinical research coordinator in the Pulmonary and Critical Care Division at Stanford University. I worked closely with lung cancer patients and their families, witnessing the physical and emotional challenges that they had to face. The experiences motivated me to become a knowledgeable and compassionate acute care nurse practitioner, specializing in lung cancer. Yale School of Nursing (YSN) has a rigorous educational program that prepares me to treat and manage acute and advanced diseases. The Oncology Concentration provides comprehensive classes and clinical skills specific to the care of adults with cancer.

I also chose YSN because of its mission to "provide better health for all people" through the integration of research and clinical practice. Lung cancer is the leading cause of cancer-related deaths globally, affecting people across racial and socio-economic groups. My previous research studies on the early detection of lung cancer helped me realize that it is a multifaceted problem with serious impacts on patients' psychosocial wellbeing. During my time at Yale and for future PhD work, I will further investigate new methods for lung cancer detection and the effects of screening processes on patients. The Graduate Scholarship in Cancer Nursing Practice will support my research and my goal of becoming a certified cancer nurse practitioner.

Grant Profile Information

Rachel Niederer, PhD

Quantification of Translational Control by Transcript Leader Elements

Yale University
Department of Molecular Biophysics and
Biochemistry
266 Whitney Avenue
New Haven, CT 06520

Grant No. PF-19-092-01-RMC
Division: Northeast
Term of Grant: 07/01/2019-06/30/2021
Total Award: \$111,500
Total ACS Support: \$111,500

Mentor: Wendy Gilbert, PhD

Area of Research:	Normal Functioning			70%
	Cancer Initiation: Oncogenes and Tumor Suppressor Genes			30%
Types of Cancer:	Breast Cancer	20%	Lung Cancer	20%
	Cervical Cancer	20%	Prostate Cancer	20%
	Colon and Rectal Cancer	20%		

Project Summary

Regulation of gene expression is a highly complex, multi-step process that is essential for many aspects of life from cellular differentiation to stress response. The expression of many genes is regulated at the level of protein synthesis, or translation. Cancer cells undergo widespread changes in which genes are translated, but exactly how these changes occur is poorly understood. The goal of this proposal is to understand how different genes are targeted for translation under different conditions.

First, I will establish a quantitative high-throughput assay to measure recruitment levels of the ribosome, the macromolecular machine responsible for carrying out protein synthesis. This will enable me to identify specific elements within mRNAs that are associated with either high or low levels of ribosome recruitment. With a complete profile of these elements we can begin to predict the protein output of a given gene as well as predict any alterations that arise in response to tumorigenesis or other disease states.

Next, I will use the assay described above to examine an unconventional mechanism of protein synthesis that is critical in cancer cells. Most ribosome recruitment proceeds via recognition of a specialized structure at the end of mRNAs known as the cap. However, in many cancer cells the machinery that recognizes the cap is downregulated. Cancer cells circumvent this by using cap-independent mechanisms of translation, however which genes undergo this type of translation and exactly how they do so is unclear. Using the assay described above I will identify all the genes that can undergo cap-independent translation and then explore the pathways responsible.

Finally, I will study the role of the core translation factor known as eIF4E in promoting the selective translation of specific genes. eIF4E is a proto-oncogene whose overexpression is sufficient to drive oncogenic transformation in cell lines. Overexpression of eIF4E drives the selective expression of a subset of genes. I will measure the responsiveness in ribosome recruitment of different genes to different levels of eIF4E. This will enable me to identify sequence or structural elements that are targeted by eIF4E.

Grant Profile Information

Megan L. Norris, PhD

Role and Regulation of RNA Localization in Cellular Migration and Invasion

University of Texas Southwestern Medical
Center, Dallas
Department of Molecular Biology
5323 Harry Hines Boulevard
Dallas, TX 75390-9020

Grant No. PF-19-043-01-RMC
Division: South
Term of Grant: 07/01/2019-06/30/2022
Total Award: \$163,500
Total ACS Support: \$163,500

Mentor: Joshua T. Mendell, MD, PhD

Area of Research:	Normal Functioning	60%
	Cancer Progression and Metastasis	40%
Types of Cancer:	Melanoma	90%
	Neuroblastoma	10%

Project Summary

Cancer metastases, as opposed to primary tumors, account for 90% of cancer-related deaths but our understanding of metastasis lags behind other cancer research disciplines. A powerful way to get around this obstacle is to first understand how healthy cells function, which will make defects in cancer cells more obvious. In a growing embryo, it is good for cells to rapidly divide and migrate throughout the body. However, cancer cells will often borrow these behaviors in order to metastasize. In healthy babies, cells called neural crest give rise to the face and skull, much of the nervous system, and pigment cells called melanocytes. The goal of my research is to understand how the migration of these cells is abused to give rise to malignant melanoma. Although decades of study have previously failed to uncover how this process works, recent evidence suggests it depends on where RNA molecules are inside the cell. In my work, I have already discovered that melanoma cells organize their RNAs in a very specific way. Next, by comparing the RNA of melanoma cells to neural crest cells, I will be able to find RNAs that behave differently in cancer vs healthy cells. After identifying the most unique RNAs, I will find what other cellular molecules control the RNA and affect where it is in the cell. These other molecules, and the RNAs themselves, may prove to be important biomarkers of cancer, or even therapeutic targets. Lastly, I will use gene-editing technologies to manipulate the RNAs and see how it affects cancer onset and progression – first in cell culture, then in mice. In the short term, this work will help break through the historical barriers in understanding neural crest cell and cancer migration on a fundamental level. In the future, this foundation can be expanded to other cell types and may provide ways to detect, treat or even prevent cancer of all kinds.

Grant Profile Information

Steve Oghumu, PhD

Mechanisms of MIF in Oral Cancer: Applications for Prevention and Treatment

Ohio State University
Department of Pathology
1960 Kenny Road
Columbus, OH 43210

Grant No. RSG-19-079-01-TBG
Division: North Central
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$786,000
Total ACS Support: \$786,000

Area of Research:	Endogenous Factors in the Origin and Cause of Cancer	50%
	Complementary and Alternative Treatment Approaches	50%
Types of Cancer:	Oral Cavity and Lip Cancer	100%

Project Summary

Oral cancer kills one person every hour every day in the United States. Worldwide, 450,000 new cases and 127,000 deaths are reported every year. New forms of treatment have not significantly improved the survival rates of oral cancer. Therefore, new and effective oral cancer prevention and treatment strategies are desperately needed. Our research has identified a protein that is important for the development of oral cancer. This protein is termed macrophage migration inhibitory factor (MIF). Levels of MIF have been found to be elevated in tumors of oral cancer patients compared to surrounding normal oral tissue. In mice that have MIF genetically removed, the development of oral cancer is significantly reduced compared to normal mice that have the MIF gene intact. These results show that MIF can potentially be targeted for oral cancer prevention and treatment. However, important questions remain, such as (i) how does MIF promote oral cancer, and (ii) can agents that inhibit MIF be used in combination with other oral cancer agents to improve oral cancer treatment outcomes? This project will investigate the mechanisms that underlie MIF-associated promotion of oral cancer and will evaluate the effectiveness of MIF inhibitors in combination with other treatments in oral cancer treatment. Based on our recent studies, we have identified a population of cells in oral tumors that we believe are responsible for the effects of MIF on oral cancer. These cells are called myeloid derived suppressor cells (MDSCs). We have recently generated a novel genetically modified mouse model that allows us to delete MIF in MDSCs so we can fully explore the role of MDSCs in MIF-associated promotion of oral cancer. We have also identified a novel small molecule that inhibits MIF (CPSI-1306), which can potentially improve the effectiveness of oral cancer treatment, when strategically combined with established oral cancer treatments. We will therefore evaluate combinations of CPSI-1306 with immune checkpoint inhibitors or a growth factor inhibitor to inhibit oral cancer in mouse models. With the complementary expertise of our investigative team coupled with the unique and novel tools we have generated, we will be able to successfully complete the aims proposed in this application. Successful completion of these studies will increase our understanding of how MIF promotes oral cancer, and will open up novel opportunities for oral cancer treatment using combinations with MIF inhibitors. Ultimately, we expect that these strategies can eventually be advanced to clinical trials in the treatment of oral cancer. Knowledge gained from these studies can also be applied to the treatment of other cancers.

Grant Profile Information

Eleanor C. Ory, PhD

Microtentacle Mechanics in Reattachment of Metastatic Tumor Cells

University of Maryland, Baltimore
Department of Oncology
655 West Baltimore Street
Baltimore, MD 21201

Grant No. PF-19-017-01-CSM
Division: Northeast
Term of Grant: 07/01/2019-06/30/2022
Total Award: \$163,500
Total ACS Support: \$163,500

Mentor: Stuart S. Martin, PhD

Area of Research:	Cancer Progression and Metastasis	80%
	Technology Development and/or Marker Discovery	20%
Types of Cancer:	Breast Cancer	100%

Project Summary

Cancer continues to be an epidemiologically significant disease responsible for killing approximately 590,000 people every year and 90% of those fatalities are due to metastasis or when the disease spreads to a distant site. Despite this fact, only 5% of research funding focuses on metastasis resulting in a lack of treatment options to prevent cancer from spreading. Cancer spreads throughout the body by entering the bloodstream as a circulating tumor cell, reattaching to the walls of the blood vessels, and finally forming a secondary tumor or micrometastasis. The lab I work in has discovered cytoskeleton based protrusions in Circulating Tumor Cells which we named microtentacles. Work from our lab has determined that Circulating Tumor Cells with microtentacles increase the likelihood that cells will get trapped in the lungs and form a metastasis. Microtentacles form either when inward pulling parts of the cytoskeleton called the actomyosin cortex are weakened or when outward pushing parts of the cytoskeleton called microtubules are stabilized. The goal of this study is to use quantitative methods to better understand how changes to the cytoskeleton affect the quantity, length, and dynamics of microtentacles as well as determine how microtentacles aid CTC attachment to the blood vessels. The work proposed in my application has 2 potential impacts on cancer treatments. 1) Improved understanding of the mechanics behind microtentacle formation could identify targets for drug treatments that will help prevent metastasis. 2) Combining the results and analysis techniques outlined in this study with emerging CTC isolation technologies could help clinicians better assess risks for metastasis and prescribe optimal personalized treatment plans.

Grant Profile Information

Kelli Passalacqua, MSSW

Master's Training Grant in Clinical Oncology Social Work

Mayo Clinic Cancer Center
School of Social Work
200 First Street SW
Rochester, MN 55905

Grant No. MSW-19-068-08-SW
Division: North
Term of Grant: 07/01/2019-06/30/2021
Total Award: \$24,000
Total ACS Support: \$108,000

Project Summary

It has been my sincere pleasure to have just finished another summer block placement with an intern from St. Thomas/St. Catherine's University (Minneapolis, MN). I have had 12 interns over the course of my career and this is the eighth Master's Level Training Grant in Oncology Social Work recipient. I am grateful for the opportunity to have been accepted these past years for this grant as it continues to provide me with personal and professional growth as I educate interns who have a hunger for understanding our importance in the field of social work and the work we do with a fragile pediatric oncology population. I am humbled with every intern as I am able to view a case through the eyes of a learner who offers different impressions and perspectives. Although, I have been out of graduate school for 21 years, the opportunity for continued learning serves me well through the field instructor platform.

In terms of the selected interns through this grant, it gives them an opportunity to focus fully on their work due to the generous amount the grant fund and allows them flexibility to focus on all aspects of the work to obtain competency across the spectrum for psychosocial attention. The intern is able demonstrate knowledge of the inter and intra-professional collaboration and team practice, obtain knowledge of the epidemiology of different cancers which impact social and environmental risk factors, understand health care policy and resources, financing of health care with legal and ethical responsibilities, knowledge of the impact of a cancer diagnosis on the psychosocial, emotional, economic and physical functioning of the patient and family, knowledge and ability to conduct an oncology specific clinical assessment and make clinical treatment interventions, and the knowledge and ability to educate patients, families and colleagues about the psychosocial implications of illness and treatment.

Mayo Clinic continues to serve a large volume of patients with cancer and it remains an exceptional environment to receive training on the delivery of services to pediatric patients with cancer. The continued importance with the integration of practice, research and education continues to provide opportunities and access to the latest developments in the diagnosis and treatment of cancer and continues to serve as an excellent training foundation for the pediatric oncology intern who wishes to develop a career in the area of pediatric oncology. This opportunity for an intern is enhanced by the generous grant of the American Cancer Society as well as the additional opportunities that I am able to receive through the funds offered for education. You have my heartfelt gratitude and thank you for considering another opportunity for all involved.

Grant Profile Information

Huadong Pei, PhD

Investigate the Role of USP15 in Breast Cancer Radiochemotherapy

George Washington University
Department of Biochemistry and Molecular
Medicine
Science and Engineering Hall
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Washington, DC 20052

Grant No. RSG-19-032-01-DMC
Division: Northeast
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$792,000
Total ACS Support: \$792,000

Area of Research:	Cancer Initiation: Alterations in Chromosomes	50%
	Cancer Initiation: Oncogenes and Tumor Suppressor Genes	50%
Types of Cancer:	Breast Cancer	100%

Project Summary

The genome DNA of a cell is under constant attack from exogenous and endogenous DNA damaging factors such as radiation, carcinogens and reactive radicals. To maintain genomic stability, cells have developed an elaborate DNA damage response (DDR) system, which is responsible for sensing DNA damage, halting the ongoing cell cycle, and repairing DNA damage. Failure to detect and repair DNA damage leads to genomic instability, which in turn can drive tumorigenesis. Many human genetic cancer predisposition syndromes are linked to defective DDR. For example, mutations in the BRCA1 gene were found in about 50% of familial breast cancer cases. Because individual tumors often have unique defects in the DDR pathway, insight into the basic mechanisms by which cells repair different DNA lesions could also guide individualized therapy. A promising example is the use of PARP inhibitors in cancers with BRCA1 and BRCA2 mutations. PARP inhibitors offer a promising strategy, but many questions apart from clinical efficacy remain unanswered. For example, there is evidence for the utility of PARP inhibitors in ovarian cancers in the absence of BRCA mutations, presumably resulting from other molecular deficiencies in DNA repair. So there is a continual demand to identify BRCA-like and other genomic signatures that may expand benefit from PARP inhibitor. On the other hand, many studies suggest that overexpression of DNA repair factors could contribute to resistance to chemoradiotherapy. Therefore, studying this pathway has important implications in cancer pathogenesis and cancer therapy. Our long term goal is to understand the molecules and mechanisms that control DNA repair, genome stability and breast cancer. Towards this aim, we have begun to analyze a critical deubiquitylating enzyme, appropriately named USP15, which functions as a homologous recombination player to control genome stability and prevent breast cancer. In this proposal, we will investigate the detailed functions and mechanisms of USP15 in HR, breast cancer initiation and breast cancer response to radiochemotherapy. Ultimately, we hope to translate this knowledge into new strategies for detecting and treating breast cancers.

Grant Profile Information

Christopher Petell, PhD

Decoding the Role of the PBRM1 BAH Domains in Tumorigenesis

University of North Carolina, Chapel Hill
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CB 7295
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Chapel Hill, NC 27599

Grant No. PF-19-027-01-DMC
Division: Southeast
Term of Grant: 07/01/2019-06/30/2022
Total Award: \$163,500
Total ACS Support: \$163,500

Mentor: Brian Strahl, PhD

Area of Research: Cancer Initiation: Alterations in Chromosomes 100%
Types of Cancer: Not Site-Specific Cancer 100%

Project Summary

Cells are the basic unit of the human body, with each person possessing over 200 different cell types that each have a different function. Remarkably, despite having over 200 cell types, every one of these cells has the same set of instructions or “blueprints” in the form of DNA. How the same set of instructions can lead to all of these cell types is one of the major outstanding questions and wonders in biology.

Recent evidence points to an area of biology called “epigenetics”, which begins to explain how one set of instructions, or genes, can lead to all of the cellular diversity in humans. Epigenetics refers to the ability to control the “when” and “where” our genes within these instructions are used. Most often, thousands of genes are carefully – almost like an orchestra – turned on or off by this epigenetic process to create each unique cell type, and to instruct what each cell must do to contribute to the whole organism. However, when epigenetics goes awry, cells become confused and begin to behave like another cell type – often like how the first cells to emerge from fertilization have instructions to divide, but without the control to stop doing so. This is one way to think of how cancer arises, and importantly, how we have recently learned how mutations or disruptions of the epigenetic machinery lead to cancer.

My proposal seeks to define one of the most mutated genes in all of cancer. It is called PBRM1 and it is part of an epigenetic machine that is involved in the opening of our genome to allow genes to be turned on. PBRM1 is known for making cancer cells susceptible to killing by your own immune cells. While PBRM1 has been widely examined, no one has yet explored a particular region in this protein (a region containing several domains called BAH domains) on its function. With this fellowship, I will determine the normal role for the BAH domains in PBRM1 function. This will be compared to how mutations in these domains found in cancer disrupt normal PBRM1 function. By learning how the BAH domains work in normal or mutant PBRM1, new therapeutic targets will be made available to the drug discovery pipeline.

An important facet of this study will be the characterization of other BAH domains. These domains are found in equally important genes that are known to drive the development of cancer or support its growth. My goal is to determine what role the other BAH domains have in these proteins. This will be a resource that other researchers can use as a better starting point to figure out the impact of mutant BAH domains in other cancers and diseases. This screen will provide the foundation for many previously unknown targets for cancer drugs or other therapies.

Grant Profile Information

Jenifer Prosperi, PhD

APC Regulation of Doxorubicin Resistance in Breast Cancer

Indiana University, Indianapolis
Department of Biochemistry and Molecular
Biology
1234 Notre Dame Avenue
South Bend, IN 46617

Grant No. RSG-19-093-01-TBG
Division: North Central
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$792,000
Total ACS Support: \$792,000

Area of Research:	Cancer Progression and Metastasis	50%
	Combinations of Localized and Systemic Therapies	50%
Types of Cancer:	Breast Cancer	100%

Project Summary

Our laboratory works on a tumor suppressor called Adenomatous Polyposis Coli (APC), which is lost in up to 70% of breast cancers. Breast cancer is the leading cause of cancer-related deaths in non-smoking women in the United States. Over the past 10-15 years, it has become evident that breast cancer is not one disease, but is divided into multiple subtypes that differ in their gene expression, ability to form distant metastases, and response to chemotherapeutic treatment. It is known that breast (and other solid) tumors acquire resistance to commonly used chemotherapeutic agents. In my laboratory, we use model systems that mimic early and late tumor development and progression with varied levels of APC. While much is known about how APC impacts the development of inherited and sporadic colorectal cancer, significantly less is known about its role in breast cancer. APC interacts with proteins that are involved in the process of DNA repair and replication, such as topoisomerase II. We have identified that breast cancer cells with decreased APC become resistant to treatment with chemotherapeutic agents that are used to treat breast cancer. The focus of this proposal is on a drug called doxorubicin (Adriamycin), an anthracycline that blocks the function of topoisomerase II. Emphasizing the gap of knowledge and innovation of this project, these pathways are understudied in breast cancer. We hypothesize that APC loss mediates the development of therapeutic resistance as a result of the "normal," cell maintenance functions of APC, and we are able to test this using models that we have in the laboratory. We will use standard chemotherapeutic agents in combination with targeted inhibitors of APC-mediated pathways to define a treatment regimen that would be most beneficial for patients with APC-null breast cancer. In addition, we will identify which how APC mediates therapeutic response through DNA repair pathways through a study of multiple repair pathways, and the steps from drug treatment through cell death. Finally, we will correlate APC status in breast cancer patients to drug response using tissues from the IU Simon Cancer Center. Future studies will investigate other chemotherapeutic agents in combination with DNA repair pathways specific for those drugs. Our work has the potential to decrease breast cancer mortality through the understanding, and further application, of the modalities involved in specific subtypes of breast cancer. These studies will allow the discovery of novel targeted therapies and the ability to predict therapy response based on expression of the APC tumor suppressor.

Grant Profile Information

Malavika Raman, PhD

VCP-UBXN1 Regulation of the ER Stress Response in Multiple Myeloma

Tufts University
Department of Developmental Molecular and
Chemical Biology
J612
150 Harrison Avenue
Boston, MA 02111

Grant No. RSG-19-022-01-CSM
Division: Northeast
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$775,000
Total ACS Support: \$775,000

Area of Research:	Normal Functioning	50%
	Endogenous Factors in the Origin and Cause of Cancer	50%
Types of Cancer:	Blood Cancer	100%

Project Summary

Cancer cells often contain duplications of entire chromosomes. These extra copies of DNA in turn produce extra copies of proteins, that are superfluous and have no function. The burden of having hundreds or thousands of extra proteins can result in the death of the cancer cell. To circumvent this problem, cancer cells come to rely on cellular components that can remove these extra proteins. The main component of the cells that eliminates proteins in a machine known as the proteasome, which functions in a manner similar to a kitchen insinkerator; proteins that are fed into the proteasome are chewed up and destroyed. Proteins to be destroyed by the proteasome are "flagged" by a small molecule called ubiquitin. Specific proteins in the cell will recognize the ubiquitin-tagged protein and deliver it to the proteasome for disposal. Because cancer cells rely on this disposal system for survival, drugs that interfere with these processes cause a backup in the system which eventually becomes toxic to the cancer cell eventually causing death. This observation resulted in the development of proteasome inhibitors that are particularly efficient in treating a variety of blood cancers. However, because the proteasome is also essential for the functioning of healthy or normal cells, proteasome inhibitors have many harmful side-effects. Therefore, there is a need to identify proteins within these degradation pathways that when targeted may be more specific in inducing the death of the cancer cell while sparing normal cells. One protein that may be amenable to targeting is known as VCP, which is a ubiquitin recognition protein that identifies targets to be degraded and delivers them to the proteasome. Indeed, VCP protein levels are highly increased in many cancers and correlate with poor clinical outcomes. Our long-term goal is to understand how VCP recognizes proteins for degradation so that we can develop ways to inhibit this process and treat cancers. We have identified a new role for VCP in degrading proteins that are secreted from the cell (for example antibodies from immune cells). Many blood cancers (e.g. multiple myeloma) aberrantly secrete large amounts of antibodies and are reliant on the proteasome and associated pathways to degrade these non-functional antibodies. In this proposal, we will use a number of complementary approaches to determine (1) how VCP recognizes this class of ubiquitin-modified substrate, (2) the identity of the proteins VCP helps degrade and (3) whether interfering with this specific VCP function is sufficient to cause cancer cells to die. Ultimately, the goal is to develop a molecular understanding of these pathways so that we can develop drugs that will target this Achilles heel in cancer.

Grant Profile Information

Ranjith Ramasamy, MD

Nitric Oxide Based Immunotherapy for Castration Resistant Prostate Cancer

Miller School of Medicine, University of Miami
Department of Urology
#1551
1120 NW 14th Street
Miami, FL 33136

Grant No. CSDG-19-016-01-CSM
Division: Southeast
Term of Grant: 07/01/2019-06/30/2024
Total Award: \$729,000
Total ACS Support: \$729,000

Area of Research:	Cancer Progression and Metastasis	50%
	Systemic Therapies - Discovery and Development	50%
Types of Cancer:	Prostate Cancer	100%

Project Summary

Prostate cancer growth is often driven by male sex hormones called androgens, which include testosterone. Because of this, a common treatment option for prostate cancer is to lower the levels of androgens in a man's body. Androgen levels can be lowered by surgically removing the testicles or with drugs that stop the testicles from making androgens or block how they affect the body. This type of treatment is called hormone therapy or androgen-deprivation therapy. If the cancer spreads to other parts of the body beyond the prostate in a process called metastasis, hormone therapy is usually continued. Eventually, many men with metastatic prostate cancer develop castration-resistant disease. This means that the cancer is able to grow and continue to spread despite using hormone therapy. For men with this type of disease, additional treatment is needed to help control the growth of the cancer. Our long-term goal is to develop curative therapies for patients with castration resistant prostate cancer by focusing on under studied aspects of tumor micro-environment. By understanding what critical changes occur in the microenvironment, we hope to identify drugs that can be targeted to treat patients with this lethal illness. To achieve this goal, we are using a drug that increases the levels of nitric oxide. The critical association of nitric oxide with tumor microenvironment in castration resistant prostate cancer remains unknown. It is anticipated that the results of this proposal will determine the impact and mechanism of nitric oxide on castration resistant prostate cancer. Successful completion of this proposal will establish not only the clear understanding of role of nitric oxide in castration resistant prostate cancer but could also potentially lead to development of a new drug that can be used to cure castration resistant prostate cancer.

Grant Profile Information

Matthew R. Ramsey, PhD

Dissecting the Functions of Basonuclin 1 in Squamous Cell Carcinoma

Brigham and Women's Hospital
Department of Dermatology
77 Avenue Louis Pasteur
Boston, MA 02115

Grant No. RSG-19-021-01-CSM
Division: Northeast
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$792,000
Total ACS Support: \$792,000

Area of Research:	Cancer Initiation: Oncogenes and Tumor Suppressor Genes	60%		
	Cancer Progression and Metastasis	40%		
Types of Cancer:	Head and Neck Cancer	30%	Oral Cavity and Lip Cancer	20%
	Lung Cancer	10%	Skin Cancer (non-melanoma)	40%

Project Summary

Squamous Cell Carcinoma (SCC) is a common cancer that develops most often in the skin, the mouth, and the lungs. Standard treatments for patients include radiation, cis-platin, 5-fluorouracil, and paclitaxel, which are only modestly effective and have many toxic side effects, resulting in approximately 45,000 deaths every year. While advances in immunotherapy have improved patient outcomes compared to standard therapy, many patients do not respond, leading to a need for new approaches to treatment. Like most other cancers, outcomes are worse in late stage disease, and most deaths are the result of metastatic spread. However, despite a great deal of effort, very few genes have been found that are specifically altered in metastatic tumors compared to the primary tumor. Instead, it is becoming increasingly clear that metastatic cells employ normal cellular motility pathways to move throughout the body. Thus, understanding the mechanisms that control normal cell movement is likely to shed light on the metastatic process.

A key feature common to tissues that develop SCC is that they form a barrier to protect tissues from the outside environment. Upon tissue damage, cells stop dividing, and then migrate across the wound area to complete the repair process. We have identified the Basonuclin 1 (BNC1) transcription factor as a key modulator of the cell division to migration switch essential for proper completion of wound healing. Interestingly, BNC1 is specifically expressed in SCC, but not other tumor types such as Adenocarcinoma, suggesting an important role in SCC. The goal of this project is to elucidate how BNC1 functions to control the switch from cell division to migration, and how this may promote metastatic spread of SCC cells. We will employ pre-clinical tumor initiation models driven by environmental carcinogens such as UV to test the requirement of BNC1 in early tumor formation. We will take advantage of our novel inducible CRISPR/Cas9 genome editing system to test whether BNC1 loss in late stage tumors can lead to metastatic spread. To complement these studies, we will explore the contributions of a number of newly identified BNC1-associated proteins to the regulation of cell division and migration. We hypothesize that BNC1 will work together with unique protein partners to control different sets of genes that are needed for processes such as cell division and migration. Importantly, many of these protein partners have enzymatic activities that have the potential to be therapeutically targeted. In total, these experiments aim to dissect the complex contributions of BNC1 to SCC tumorigenesis, with the goal of developing ways of blocking both proliferation and metastatic spread.

Grant Profile Information

Jill M. Randall, MSW

Development of a Pre-Transplant Psychosocial Assessment Tool

University of Louisville Research Foundation,
Inc.
Kent School of Social Work
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Louisville, KY 40202-1959

Grant No. DSW-19-064-01-SW
Division: North Central
Term of Grant: 07/01/2019-06/30/2021
Total Award: \$40,000
Total ACS Support: \$40,000

Area of Research:	Patient Care and Survivorship Issues	100%
Types of Cancer:	Blood Cancer	100%

Project Summary

Hematopoietic cell transplantation (also known as bone marrow transplant) is a potentially curative therapy that is used in adults primarily to treat blood cancers such as leukemia and lymphoma. Transplant is an arduous process entailing psychosocial challenges that can endure for years. Examples of these include financial burden, caregiver stress, anxiety, depression, and post-traumatic stress disorder. Given these challenges, patients undergo a psychosocial assessment before transplant to identify high risk factors that require intervention before, or close monitoring throughout, transplant. Examples of high risk factors include suicidal thoughts, suicide attempts, illicit drug use, history of noncompliance with medical treatment, no caregiver, alcoholism, cognitive impairment, and major mental illness.

While there is general agreement that pre-transplant psychosocial assessment is important, there are no standard practice guidelines for it. Thus, the content (what) and process (how) of the assessment varies among transplant centers. The lack of consistent screening practices results in disorganized psychosocial data and is therefore a barrier to conducting high quality psychosocial research. A standardized pre-transplant psychosocial assessment tool would bring consistency and set a standard for comprehensive pre-transplant psychosocial assessment.

Using survey and focus group methods, this research will develop an assessment tool that can be implemented across transplant centers. The tool will be informed by research on psychosocial factors that influence transplant outcomes. The workability of the tool will be tested by a small group of transplant social workers, and changes will be made accordingly before broad implementation at transplant centers. Social work leaders currently practicing in four transplant centers across the U.S. are collaborating on this research.

Grant Profile Information

Jennifer L. Raybin, MSN

Evaluation of a Quality of Life Biomarker in Children with Cancer

University of Colorado, Denver
1465 S. Steele Street
Denver, CO 80210

Grant No. DSCN-19-050-01-SCN
Division: North
Term of Grant: 07/01/2019-06/30/2021
Total Award: \$30,000
Total ACS Support: \$30,000

Mentor: Catherine Jankowski, PhD

Area of Research:	Technology and/or Marker Testing in a Clinical Setting	30%
	Complementary and Alternative Treatment Approaches	30%
	Patient Care and Survivorship Issues	40%
Types of Cancer:	Not Site-Specific Cancer	100%

Project Summary

As of 2017, more than 40 children in the United States are diagnosed with cancer every day. Although the survival rate is now over 80%, children with cancer still experience distress related to the disease and treatment. The World Health Organization has mandated that all children with life-threatening diseases like cancer receive palliative care to decrease their suffering and improve quality of life. Complementary and alternative therapies have been associated with improved symptom management and therefore quality of life for children with cancer. Creative arts therapy is a complementary therapy that is especially useful for this population. Research studies of creative arts therapies have used questionnaires to measure self-reported quality of life changes. While an abundance of cancer research strives to find reliable biological markers (biomarkers) to assess disease treatment, it is equally important to find an objective biomarker of quality of life. In children with cancer, biomarkers found in blood can be difficult to interpret due to cyclical cancer treatments and disease processes. I propose that physical posture can be used as an objective measure of quality of life in children undergoing chemotherapy. Physical posture will represent changes in a child's sense of well-being and body image during cancer treatment and in response to creative arts therapy.

The purpose of the proposed study is to determine if physical posture as a biomarker is significantly related to quality of life in children undergoing cancer chemotherapy. The aims of the study are: 1) to determine the relationship between posture and creative arts therapy in children receiving chemotherapy and 2) to determine if children with a central venous catheter have worse posture and if their posture improves compared to children without a central venous catheter in response to creative arts therapy interventions. In my published pilot study, preliminary data suggested that creative arts therapy improved self-reported quality of life for children with cancer. My ongoing study with a larger sample size will attempt to confirm these results. The current proposed study will be a secondary analysis of a posture measure to examine more closely its possibility for use as a biomarker. By using posture as a biomarker, we may be able to more easily measure changes due to creative arts therapy or other complementary therapies intended to reduce distress for children with cancer.

The American Cancer Society Doctoral Scholarship will support my goal to become an independent nurse scientist who will investigate the use of creative arts therapy to reduce distress in children with cancer and other chronic conditions. As we continue to cure cancer, children are enduring increasingly intensive treatments with more suffering. In pursuit of the American Cancer Society vision, we must not only strive to help these children survive cancer, but ensure they are free from pain and suffering.

Grant Profile Information

Michaela R. Reagan, PhD

Marrow Niche Modulation of Myeloma Progression

Maine Medical Center
Maine Medical Center Research Institute
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Scarborough, ME 04074-7204

Grant No. RSG-19-037-01-LIB
Division: Northeast
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$792,000
Total ACS Support: \$792,000

Area of Research:	Cancer Progression and Metastasis	40%
	Localized Therapies - Discovery and Development	60%
Types of Cancer:	Bone Cancer	10%
	Myeloma	90%

Project Summary

Cancer develops and spreads because of the nature of the tumor and the environment or 'soil' in which the tumor is embedded. Multiple myeloma is a blood cancer that results from mutations in a type of blood cell called the plasma cell. Multiple myeloma cells grow in the rich soil of the bone marrow, first very slowly, causing no damage or symptoms, and then more quickly and aggressively, causing degradation of the bone and development of drug resistant clones. The risk of developing myeloma is greater in older individuals and people with high body mass index. These patients also typically have more bone marrow adipose tissue, or fat, than younger or leaner individuals. However, the ways in which bone marrow adipocytes (fat cells) modulate disease progression are not well understood. Thus, we hope to shed light on new therapeutic avenues to halt multiple myeloma by targeting the interactions between myeloma cells and bone marrow adipocytes that will one day have a huge impact on patients. Due to the potentially inflammatory nature of bone marrow adipose tissue, and its ability to act as a source of fatty acids and adipokines, we wanted to explore how bone marrow adipose tissue affects myeloma tumor cells. Our cell culture studies suggest bone marrow adipocytes induce drug resistance in myeloma cells through a protein called fatty acid-binding protein 4 (FABP4). In this proposal, we will analyze how bone marrow adipocytes contribute to myeloma by using novel, three-dimensional (3D), tissue engineered cancer models. Compared to two-dimensional (2D) cultures, 3D cultures much more realistically recapitulate what happens in the human body. The tissue engineered models are made from silk scaffolds, bone marrow adipocytes, and cancer cells. By growing myeloma cells in these 3D mini-bone environments, we can determine how myeloma cells change in response to adipocytes and discover new ways to target this interaction. The second part of our project will use mouse models to study bone marrow adipocyte and myeloma crosstalk. Our mouse models recapitulate very closely how tumors grow in patients. We will test how increasing or removing bone marrow adipocytes in mice affects tumor growth and drug resistance, and we will test specifically the role of FABP4 in this process. We will use these in vitro and in vivo models, which we have already developed and optimized in our lab, to better understand how cancer hijacks the bone marrow niche for its own purposes. Our long-term goal is to understand molecules and mechanisms driving multiple myeloma growth in the bone marrow. This proposal feeds into that by interrogating a novel part of the cellular "soil" (the bone marrow adipocyte), in which tumor cells, or "seeds" land and grow. In sum, our research will identify feedback loops between host and cancer cells, indicate mediators of this interaction, and propose paradigm-shifting concepts to guide the development of new anti-myeloma therapies.

Grant Profile Information

Sergi Regot, PhD

Single Cell Analysis of Tissue-level Signaling Dynamics During Cancer Onset

Johns Hopkins University
Department of Molecular Biology and Genetics
515A Pre Clinical Teaching Building
725 N Wolfe Street
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Grant No. RSG-19-005-01-CCG
Division: Northeast
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$792,000
Total ACS Support: \$792,000

Area of Research:	Normal Functioning	40%		
	Cancer Initiation: Oncogenes and Tumor Suppressor Genes	40%		
	Cancer Progression and Metastasis	10%		
	Technology Development and/or Marker Discovery	10%		
Types of Cancer:	Breast Cancer	40%	Skin Cancer (non-melanoma)	20%
	Gastrointestinal Tract	40%		

Project Summary

Cancer arises from a malfunction of the mechanisms that control cell proliferation, programmed cell death and other irreversible decisions. These critical decisions are made by integrating a variety of internal and external parameters in a very dynamic process that involves a network of clinically relevant protein kinases (Mitogen Activated Protein Kinases or MAPKs). In a live tissue such as the breast or the gut epithelium, the decision to divide or die can dramatically impact neighboring cells and therefore must be coordinated at the tissue level. Our current understanding of how the MAPK signaling network works to coordinate cell fate choices within tissues is incomplete due to the lack of methods to measure MAPK signaling in each individual cell of a living tissue in real time.

To address this limitation, my laboratory has pioneered a new technology that enables measuring MAPK signaling dynamics in single cells of a living tissue. Using this technology, we have implemented a series of assays in cell culture, primary tissues and in vivo that enable for the first time addressing the question of how cells make decisions in a coordinated manner. In particular, we have focused our efforts in characterizing the cell-cell communication and cell fate choices that occur when certain cells within a tissue express a cancer driver mutation. Our preliminary data shows that oncogenic cells trigger massive MAPK signaling responses in the neighboring healthy cells that are often required to clear the diseased cells from the tissue. The work we propose here seeks to understand these horizontal signaling events at the cellular and multicellular levels to provide a better understanding of the naturally occurring defense mechanisms against aberrantly signaling cells.

Grant Profile Information

Derek Rhoades, PhD

Development of Spliceosome Modulating Agents for MYC-Driven Breast Cancer

Baylor College of Medicine
Department of Pharmacology and Chemical
Biology
One Baylor Plaza
Houston, TX 77030

Grant No. PF-19-007-01-CDD
Division: South
Term of Grant: 07/01/2019-06/30/2021
Total Award: \$111,500
Total ACS Support: \$111,500

Mentor: Jin Wang, PhD

Area of Research:	Systemic Therapies - Discovery and Development	100%
Types of Cancer:	Breast Cancer	100%

Project Summary

Despite recent advances in targeted therapies for breast cancer, the need for new and improved medicines is still desperately needed. This is especially true for triple negative breast cancer (TNBC), a highly aggressive type of breast cancer in which no targeted therapies exist. Consequently, TNBC patients rely solely on toxic chemotherapy as their only treatment option. Thus, the discovery and development of novel therapeutics for TNBC that are safe and effective would revolutionize treatment for this aggressive form of breast cancer.

A primary driver of TNBC, and many other types of cancer, is the notorious gene (or oncogene) known as MYC. Although MYC has been known to be a major culprit in the onset and progression of cancer for decades, it has long been thought to be “undruggable.” Recently, it has been demonstrated that MYC-driven breast cancers, including TNBC, are therapeutically vulnerable to small molecule spliceosome modulators, an emerging new class of anticancer agents. Interestingly, and in contrast to classical chemotherapies that preferentially target rapidly dividing cancer cells, spliceosome modulators have also been shown to effectively kill both slowly and rapidly dividing cancer cells. Taken together, small molecule spliceosome modulating natural products hold tremendous promise as a transformative therapy for MYC-driven breast cancer, such as TNBC.

This proposal seeks to utilize the pladienolide class of spliceosome modulating natural products for the purposes of breast cancer drug discovery. Specifically, this project aims to develop and implement a fully synthetic chemical route for accessing pladienolide B and a series of its designed analogues in order to enhance their druglike properties. Next, all of the newly synthesized pladienolide compounds will be evaluated for their biological activity, including side effect profiles in mice. Finally, the most promising pladienolide analogue will be rigorously evaluated in a mouse model of human TNBC, with the ultimate goal of realizing a novel therapeutic candidate for treating breast cancer that is both safe and effective.

Grant Profile Information

Tyler Risom, PhD

Determining Breast Cancer Invasion Risk Through Novel Multiplexed Imaging

Stanford University, Palo Alto CA
Department of Pathology
Stanford Blood Center
3373 Hillview Avenue
Palo Alto, CA 94304

Grant No. PF-19-002-01-CCE
Division: West
Term of Grant: 07/01/2019-06/30/2022
Total Award: \$163,500
Total ACS Support: \$163,500

Mentor: Robert M. Angelo, MD, PhD

Area of Research:	Cancer Progression and Metastasis	20%
	Technology Development and/or Marker Discovery	60%
	Technology and/or Marker Evaluation With Respect to Fundamental Parameters of Method	20%
Types of Cancer:	Breast Cancer	100%

Project Summary

Breast cancer is the number one cancer affecting women in the United States. Many of these patients are first diagnosed with a pre-invasive, non-deadly, form of the disease termed Ductal Carcinoma in Situ (DCIS). From historical studies we know that around one third of DCIS patients would progress to invasive cancer if left untreated, however, we are currently blind to which patients are at risk of progressing from DCIS to invasive cancer due to lack of a clinical test to identify at-risk patients. Oncologists therefore have no choice but to treat all patients with the same surgery, radiation, and possible hormone therapy. Consequently, this current practice imparts significant treatment-related side effects, health issues, anxiety, and cost to tens of thousands of patients per year that had no risk of progression. Furthermore, many patients that receive therapy still progress to invasive breast cancer. These findings highlight two dire needs in breast cancer: 1) a clinical test to identify which patients are at risk of progressing from DCIS to invasive cancer, and 2) new effective therapies for those women who are at risk of progression.

This project seeks to solve both of these issues by identifying the differences in DCIS tumors that did or did not go on to progress to invasive breast cancer, through the use of a new microscope technology. Multiplexed Ion Beam Imaging (MIBI) allows us to see 40+ distinct protein markers simultaneously within a single tumor image. While past microscopes were unable to measure the profound cellular diversity in breast tumors and thus failed to identify predictive biomarkers of DCIS progression, MIBI can simultaneously measure every type of immune cell, tumor cell, stromal cell, and other progression-supporting processes. Using this technology I will image hundreds of archival DCIS patient tumors where patients either progressed to invasive cancer, or did not progress to invasive cancer within 10 years of follow up. In this way I can identify which features were specific to cases that progressed, identifying biomarkers of DCIS progression that could be used in future clinical risk-test development. Second, by looking at the cellular changes as breast tissue goes from a normal state, to in situ cancer, and onto invasive cancer, I can identify what immune cell types, immune regulatory proteins, and other processes change throughout this continuum. Such factors may be important targets for new therapies that could prevent cancer progression from an early stage.

By combining this new microscope technology with a meticulously collected set of patient samples with known outcomes, we will for the first time have capability to overcome the profound diversity of breast tumors in order to identify the molecular 'needles in the haystack' that can predict patient outcomes and lead to new clinical test and therapeutic development. The outcomes of this work will greatly reduce patient over-treatment and expand the availability of effective drugs for the patients that need it.

Grant Profile Information

Christa Roe, BS, RN,

Graduate Scholarship in Cancer Nursing Practice

Yale University
Yale School of Nursing
400 West Campus Drive
Orange, CT 06477

Grant No. GSCNP-19-060-01-SCN
Division: Northeast
Term of Grant: 07/01/2019-06/30/2021
Total Award: \$20,000
Total ACS Support: \$20,000

Mentor: Mark Lazenby, PhD

Area of Research:	Resources and Infrastructure Related to Prevention	50%		
	Patient Care and Survivorship Issues	50%		
Types of Cancer:	Blood Cancer	20%	Leukemia / Leukaemia	20%
	Breast Cancer	20%	Non-Hodgkin's Lymphoma	20%
	Hodgkin's Disease	20%		

Project Summary

Yale University School of Nursing provides an environment that is conducive for the success of its students fostering knowledgeable, collaborative, innovative, dignified, and respectful adult gerontological primary care nurse practitioners. Thus, creating better health for all, including those diagnosed with cancer.

Cancer does not discriminate, and leaves an unfathomable burden on humanity, as it is one of the leading causes of death in the US and around the world. However, much of the disease burden is preventable. Through education and emphasis on cancer prevention, including healthy lifestyle choices, avoidance of cancer causing agents such as tobacco, and wholesome nutrition, the burden can be drastically reduced. Advanced registered nurse practitioners play a pivotal role in preventative measures for cancer, along with expanding access to healthcare generating more positive outcomes and a greater quality of life for those afflicted. In my practice experience at two large oncology academic centers, and abroad in oncology institutions located in lower and middle-income countries, I have seen the difference advanced registered nurse practitioners make for their patients, their colleagues, and in the prevention, diagnosis, treatment of cancer. My passion for cancer research has led to poster and oral presentations, along with peer reviewed journal article publications which demonstrate my commitment to improving the lives of patients diagnosed with cancer. The Graduate Scholarship in Nursing Practice Scholarship will provide me with support that I need in order to achieve my goal of contributing to the prevention and cure of cancer in the US and globally.

Grant Profile Information

William Rosa, MS

Analgesic Nonadherence in the Outpatient Oncology Setting

The Trustees of the University of Pennsylvania
60 West 68th Street Apt 6F
New York, NY 10023

Grant No. DSCN-19-054-01-SCN
Division: Northeast
Term of Grant: 07/01/2019-06/30/2021
Total Award: \$30,000
Total ACS Support: \$30,000

Mentor: Salimah Meghani, PhD

Area of Research:	Patient Care and Survivorship Issues	50%
	Population-based Behavioral Factors	50%
Types of Cancer:	Not Site-Specific Cancer	100%

Project Summary

Pain is one of the most common symptoms negatively affecting the quality of a person's life throughout the cancer experience. Healthcare providers often prescribe a combination of medications to effectively manage pain and improve physical and social independence. Despite experiencing pain, patients often deviate from a recommended pain medication plan or stop taking these medications altogether. This is referred to as "nonadherence". Patients demonstrate nonadherent behavior for a number of reasons, including individual beliefs and preferences, family members' hesitancy in using pain medications, and difficulty obtaining medications due to issues beyond their control, such as a lack of prescription coverage. Poor pain medication adherence leads to poor patient outcomes and increased healthcare resource use. A major component of understanding pain medication adherence relates to health disparities. Significant findings in the literature point to cancer pain disparities that disproportionately impact racial and ethnic minorities. For example, African Americans may be less likely to receive an optimal pain medication and may be in more severe pain more often than Whites. As a result, African Americans may be at a higher risk for becoming nonadherent to medications for cancer pain, potentially leaving them vulnerable to poorer pain and health outcomes.

How do healthcare providers address pain medication nonadherence? Unfortunately, many of the educational interventions offered to patients and families to improve adherence rates do not work. In addition, the current opioid crisis is shifting the way prescribers and patients think about and use pain medications, which may be leading to more opioid stigma, increased nonadherence, and more severe pain and associated suffering. Despite the research related to pain medication nonadherence for cancer pain, little is known about the related factors that contribute to nonadherent behaviors and some studies disagree on findings. Further research is needed to 1) explore the related factors that contribute to increased pain medication nonadherence and 2) assess how patients make decisions that result in nonadherent behaviors. Additionally, more research needs to address disparities between African American and White patients while considering a number of other social factors, such as socioeconomic status and level of education. In order to optimize patient and health outcomes and effectively manage cancer pain, scientists need a clearer understanding of what determines adherence to prescribed pain medication regimens and what healthcare providers can do to provide better solutions to improve adherence. By doing so, we may become better able to decrease cancer pain and associated suffering for individuals, their families, and our communities at large.

This proposal takes a scientific step toward the American Cancer Society's vision of a "world free from the pain and suffering of cancer" and their desire to understand healthcare barriers for minority groups and create strategies to overcome them.

Grant Profile Information

Sandra Sabatka, MSW

Master's Training Grant in Clinical Oncology Social Work

University of Rochester
School of Social Work
518 Hylan Building RC
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Rochester, NY 14627

Grant No. MSW-19-069-01-SW
Division: Northeast
Term of Grant: 07/01/2019-06/30/2021
Total Award: \$24,000
Total ACS Support: \$24,000

Project Summary

The Social Work Intern Program at the Wilmot Cancer Institute prepares master's level social work interns to provide clinical services to adult patients and their care partners as a valued member of an interdisciplinary team.

Advanced training focuses on assessing patient/family needs using a strengths oriented approach. Interns learn how to identify and remove barriers to care, assist with navigation of complex medical and social service systems, mobilize community resources, address psycho-social distress and provide supportive counseling related to adjusting to diagnosis, treatment and survivorship. They are expected to network with community partners such as the American Cancer Society, Gilda's Club, 13-Thirty and the Breast Cancer Coalition of Rochester through tours, participation in community events and referrals.

Interns are quickly familiarized with institutional, community and national policies that impact patients and their care. They are encouraged to seek ways to effect change and advocate for patients at both the micro and macro levels.

The Wilmot Cancer Institute is comprised of 86 inpatient beds and 11 outpatient locations serving patients across upstate New York. This affords interns the opportunity to develop skills working with patients of diverse cultural and socioeconomic backgrounds from both urban and rural settings.

An evidence-based Integrative Oncology and Wellness Center serves to familiarize interns with complementary modalities such as Acupuncture, Yoga, Qi Gong, Journaling, Plant-Based Cooking for Wellness Classes, Integrative Health & Wellness Lectures and Massage Therapy. Robust Survivorship and Palliative Care Programs provide interns with occasions to follow a patient through transitions such as re-integrating to work or pursuing a comfort oriented approach.

The Oncology Social Work staff is highly regarded at Wilmot and facilitates a number of support groups and programs. Interns are introduced to group work and expected to help facilitate an existing support group, assist with community needs assessments and participate in program and group development.

As part of the University of Rochester Medical Center, interns are encouraged to avail themselves of interdisciplinary educational opportunities such as Schwartz Rounds, Palliative Care Rounds, Ethics Conferences, Social Work and Survivorship Conferences and Well-U offerings promoting self-care.

The Social Work Staff is committed to mentoring interns supervising and has a great deal of experience. Several have been recognized with awards for leadership, program innovation and clinical expertise. They are frequent guest lectures for area Social Work programs and Oncology Conferences. The Wilmot Cancer Institute provides a unique experience for qualified candidates to develop the skills necessary for a career in oncology social work.

Grant Profile Information

Daniel Savic, PhD

Characterizing Variants at GWAS Loci for Acute Leukemia Treatment Outcome

St. Jude Children's Research Hospital
Department of Pharmaceutical Sciences
CCC Room I5103A
262 Danny Thomas Place
Memphis, TN 38105-3678

Grant No. RSG-19-083-01-TBG
Division: North Central
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$791,000
Total ACS Support: \$791,000

Area of Research: Systemic Therapies - Discovery and Development 100%

Types of Cancer: Leukemia / Leukaemia 100%

Project Summary

Acute lymphoblastic leukemia (ALL) is the most prevalent childhood cancer, and although overall survival rates of ALL have substantially improved, resistance to chemotherapeutic agents remains a major clinical concern. Chemotherapeutic drug resistance is predictive of poor disease outcome and is commonly observed in ALL patients that have relapsed, who have a low overall survival rate of only 40%. The underlying biological reasons for why ALL patients relapse and become resistant to chemotherapeutic drugs remain poorly understood. To identify genetic causes for ALL relapse and drug resistance, large genetic mapping studies in ALL patients were performed and identified regions of the genome that contain inherited "genetic variants" that contribute to ALL relapse. These genetic variants are common, naturally-occurring DNA mutations that are found in all humans. However, because the genomic regions identified by these mapping studies are large and contain hundreds of genetic variants, identifying which are important and contribute to ALL relapse has been extremely challenging. Notably, these functionally important variants are predicted to contribute to ALL relapse by altering the activity of a neighboring gene. This proposal will employ an integrative strategy that will follow-up on these genetic mapping studies by identifying genetic variants that are important for ALL treatment outcome and the target genes they act upon. This proposal will also determine how these variants and their target genes contribute to ALL relapse by assessing their effects on chemotherapeutic drug resistance in leukemia cells. Consequently, the results generated by this proposal will uncover novel biological mechanisms of chemotherapeutic drug resistance, and these data can be used to improve treatment strategies for newly diagnosed and for relapsed ALL by aiding in the development of novel therapeutics that can combat drug resistance in ALL patients. In addition, these data can inform approaches to circumvent resistance in the clinic, and be used to improve initial treatment, as well as guide therapy for relapsed disease through precision medicine and more personalized treatment regimens.

Grant Profile Information

Christal Sohl, PhD

Mechanisms of Isocitrate Dehydrogenase Variants in Cancer

San Diego State University
Department of Chemistry and Biochemistry
CSL 326
5500 Campanile Drive
San Diego, CA 92182

Grant No. RSG-19-075-01-TBE
Division: West
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$792,000
Total ACS Support: \$792,000

Area of Research:	Normal Functioning	20%		
	Cancer Initiation: Oncogenes and Tumor Suppressor Genes	80%		
Types of Cancer:	Brain Tumor	35%	Not Site-Specific Cancer	20%
	Leukemia / Leukaemia	30%	Sarcoma (soft tissue)	15%

Project Summary

The development of cancer requires acquisition of errors in the genome that usually either activates genes involved in activities like cell growth and division, or deactivates genes supporting pathways like genome repair or cell death. However, mutations in the gene encoding isocitrate dehydrogenase 1 and 2 (IDH1 and IDH2) are very unusual. These mutations not only deactivate the normal activity of balancing the production of small molecules used during metabolism, but they also allow the proteins to perform a new activity. This new activity is the production of the chemical D-2-hydroxyglutarate (D2HG), which drives the formation of tumors. IDH1 and IDH2 mutations are seen in > 80% of patients with lower grade brain cancers and secondary glioblastomas, and in 20% of patients with acute myeloid leukemia. We do not yet fully understand how these mutations allow the protein to make this new molecule. We also do not yet know if this molecule acts like an on/off switch, where any production of D2HG drives cancer, or if it is more like a rheostat, where more D2HG causes a more severe response in the tumor. Our long-term goals are to establish the specific properties of mutations found in cancer patients, to understand how these properties impact the cancer, and to establish new pathways affected by these mutations. To address these goals, we have developed an interdisciplinary research proposal where we will use methods to understand the mechanistic features and consequences of IDH1 and IDH2 activity. This includes addressing questions such as: how do IDH1 and IDH2 reroute metabolism in cancer? How much D2HG is produced by each mutation? How does the mutant form of the protein change its 3D shape? How well can we target each mutation therapeutically? We will also establish how the molecular mechanisms of IDH1 and IDH2 activity affect the cancer cell and animal models of cancer (does efficient production of D2HG cause more severe cancer characteristics? Why do prognoses vary in patients depending on the mutation type? What are the consequences of D2HG synthesis?). After identifying several mutations that allow us to understand the molecular mechanisms of IDH1 and IDH2 activity, we have developed new protein, cellular, and animal models to allow us to answer these questions. Overall, this work will enable us to establish the fundamental activities of normal and mutant IDH1 and IDH2, provide tools for predicting patient prognosis depending on their IDH mutation, and identify patients most likely to respond to personalized medicines.

Grant Profile Information

Jennifer Stewart, BSN

Graduate Scholarship in Cancer Nursing Practice

Duke University
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Central Office: 2200 W. Main Street, Suite 820
Durham, NC 27705-4677

Grant No. GSCNP-19-063-01-SCN
Division: Southeast
Term of Grant: 07/01/2019-06/30/2021
Total Award: \$20,000
Total ACS Support: \$20,000

Mentor: Susan M. Schneider, PhD, RN, AOCN,
FAAN

Area of Research:	Interventions to Prevent Cancer: Personal Behaviors (Non-Dietary) that Affect Cancer Risk	30%
	Resources and Infrastructure Related to Treatment and the Prevention of Recurrence	30%
	Patient Care and Survivorship Issues	25%
	Education and Communication Research	15%
Types of Cancer:	Breast Cancer	70%
	Not Site-Specific Cancer	30%

Project Summary

It is an honor to attend Duke University School of Nursing in the BSN to DNP program to become an Adult Gerontology Primary Care Nurse Practitioner with an oncology concentration. At the conclusion of this program, I will have developed the skills and knowledge to be a certified Adult Gerontology Primary Care Nurse Practitioner. Then, I will obtain my certification as an Advanced Oncology Certified Nurse Practitioner. As a Nurse Practitioner, I will be able to diagnose medical conditions and prescribe medicines and therapies. Being a primary provider managing the care on oncology patients is my goal. I plan to continue at Duke University to pursue my Doctor of Nursing Practice after obtaining my Master's degree.

I currently work as an intermediate float pool nurse at Brigham and Women's Hospital in Boston, MA. I float to all units in the hospital taking care of patients from all specialties. The majority of my patients are oncology patients receiving treatment for cancer. Being in the float pool has allowed me the opportunity to experience all varieties of oncology care, including surgical oncology, medical oncology, chemotherapy, bone marrow transplant, pain and palliative care. This diverse experience provides me with an excellent background and foundation in oncology care and has prepared me to become an advanced care provider.

My career goals as a Nurse Practitioner include working at an outpatient oncology clinic. This will allow me to provide care to patients on a regular basis who are receiving oncology treatment. Nurse practitioners are gaining major roles in outpatient settings. It is my goal to be the primary provider for my patients. Throughout my career as a nurse practitioner, I plan to continue being an active participant in professional organizations. Being a nursing leader is extremely important, and I plan on being an active member in the leadership community. Continuing to be an active member in professional organizations will allow me to collaborate with all healthcare disciplines, expand my oncology and medical knowledge and stay up to date on quality, patient-centered care.

Throughout my career as a nurse practitioner, I plan to engage in clinical trials and evidence based practice projects to provide quality, holistic care to meet the growing needs of the oncology population. Patient centered care is of utmost importance in oncology nursing. Focus on early detection of cancer and symptom management are areas of interest. Continuing to be involved in evidence-based practice ensures that as I move throughout my career, I will always be provided evidence supported best quality care to my patients. It will be my privilege to provide effective care to my patients and witness the ever-changing profession of oncology care due to technological and medical advances.

The Duke University School of Nursing will continue to provide me the strong clinical foundation to be an advanced practice provider.

Grant Profile Information

Richard Anthony Taylor, DNP

Lifespace Mobility in the Elderly, Rural Community-dwelling Cancer Survivor

The University of Alabama at Birmingham
Department of Acute, Chronic and Continuing
Care
1701 University Boulevard NB 536
Birmingham, AL 35294

Grant No. DSCN-19-051-01-SCN
Division: South
Term of Grant: 07/01/2019-06/30/2021
Total Award: \$30,000
Total ACS Support: \$30,000

Mentor: Marie Bakitas, DNSc

Area of Research:	Normal Functioning	25%
	Patient Care and Survivorship Issues	75%
Types of Cancer:	Not Site-Specific Cancer	100%

Project Summary

Life-space mobility (LSM) is a measure of community mobility and social participation related to the older adult's level of independent mobility, frequency, and distance as they move through their environment (life-space level), from their bedroom to beyond their town of residence. Life-space level declines or restrictions are associated with poorer quality of life (QOL) and well-being, higher health care utilization, psychological and spiritual distress, long-term disability, cognitive impairment, and poorer self-management. A higher incidence of decline in LSM occurs in the elderly (> 65 years) rural population. There is no evidence-based literature regarding factors that affect LSM and QOL across the elderly's cancer journey, particularly in the rural population. By 2040, the United States (US) is projected to have 26.1 million cancer survivors. Of this number, the percentage of elderly is expected to increase from the current 61% to 73%. The elderly population is highest in the rural areas and is expected to increase over time as they elect to age in place. With the expected population increase of the elderly cancer survivors in the US over the next 20 years and the consequences of them are having a restricted LSM, this area of research is critically significant.

The purpose of my dissertation research is to: 1) Determine the factors that affect LSM in the elderly rural cancer survivor 2) Identify the differences between the factors that affect LSM in the elderly rural and urban cancer survivor.

An analysis of the existing data from the National Institute on Aging (R01-AG15062), UAB Study of Aging (Mobility Among Older African Americans and Whites) will be conducted to answer the research questions. This prospective, observations study of rural and urban dwelling 65-years and older in the Deep South measured LSM and multiple physiological, qualitative, and quantitative variables, including QOL, over a ten year period. The total study population is 8,000 of which 35% are African American.

My area of research interest applies to the priority content area of aging and is cross-cutting over multiple content areas of the ONS 2014-2018 Research Agenda. The knowledge generated through this program of research could inform oncology clinical practice to lessen the loss of function and independence, improve health and QOL, and prevent long-term disability in this population across the cancer survivorship period. The knowledge and resulting invention could be integrated into existing cancer rehabilitation programs, oncology inpatient and outpatient units, skilled nursing facilities, academic educational programs for oncology nursing, interdisciplinary healthcare team members, home health, palliative, and hospice programs.

Grant Profile Information

Tess Thompson, PhD

Analyzing Outcomes for African American Breast Cancer Patients & Caregivers

Washington University, St. Louis
Brown School of Social Work
One Brookings Drive
Campus Box 1196
St. Louis, MO 63130

Grant No. MRS-19-086-01-CPPB
Division: North
Term of Grant: 07/01/2019-06/30/2024
Total Award: \$728,000
Total ACS Support: \$728,000

Area of Research:	Patient Care and Survivorship Issues	100%
Types of Cancer:	Breast Cancer	100%

Project Summary

Researchers and clinicians often think of cancer as a "family affair" because it affects both patients and people close to them. Informal caregivers such as spouses, family members, or friends provide unpaid support to patients. Informal caregivers may help patients with their medical care, for example, or calm their fears. Research has shown that cancer patients and caregivers affect each other's mental and physical health during cancer treatment and survivorship, but most of this research has been done in samples that are primarily White. To support diverse patients and their caregivers, it is important to understand the needs and concerns of African American cancer patients and caregivers. Breast cancer is particularly crucial to study because it is the most commonly diagnosed non-skin cancer among African American women. This research and training plan will develop the career of Dr. Tess Thompson, whose long-term goal is to improve outcomes for diverse breast cancer patients and their caregivers. This plan brings together ideas from disciplines including psychology, medicine, and public health. The proposed mixed methods research has two aims. AIM 1: Describe how caregivers of African American breast cancer patients were involved during patients' treatment and during the survivorship care planning process. Six focus groups will be held with 5-8 caregivers each. Transcripts will be analyzed to examine how caregivers supported patients, whether caregivers were aware of patients' getting a survivorship care plan, whether caregivers know about long-term side effects of cancer, and whether/how caregivers would prefer to be involved in the survivorship care planning process. AIM 2: Conduct a study of 110 pairs of African American breast cancer patients and their informal caregivers from the time of diagnosis through receipt of a survivorship care plan. Patients and caregivers will be interviewed separately three times over the 18 months after diagnosis. Data will be analyzed to determine how mental and physical health are related in patient-caregiver pairs and how patients and caregivers influence each other over time. This information will help clinicians know how best to help patients and caregivers. Dr. Thompson will follow her career and training objectives to learn specialized methods for conducting focus groups and analyzing data from pairs of people over time. She will also build skills in intervention development and deepen her understanding of the clinical context in which cancer patients receive care. Her mentors are experts in these areas and will provide information about research, clinical care, health disparities, and cancer survivorship. This work will launch a program of health disparities research and help Dr. Thompson achieve her goal of promoting health equity by improving outcomes for diverse breast cancer patients and their caregivers.

Grant Profile Information

Susan T. Vadapampil, PhD, MPH, MHSE

Cervical Cancer: PROGRESS for Prevention

H. Lee Moffitt Cancer Center and Research
Institute, Inc
Department of Health Outcomes and Behavior
MFC-CRISP
12902 Magnolia Drive
Tampa, FL 33612

Grant No. RSG-19-011-01-CPHPS
Division: Southeast
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$736,000
Total ACS Support: \$736,000

Area of Research:	Health Services/ Economic and Health Policy Analyses	100%
Types of Cancer:	Cervical Cancer	100%

Project Summary

Organized cervical cancer screening programs have reduced cervical cancer rates by up to 80%. Current guidelines try to reduce unnecessary testing while providing excellent cancer protection. However, they require that providers assess each patient's risk level based on prior history of cervical disease, current medical conditions, and the results of up to three screening tests (cytology or Pap tests, Human Papillomavirus (HPV) testing, and HPV genotyping) to determine the next steps of screening and treatment. Failure to properly apply guidelines may result in over-screening of low-risk women and under-screening of high-risk women, with the potential for significant harm: unnecessary invasive testing in one group and failure to prevent cancer in the other.

Recognizing the need to update existing guidelines, professional organizations have begun planning revisions of cervical cancer screening and abnormal result management guidelines. Guideline revisions will utilize extensive clinical data on the natural history of HPV infection and the evolution of cellular abnormalities, allowing for individualized and precise screening and management protocols. However, these protocols function only to the extent to which they are applied correctly by providers with variable training and expertise. Yet, information regarding provider practices, needs, and preferences related to cervical cancer screening guidelines is scarce.

To fill this gap in knowledge, we propose to examine current practices related to cervical cancer screening, barriers and facilitators of guidelines adoption, and preferences around guidelines, which will then be used to inform planned guideline revision processes. We will survey providers to determine their knowledge of and attitudes toward current guidelines, and will then perform in-depth interviews to assess their opinions on revisions to help plan dissemination at the national level.

As we learn more about the natural history of HPV infection and develop more sophisticated tests and algorithms, we gain the capacity to decrease cancer rates while reducing unnecessary screening and treatment—but only if the content and format guidelines are sufficiently user-friendly to facilitate broad adoption by the majority of providers. The inclusion of rigorously collected provider preferences in guideline revisions is a necessary innovation that should facilitate rapid adoption. To ensure the maximum and immediate impact of this work, study results will be used immediately to inform the multiyear guideline revision process of the American Society of Colposcopy and Cervical Pathology (ASCCP), the guideline organization that creates the most comprehensive and widely used management guidelines. The goal is to facilitate creation of user-friendly guidelines that will improve care, reduce harms, and decrease cervical cancer rates.

Grant Profile Information

Rachel I. Vogel, PhD

Wearable Device Intervention to Improve Sun Behaviors in Melanoma Survivors

University of Minnesota Medical School
Department of Obstetrics, Gynecology and
Women's Health
MMC 395
420 Delaware Street SE
Minneapolis, MN 55455

Grant No. RSG-19-014-01-CPPB
Division: North
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$792,000
Total ACS Support: \$792,000

Area of Research:	Interventions to Prevent Cancer: Personal Behaviors (Non-Dietary) that Affect Cancer Risk	50%
	Patient Care and Survivorship Issues	50%
Types of Cancer:	Melanoma	100%

Project Summary

Over 5 million new cases of skin cancer are diagnosed in the United States each year, more than all other cancers combined. Most of these cases are caused by excess exposure to ultraviolet radiation from the sun and artificial sources such as indoor tanning. Melanoma, approximately 87,000 of the annual skin cancer cases and one of the more deadly skin cancers, is on the rise. Previous research on these individuals suggests that while some change how much time they spend in the sun and adopt ways to protect themselves when in the sun, many do not. In our previous study, we found that 20% of melanoma survivors reported a sunburn in the past year and 10% intentionally went outside for a tan, both strong indicators of inappropriate sun exposure. Melanoma survivors are at high risk of second melanomas, making it critical that they spend less time in the sun or take actions to protect themselves when they are in the sun.

No studies to date have investigated technology-based strategies in melanoma survivors to improve sun exposure and protection behaviors. This project will test whether a wearable device that tracks sun exposure and provides alerts regarding sun exposure and protection behaviors will increase sun protection behaviors in melanoma survivors. The use of wearable technology devices (e.g., Fitbit) has grown quickly over the last decade and studies using these devices to promote physical activity and weight loss have been promising. We will test the technology device versus a similar control device in 248 melanoma survivors and compare sun protection behaviors between the two groups.

This project has the potential to identify a strategy that could significantly lower the number of melanoma survivors who go on to have a second melanoma diagnosis. Importantly, this easy to use technology could also be utilized by survivors' family members, who are also at higher risk for melanoma, and the general population as a means to reduce risk of all forms of skin cancer.

Grant Profile Information

Setu Vora, PhD

Signaling Functions of the Myddosome and Consequences on B cell Lymphoma

Boston Children's Hospital
Department of Cellular and Molecular Medicine
300 Longwood Avenue
Boston, MA 02115
Boston, MA 02115

Grant No. PF-19-034-01-LIB
Division: Northeast
Term of Grant: 07/01/2019-06/30/2022
Total Award: \$163,500
Total ACS Support: \$163,500

Mentor: Hao Wu, PhD

Area of Research:	Normal Functioning	50%
	Endogenous Factors in the Origin and Cause of Cancer	25%
	Technology and/or Marker Evaluation With Respect to Fundamental Parameters of Method	25%
Types of Cancer:	Non-Hodgkin's Lymphoma	100%

Project Summary

Cells gauge their environment to make decisions that are essential to an organism's survival. They can accomplish this task using signal transduction pathways - highly organized communication networks between molecules in the cell - to relay information about the cell's environment and ultimately trigger a response. Signal transduction processes are disrupted in all cancers. Some signal transduction pathways depend on the ability of molecules to arrange themselves into large assemblies to transmit information throughout the cell. Disruption of these enigmatic "higher-order" assemblies is likely to contribute to cancer yet we know virtually nothing about them. A barrier to our understanding of higher-order assemblies is that we have no way of measuring them in cells. Our research seeks to develop an experimental and analytical framework for labeling higher-order assemblies on a cell by cell basis. Specifically, we are interested in an assembly called the Myddosome, an assembly that forms when cells encounter certain pathogens and triggers an immune response. Mutations in Myddosome components are commonly recurrent in various lymphomas and are thought to promote survival of malignant B cells. We hypothesize that Myddosome assembly functions as an all-or-none binary switch that prohibits cellular response to pathogen signals below a threshold and that its formation is thus uniform among lymphoma cell populations with mutated Myddosome components. We will visualize Myddosome assembly in single to determine if its assembly is switch-like and characterize its uniformity in lymphoma populations. This study will allow us to investigate Myddosome formation in various lymphomas and determine how they process and relay information throughout the cell to initiate cellular responses necessary for malignant cell survival.

Grant Profile Information

Daniel R. Wahl, MD, PhD

Targeting De Novo Nucleotide Synthesis to Overcome Radioresistance in GBM

University of Michigan
Department of Radiation Oncology
1500 E. Medical Center Drive
Ann Arbor, MI 48109

Grant No. CSDG-19-077-01-TBG
Division: North Central
Term of Grant: 07/01/2019-06/30/2024
Total Award: \$729,000
Total ACS Support: \$729,000

Area of Research:	Systemic Therapies - Discovery and Development	20%
	Combinations of Localized and Systemic Therapies	80%
Types of Cancer:	Brain Tumor	100%

Project Summary

Glioblastoma (GBM) is the most common brain tumor in adults and is nearly universally fatal within five years of diagnosis. Despite aggressive treatment with surgery, radiation and chemotherapy, nearly all GBMs recur locally (e.g., within the region of the brain that was irradiated), which suggests that poor clinical outcomes may be due to the intrinsic radioresistance of GBM. Like many cancers, GBMs rewire cellular metabolism to utilize nutrients at high rates, which allows them to proliferate and invade nearby tissues. Our group believes that these metabolic adaptations also make GBMs resistant to radiation. To test this hypothesis, we comprehensively analyzed the metabolomic profile of more than 20 laboratory models of GBM to determine which metabolites are most associated with radiation resistance. We found that GBMs able to maintain high levels of free purines and pyrimidines (the building blocks of DNA) are most resistant to radiation, presumably because high levels of these metabolites allow GBMs to repair radiation-induced DNA damage.

In this project, we now ask how radiation interacts with the pathways used to make purines and pyrimidines and whether inhibiting these pathways can overcome GBM radioresistance. Drugs that inhibit the ability of cells to make purines or pyrimidines from scratch are currently used in patients to treat viruses and autoimmune diseases, but have not been used in combination with radiation or to treat patients with GBM. We will now combine these drugs with radiation in patient-derived models of GBM in vitro and in vivo to determine if they make radiation treatment more effective. Because most cancers make purines and pyrimidines from scratch, while normal tissues such as the brain re-use existing purines and pyrimidines, we believe that these drugs will selectively target GBMs while sparing normal brain. Enhancing the effectiveness of radiation by inhibiting purine and pyrimidine synthesis may also be effective in other cancers characterized by radioresistance such as pancreatic cancer.

Grant Profile Information

Lauren P. Wallner, PhD, MPH

Disparities in the Delivery and Quality of Breast Cancer Survivorship Care

University of Michigan
Department of Internal Medicine
3003 S. State Street
Ann Arbor, MI 48109-1274

Grant No. RSG-19-015-01-CPPB
Division: North Central
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$1,203,000
Total ACS Support: \$1,203,000

Area of Research:	Patient Care and Survivorship Issues	50%
	Health Services/ Economic and Health Policy Analyses	50%
Types of Cancer:	Breast Cancer	100%

Project Summary

Early-stage, favorable prognosis breast cancer is now a survivable condition for many women, as a result of advances in early-detection and curative therapies. However, providing high-quality, comprehensive survivorship care long term remains significantly challenging. In addition, notable socioeconomic disparities in both the morbidity and mortality related to breast cancer exist. Addressing the complex needs of aging breast cancer patients, both those resulting from their cancer and those related to aging, requires the involvement of multiple providers over time, which makes coordination of their care difficult. As a result, many survivors are not getting the comprehensive survivorship care they need. In response to these challenges and a growing workforce shortages that makes an oncology dominant model of survivorship care no longer sustainable, the National Academy of Medicine recommends that oncologists work together with primary care providers (PCP) to deliver shared cancer care. However, implementing this shared care approach has been difficult in practice. This is due to our limited understanding about how survivorship care is delivered in community-practice settings today and whether disparities in the delivery and quality of survivorship care exist among women vulnerable to poor outcomes. Therefore, we will conduct a follow-up survey study in year 5 of survivorship of a population-based sample of 2502 women who were diagnosed in 2014-15 with early-stage breast cancer in Los Angeles County and Georgia. Using the unique data collected during initial treatment, we will first characterize provider roles in the delivery of survivorship care among vulnerable populations and identify whether disparities exist in how involved PCPs are in survivorship care. We will then examine sociodemographic disparities in the quality and coordination of breast cancer survivorship. Finally, we will assess whether more PCP involvement in survivorship care improves the quality and coordination of breast cancer survivorship care, particularly among vulnerable populations. We hypothesize that oncologists will dominate the delivery of survivorship care for most women. We also hypothesize that significant disparities will exist in PCP involvement in survivorship care, as well as the coordination and quality of survivorship care across race, ethnicity, acculturation, education, age, and literacy level. However, we expect that these disparities will be mitigated among women with more PCP involvement in their survivorship care. Findings from this study will directly inform future cancer care delivery strategies, address how survivorship care delivery patterns impact the quality of survivorship care, identify important disparities in the delivery and quality of survivorship care, and guide the development of interventions to improve survivorship care.

Grant Profile Information

Chao Wang, PhD

Define Predictive Biomarkers for ATR Inhibitors

University of Texas M.D. Anderson Cancer
Center
Department of Experimental Radiation
Oncology
6565 MD Anderson Boulevard
Houston, TX 77030

Grant No. PF-19-028-01-DMC
Division: South
Term of Grant: 07/01/2019-06/30/2020
Total Award: \$57,500
Total ACS Support: \$57,500

Mentor: Junjie Chen, PhD

Area of Research:	Endogenous Factors in the Origin and Cause of Cancer	30%		
	Technology Development and/or Marker Discovery	70%		
Types of Cancer:	Blood Cancer	20%	Lung Cancer	20%
	Breast Cancer	20%	Prostate Cancer	40%

Project Summary

Targeting ATR for cancer therapy is a promising but needs reliable biomarkers. To guide the clinical usage of ATRi, it is important to develop a comprehensive catalogue of synthetic essential genetic contexts with ATRi. We have already started functional screens to identify these coessential genetic contexts in 293A cells. In this proposal, we will perform similar functional screens in several different cell lines to obtain a profile of “core co-essentiality genes”, which are likely the best biomarkers for directing ATRi based therapies. With our further validation of these candidate genes and the use of public resources such as TCGA database, we anticipate that these studies will define the genetic contexts where single agent ATRi would be most effective and use this knowledge to direct ATRi-based clinical trials.

Grant Profile Information

Siobhan Whalen, MSW

Master's Training Grant in Clinical Oncology Social Work

University of Washington
Department of Social Work and Care
Coordination
1959 NE Pacific Street
Seattle, WA 98195

Grant No. MSW-19-067-05-SW
Division: West
Term of Grant: 07/01/2019-06/30/2021
Total Award: \$24,000
Total ACS Support: \$72,000

Project Summary

The MSW student training program at the University of Washington Medical Center (UWMC) Social Work and Care Coordination Department is aimed at teaching a 2nd year master's level social work student to provide clinical social work services and care coordination to adult patients with cancer and to provide psychosocial support to their families. The emphasis is on clinical provision of services and teaching the trainee about the psychosocial impact of cancer along the continuum of care from initial diagnosis, through complex medical treatment planning, navigating cancer resource and support options, and progressing on with survivorship or to transition towards end of life care, while realizing cancer affects the whole family system.

Trainees are taught to understand medical terminology, the cancer treatment process, do psychosocial assessments, help patients identify coping strategies and aide them in formulating new ones. Trainees are taught to recognize changes in a patient's definition of normalcy, daily personal functioning and coping, identify the resiliency of the family caregivers, and how to interact as a professional providing education on an interdisciplinary team. Trainees will develop the clinical skills to assess patient and caregivers, identify areas for strengthening the family system, provide supportive counseling and education, advocate on the patient's behalf, enhance cultural preferences and diversity norms within medical systems, and facilitate communication with teams regarding psychosocial or post-discharge care needs.

Trainees will increase their knowledge of local community, state and national resources available to support patients, and identify the areas where services are poorly funded or non-existing. Our trainee will have experience working with a national and internationally known inpatient transplant program through the Seattle Cancer Care Alliance (SCCA) and to have the opportunity to collaborate with professionals in their general oncology programs as well. Trainees will learn to assess, educate, advocate, counsel, support and implement options to build working relationships to enhance the patient/caregiver experience during hospitalization, then transition care to outpatient support networks and resources. The expanse of patient diagnoses will be broad and include rare cancers like Sarcoma and Merkel cell, which have fewer resources available for patients. The trainee will learn how a patient's experience is impacted through national and institutional policies affecting resources and access to care. The UWMC Social Work and Care Coordination Department has a wealth of experience to share with a trainee and the multidisciplinary oncology team offers numerous opportunities for collaboration and for expanding their knowledge and perspectives. Through this experience, the trainees will enhance their development as a social worker in medical oncology care and have opportunities for personal and professional growth.

Grant Profile Information

Richard M. White, MD, PhD

The Role of Adipocytes in Melanoma Progression

Memorial Sloan-Kettering Cancer Center
Department of Medicine
1275 York Avenue
New York, NY 10065

Grant No. RSG-19-024-01-DDC
Division: Northeast
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$792,000
Total ACS Support: \$792,000

Area of Research:	Cancer Progression and Metastasis	70%
	Systemic Therapies - Discovery and Development	30%
Types of Cancer:	Melanoma	100%

Project Summary

It is increasingly clear that cancer cells do not exist in a vacuum – they are surrounded by numerous other cell types in the body that exert dominant effects on their behavior. Collectively, all of the cells surrounding the cancer cells are called the tumor microenvironment, and it is composed of a vast number of cell types, including immune cells, fibroblasts, epithelial cells, neurons and many others. The most compelling evidence for the importance of the tumor microenvironment is the dramatic success of immunotherapy in melanoma – therapeutically targeting the interaction between tumor cells and T cells leads to remarkable efficacy in some patients. Outside of the immune system, relatively less attention has been paid to the large number of other cell types in the tumor microenvironment, and we feel that many of these other cell types would make excellent therapeutic targets. To address this question, my laboratory has developed an unusual model for studying melanoma – the zebrafish. Although not a typical model for cancer, the zebrafish is transparent, offering the unique capacity to visualize cancer from the moment the tumor begins all the way through to metastatic disease. In addition, the zebrafish allows us to study tumor-microenvironment interactions in an unbiased manner, without a priori suppositions on which interactions are most important. Using this model, we have uncovered an unexpected interaction between melanoma cells and the fat cells that are normally present beneath the skin. These fat cells, also called adipocytes, completely encase advanced melanomas, yet their role in melanoma is completely unexplored. In our preliminary data, we have shown that these adipocytes strongly promote melanoma cell growth and invasion, making the tumor cells more metastatic. They do this by directly transferring fat droplets into the melanoma cells, and we have identified a specific protein that mediates this fat transfer. Most importantly, we found a chemical that can completely block the transfer of fat from the adipocyte to the melanoma cell, and this chemical almost completely blocks growth of the tumors. In this grant, we wish to fully explore how these microenvironmental adipocytes interact with the melanoma cells, using both our zebrafish models but also human tissue specimens. We want to determine whether the chemical we discovered has the potential as a new therapeutic target in melanoma, and in which patients it is likely to be most useful. We believe this proposal takes advantage of a novel system for studying melanoma, and will lead to clinically meaningful insights that can be used to target a new member of the tumor microenvironment.

Grant Profile Information

Luke Wilkins, MD

Preclinical Transarterial Embolization for Hepatocellular Carcinoma

The Rector and Visitors of the University of
Virginia
Department of Radiology and Medical Imaging
Box 800170
1215 Lee Street
Charlottesville, VA 22908

Grant No. RSG-19-008-01-CDD
Division: Southeast
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$792,000
Total ACS Support: \$792,000

Area of Research:	Localized Therapies - Discovery and Development	100%
Types of Cancer:	Liver Cancer	100%

Project Summary

Hepatocellular carcinoma (HCC) is one of the most common causes of cancer deaths worldwide. Due to increasing obesity rates and increasing rates of hepatitis B and C, HCC is increasing in incidence. Most HCC patients are ineligible for liver transplant or surgery and require some other therapeutic treatment. When the blood supply to the tumor is occluded this creates low levels of oxygen (hypoxia) within the tumor that are, in theory, lethal for the tumor cells. However, this is not the case as the treatment is not considered curative and there are high rates of residual untreated tumor and tumor recurrence. A small minority of patients experience a complete response to treatment and only few patients become eligible for a curative liver transplant. A major improvement in TACE is needed to improve catheter-based treatments for HCC.

We theorize that cells of HCC survive embolization through both changing their method of metabolism and achieving inadequate levels of hypoxia. There is prior research showing that a majority of HCC cells may survive embolization by employing glycolytic metabolism. Glycolytic metabolism can function without the need for oxygen. Our recently published results show that a natural compound called caffeic acid (CA) is lethal to cellular functions that are active in both hypoxic and normoxic cellular environments. When combined with small particles (embolization) it causes extensive tumor regression. We hypothesize that this enhanced effect to embolization is because the two treatments are synergistic and affect both methods of metabolism in the HCC cell.

The objective of this project is to test if small particles loaded with caffeic acid will perform better than small particles alone in treating tumors in a large animal model (*Marmota monax*, woodchuck) of HCC. The woodchuck tumors develop spontaneously in diseased liver and are the closest analog to human HCC. They will be treated using the exact methods as done in current clinical practice. Improvements in catheter-based treatment for HCC will transform clinical practice as more patients will be cured through embolization or have improved chances at survival to curative liver transplant. The proposed research is innovative because we utilize a novel agent and delivery system that is synergistic with the hypoxic environment created by occluding the tumor blood flow. The woodchuck model is the closest analog to human HCC and an accurate model of embolization. This will allow for effective translation into a clinical trial.

Grant Profile Information

Christopher Woodrell, MD

Palliative Care for People with Hepatocellular Carcinoma

Icahn School of Medicine at Mount Sinai
Department of Geriatrics and Palliative
Medicine
One Gustave L. Levy Place
Box 1070
New York, NY 10029

Grant No. MRSB-19-040-01-PCSM
Division: Northeast
Term of Grant: 07/01/2019-06/30/2024
Total Award: \$728,000
Total ACS Support: \$728,000

Area of Research:	Patient Care and Survivorship Issues	100%
Types of Cancer:	Liver Cancer	100%

Project Summary

Liver cancer often develops as a complication of cirrhosis, or scarring of the liver caused by chronic liver disease. Liver cancer has a rapidly rising incidence in the United States because of the Hepatitis C Virus and obesity epidemics. Hepatocellular carcinoma, or HCC, is by far the most common type of cancer that originates in the liver. HCC is difficult to cure and very distressing for both patients and families. Palliative care provides specialized, interdisciplinary care which focuses on maximizing quality of life for people living with a serious illness, and may offer a beneficial approach for people with liver cancer. In other types of cancer, we know that palliative care improves quality of life, provides symptom relief, reduces the amount of time spent in the hospital, and in some cases, helps people live longer. However, little is known about the palliative care currently received by people with liver cancer, or how we can provide targeted palliative care that meets their specific needs. HCC is different from other cancers because it almost always occurs in people who are also living with cirrhosis. This results in uniquely burdensome symptoms, a more complex treatment plan, and added uncertainty about the future. Our preliminary work shows that people with liver cancer receive palliative care very late in the course of their illness, often only during the days before their death. The focus of this research is to learn more about the challenges faced by people with HCC throughout their illness; to explore how they might benefit from palliative care; and finally, to develop a palliative care intervention specifically tailored to their needs.

This study will have three parts. First, we will interview clinicians who provide HCC care to learn about their perspectives on their patients' needs, and also their opinion of palliative care. In the second part of the study, we will interview people with HCC who are not eligible for curative therapies to learn about their experience navigating the complex treatments of liver cancer, and how we can address their care needs as they live with HCC. Finally, we will use what we learn in the first two parts of the study to develop an innovative outpatient palliative care program for people with HCC in order to show that delivering palliative care earlier, and in the same medical practice where they receive their cancer care, is feasible. We will collect information about the experience of participants throughout the single-site study, and use the results to design a future study across multiple hospital systems to demonstrate how to best integrate palliative care into routine care for all people living with liver cancer.

Grant Profile Information

Andy Yuan, PhD

Reconstituting Heterochromatin and Gene Silencing in Vivo

Harvard Medical School
Department of Cell Biology
LHRRB 520
240 Longwood Avenue
Boston, MA 02115

Grant No. PF-19-091-01-DMC
Division: Northeast
Term of Grant: 07/01/2019-06/30/2020
Total Award: \$57,500
Total ACS Support: \$57,500

Mentor: Danesh Moazed, PhD

Area of Research:	Normal Functioning	25%
	Cancer Initiation: Alterations in Chromosomes	75%
Types of Cancer:	Not Site-Specific Cancer	100%

Project Summary

All cells in the human body contain the same DNA-encoded genetic information yet acquire unique identities and specialized functions during development from a single fertilized egg. Cancers are characterized by the loss of cell identity, which can manifest itself as uncontrolled cell proliferation. The specification of cell identity largely depends on which genes are turned ON or OFF in any given cell-type. Genes are packaged in chromatin, which consists of DNA wrapped around proteins known as histones. Chemical modifications to histones and chromatin-associated proteins can mark genes to be turned OFF without changing their DNA sequence. What exactly constitutes a mark, and how does such a mark turn a gene OFF? These fundamental questions remain unanswered. The proposed study aims to turn a gene OFF in yeast cells using histone modifications and chromatin-associated factors derived from or closely related to those found in human cells. This research plan will distill core principles underlying the establishment and maintenance of cell identity and thereby deepen our understanding of the causes and consequences of cancer. Such foundational knowledge will inform the design of new cancer detection and treatment strategies. Furthermore, this work has the potential to facilitate the discovery of new therapeutic drugs targeting specific chromatin-associated factors that play important roles in cancer biology. As histone modifications are reversible, these drugs may succeed in halting cancer progression by restoring cell identity.

Grant Profile Information

Vivian Zadkovich, MSW

Master's Training Grant in Clinical Oncology Social Work

Boca Raton Regional Hospital, Inc.
Department of Psychosocial Services
701 Northwest 13th Street
Boca Raton, FL 33486

Grant No. MSW-19-071-07-SW
Division: Southeast
Term of Grant: 07/01/2019-06/30/2021
Total Award: \$24,000
Total ACS Support: \$96,000

Project Summary

The Eugene and Christine E. Lynn Cancer Institute is accredited as a Comprehensive Cancer Center by the American College of Surgeons. Embarking on an internship within an oncology specialty at the Lynn Cancer Institute, an MSW student intern has a unique opportunity to gain an understanding of the intricacies of cancer care; from the initial cancer diagnosis, treatment options available and a myriad of settings where patients receive their diagnostic, medical, and psychosocial care.

As a comprehensive cancer center, the Lynn Cancer Institute at Boca Raton Regional Hospital offers a holistic approach by combining the best medical treatment, sound healthy habits and appropriate psychosocial support, and a broad range of cancer support services delivered free of charge by licensed professional oncology social workers. Within the Psychosocial Services department, the continuity of care begins with initial psychosocial assessments for patients who are newly diagnosed and participate in Multimodality Clinics and/or when beginning outpatient radiation therapy at 1 of 2 locations. Oncology social workers are also available to patients in the Medical Oncology department, a practice of over 14 Medical Oncologists and their staff, where patients are seen during their chemotherapy treatments.

The Lynn Cancer Institute offers a student intern the opportunity to work 1-on-1 with cancer patients and their families; facilitate support groups; participate in community events; connect patients and their families to concrete resources; refer patients to various wellness programs, complementary and expressive arts therapies, nutrition education, and community resources. This diverse and comprehensive internship would benefit immensely from the Master's Training Grant in Clinical Oncology Social Work, providing the student with funds in the amount of \$10,000.00 to assist with tuition, living expenses, and/or professional organization membership and conference participation, e.g., the Association of Oncology Social Work, while immersed in an educational program that will prepare the Master's level student for a professional position in Oncology Social Work and a deep understanding of oncology care. Within this setting, the student intern has access to a team of Oncology Social Workers who possess a broad range of experiences ranging from clinical; professional; both within the healthcare field and a variety of other professional settings, program development expertise, fundraising, and administrative/management experience. The remaining \$2,000.00 would be placed into a general education fund for the social work team to access, to pay for oncology related training to enhance the practice of the social workers at the Lynn Cancer Institute.

Grant Profile Information

Baochun Zhang, MD, PhD

A Novel Cytotoxic CD4+ T cell Approach for Treating B cell Malignancies -R1

Dana-Farber Cancer Institute
Department of Medical Oncology; Cancer
Immunology and Virology
450 Brookline Avenue
Boston, MA 02215

Grant No. RSG-19-035-01-LIB
Division: Northeast
Term of Grant: 07/01/2019-06/30/2023
Total Award: \$792,000
Total ACS Support: \$792,000

Area of Research:	Systemic Therapies - Discovery and Development	100%		
Types of Cancer:	Hodgkin's Disease	25%	Non-Hodgkin's Lymphoma	25%
	Leukemia / Leukaemia	25%	Primary CNS Lymphoma	25%

Project Summary

B cell malignancies – cancers arising from blood B cells – comprise a large number of different types of lymphomas and leukemia, which collectively represent the sixth leading cause of cancer death in the US. New treatments, including various immunotherapy approaches, are under active development and testing. These immunotherapy approaches predominantly utilize immune system's CD8+ T cells to identify and kill cancer cells, but they are effective only in a fraction of B cell malignancies. The cancerous B cells are potential targets of the immune system's CD4+ T cells, however, the latter normally lack the ability to kill such cancer cells. In this project, we develop a novel approach to rapidly produce CD4+ T cells capable of killing cancerous B cells; we will test the produced CD4+ T cells for treating B cell malignancies in preclinical animal models, and then prepare this approach towards clinical trials in patients with B cell leukemia. Once fully developed, this CD4+ killer T cell-based immunotherapy can be similarly applied to other B cell malignancies. In addition, the mechanistic insights derived from this work will guide development of CD4+ killer T cell-mediated immunotherapies for other cancers.