



Bankhead-Coley Cancer Research Grants

Principal Investigator	Principal Investigator's Organization	Project Title	General Project Abstract
Alan Pollack	University of Miami	Integrated Biomarker Profiling for Individualized Prostate Cancer Therapy	<p>Men who are diagnosed with prostate cancer face difficult decisions revolving around when and how to be treated. Current methods for determining a patient's need for treatment and the aggressiveness of the treatment needed remain problematic. We propose to better define key decision points in men who have different stages of the disease by investigating biomarkers from tissue and blood. Clinical trials have been designed to address key questions and gain insight into the potential applications of biomarkers when considered across patient groups. To our knowledge this approach has not been used previously and the technologies we will use to obtain and analyze prostate tissue and blood cancer cells are unique. The clinical trials will involve men with distinct options who 1) have early prostate cancer are candidates for no treatment (active surveillance), 2) have intermediate to high risk localized prostate cancer and are candidates for radiotherapy, 3) have experienced a rising PSA after surgical removal of the prostate and are candidates to receive salvage radiotherapy to the surgical area, and 4) have had spread of the cancer and have become resistant to hormone and chemotherapy. The projects are highly integrated and novel because of the application of new imaging technology to better direct prostate biopsies and analyze blood products, and the plan to investigate this in patients that have different stages of prostate cancer.</p>



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Maria Zajac-Kaye	University of Florida	Design, Synthesis and Evaluation of Novel Selective Inhibitors of FAK and IGF-1R Function in Pancreatic Cancer	<p>Pancreatic cancer (PC) is a leading cause of cancer death in the U.S and there is no effective therapy. Human cancer cells grow and survive due to the overabundance of focal adhesion kinase (FAK) and insulin-like growth factor receptor-1 (IGF-1R). FAK interacts with IGF-1R, which contributes to the malignant behavior of PC. Our data shows that inhibition of both FAK and IGF-1R increases PC death compared to inhibition of either protein alone. Scientists are evaluating many drugs that inhibit the enzyme function of FAK or IGF-1R. However, these drugs are not very specific or effective resulting in increased side effects and little ability to prevent PC growth. Recently, the approach of inhibiting direct protein interactions rather than enzyme function has been shown to be effective. Our hypothesis is that the protein interaction of FAK with IGF-1R is favorable for PC and promotes PC growth and survival. Our studies will identify novel compounds that will prevent the protein interaction of FAK and IGF-1R. These compounds will have widespread effects by inhibiting the cellular processes that FAK and IGF-1R control including cell growth and survival. In addition, this effect will be specific for FAK and IGF-1R with minimal inhibition of other molecules, therefore, decreasing potential side effects of these compounds. Targeting FAK and IGF-1R protein interactions in PC will allow for the development of more specific and effective treatments for patients with this deadly disease.</p>
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Tuya Pal	Moffitt Cancer Center & Research Institute	Inherited Cancer Registry (I CARE) Initiative	<p>The discovery of the BRCA genes almost 15 years ago, allows us to identify people who have changes in these genes. A woman with a gene change has a high chance to develop breast and ovarian cancer. Yet, it is still difficult to spot people with these changes due to the small number of medical experts familiar with the BRCA genes. As such, many practitioners and patients in the community are not aware of these genes. Roughly 5% of all people with BRCA gene change know that they carry this change. In Florida, we have the second highest number of new cancer cases and very few experts in the topic of Clinical Cancer Genetics. Because of this, many practitioners and patients are less aware about the topic of BRCA mutations, which could possibly lead to misinformed healthcare decisions. We propose to boost access of information about BRCA gene changes to healthcare providers and patients, through using an existing network of community practitioners (called the 'Moffitt Affiliate Network' (MAN)). This would allow MAN practitioners to reach to Moffitt-based experts for information on subjects related to how to identify and manage those with BRCA changes. Patients with BRCA changes from MAN sites would also be able to join our Inherited Cancer Registry (ICARE). This registry would carry out research on those with BRCA gene changes to develop better care options for them. The eventual goal of our efforts is to improve the care given to those with BRCA gene changes in Florida.</p>
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Tuya Pal	Moffitt Cancer Center & Research Institute	Black Women: Etiology and Survival of Triple-negative Breast Cancers (BEST) Study	<p>Young Black women get breast cancer less often than White women, but are more likely to die from it. This may be caused by a type of aggressive breast cancer called 'triple negative' (TN) disease, which is more common in Black women. We plan to study why young Black women get the more serious type of TN breast cancers. We will recruit 600 Black women diagnosed with breast cancer at or below age 50, through the Florida State Cancer Registry. Based on our earlier study in similar women, we believe we can accomplish our goals. We will collect information about each of the 600 participants through a detailed questionnaire, medical records review, and genetic testing. The participants will also be followed every 2 years for the duration of the study to track how they do. Our study would provide no cost genetic counseling and testing for the participants in this study.</p> <p>The test results could allow the study participants and their families to make important decisions about their healthcare. The researchers working on this study include Black community members. They help us make sure our research is relevant, the recruitment and study procedures are conducted in a sensitive manner, and help share important study findings with the Black community. Through our study, we hope to better understand why young Black women get TN breast cancers and why they die from the disease more often. Ultimately, we need this information to lower the number of TN breast cancers in these women.</p>
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Radka Stoyanova	University of Miami	Metabolic Tumor Volumes in Radiation Treatment of Brain Tumors	<p>Proton Magnetic Resonance Spectroscopy (MRS) can be used as a non-invasive tool for accurate delineation of tumor and healthy tissue in Radiation Therapy (RT) of patients with brain cancer. Currently, Magnetic Resonance Imaging (MRI) and Computerized Tomography (CT) are used to determine the treatment volumes for radiation dose distribution. Often MRI and CT are ambiguous with regard to tumor volume and tissue viability, while MRS can provide the exact position and extent of tumor infiltration; define the tumor margin and potentially identify the areas of microscopic disease. The University of Miami (UM) has a unique infrastructure for brain imaging – a high magnetic field MRI instrument and sophisticated acquisition and analysis methods which allow for detailed volumetric metabolite data over the entire brain. In this grant we propose to utilize these invaluable resources and apply MRS for brain tumor patient management.</p> <p>The goal is to provide the radiation oncologists with detailed maps of tumor-involved areas. The aberrant distribution of the metabolites will be detected in comparison with a database of information from healthy controls. UM is in the unique position to evaluate the role of MRS in reshaping treatment areas. A potential outcome of the proposed study will be a more precise radiation dose delivery to the malignant tissue, thus improving treatment efficacy. In addition, by minimizing the involvement of normal brain, the treatment will also reduce morbidity.</p>
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Sarah McLaughlin	Mayo Clinic	Enhancing the Ability to Predict Lymphedema Development Following Axillary Surgery for Breast Cancer and its Effects on Patient Survivorship	<p>Issues affecting breast cancer survivorship are of increasing importance as the number of women living years after breast cancer treatment grows. Following surgery for breast cancer, women worry about their risk of developing lymphedema (LE), an unpredictable, chronic arm swelling that can have a significant and debilitating impact on their lives. Indeed, many women experience considerable anxiety due to our current inability to accurately predict or modify their risk of LE. This anxiety negatively impacts their health and overall quality of life (QOL). Thus, our aims in this proposal are to (1) identify baseline tissue characteristics potentially predisposing women to LE, (2) identify markers and genetic risk factors that might be altered to prevent LE, and (3) prospectively document the time course to LE development and associated changes in QOL. This prospectively designed study includes analysis of collected biospecimens and QOL metrics at baseline and over 5 years follow up. The long term goal rests on the development of predictive tools that can help accurately predict LE, guide postoperative surveillance protocols, and more accurately pinpoint high-risk patients who might benefit from aggressive risk reduction strategies. Clinical application of these findings will help to improve research and treatment of LE after breast cancer through better risk stratification of patients for future clinical trial development related to the prevention and treatment of LE.</p>
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Olveen Carrasquillo	University of Miami	South Florida Center for the Elimination of Colorectal Cancer Health Disparities (SUCCESS-CRC)	<p>Our research team has previously shown that Hispanics and Haitians in Florida suffer a disproportionate burden of colorectal cancer. Therefore, and based on feedback from our community advisory groups, we propose to extend the work of our cancer health disparities center to now also address colorectal cancer among Hispanics and Haitians in Florida. In this Team Science Project, we will tackle this major public health problem through a series of three highly innovative studies. Our first project will develop better population based methods to track and describe the epidemiology of colorectal cancer among minority communities. This data is critical if we are to develop targeted preventive interventions. Second we propose to begin to test the feasibility and acceptability of more novel methods of colorectal cancer screening in some of the most vulnerable Hispanic and Haitian communities in Florida. Last, beyond screening, unique insights are also needed into the tumor biology of colorectal cancer among these vulnerable groups. This would allow for more personalized interventions. Our grant also includes a centralized core that will provide scientific oversight, research support and a mechanism for community input for all three projects. This TSP will also be critical in helping us secure additional federal support to continue our ongoing work in cancer health disparities.</p>
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Kevin Brown	University of Florida	Epigenetic Basis of Neoplastic Progression in Human Cancers	<p>Cancer arises and progresses due to alterations within DNA stemming from both changes in DNA sequence (genetic alterations) and DNA structure (epigenetic alterations). This Bankhead-Coley Team Science Project, an inter-institutional effort between investigators at the University of Florida and the Moffitt Cancer Center, is focused on understanding how epigenetic alterations impact the process of colorectal and cervical cancer progression and if these alterations can be used as markers to predict disease behavior. Project 1 focuses on discovering epigenetic events useful in the identification of women at risk of developing more aggressive forms of cervical cancer. This will be done using state-of-the-art molecular methodologies to measure DNA methylation at various stages of cervical cancer progression coupled with rigorous epidemiological analyses. Project 2 is focused on using an innovative technology developed by our group that examines DNA structure at the molecular level and will be used to study changes in DNA structure during colorectal tumor progression. Project 3 focuses on CTCF, a known epigenetic modulator, and how this molecule controls blood vessel development during colorectal cancer progression. This set of overlapping research projects will provide us with needed knowledge on how epigenetics impacts cancer progression, and has strong potential to discover molecular events that can be used clinically to predict tumor behavior at early disease stages.</p>
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Lori Hazlehurst	Moffitt Cancer Center & Research Institute	Targeting the Tumor Microenvironment in Multiple Myeloma	<p>Multiple myeloma (MM) often responds well to standard therapy initially. However, drug resistance inevitably emerges, and all patients eventually die of recurrent disease that is resistant to available treatments. Therefore, identification and validation of novel therapeutic strategies and understanding the evolutionary dynamics of resistance are essential for improving the clinical outcome of patients with MM. In this grant, our group, composed of investigators with expertise in biology of myeloma, mathematical modeling, clinical investigations, pharmacology, and chemistry, will use diverse hypothesis-driven strategies to target MM cells residing in the bone marrow. Our grant consists of 5 projects: Project 1 will focus on pre-clinical development of c-HYD1, a cyclized peptide targeting VLA-4-CD44 containing complexes; Project 2 will test novel CRM1 inhibitors for increasing the efficacy of topoisomerase II inhibitors; Project 3 is based on an interesting observation that Notch inhibitors are devoid of activity in vitro yet have significant anti-MM activity using in vivo models; Project 4 will examine the role of the FA pathway in mediating de novo and acquired resistance using a co-culture model system; and Project 5 will develop evolutionary based models for testing strategies for combining therapeutic agents for maintenance of minimal residual disease.</p>
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David Reisman	University of Florida	Validate BRM polymorphism as a Biomarker for lung cancer risk	<p>Our success in treating cancers has been hampered because many cancers are not detected until the cancer is very advanced and thus incurable. Early-stage lung cancer can be cured with surgery, and CT scanning is an effective radiological method to detect cancers early. But CT scanning is an expensive, so determining who will benefit from such monitoring remains a challenge. While smoking is the primary risk factor for lung cancer, only 10 percent of smokers develop lung cancer; thus, screening all smokers is cost-prohibitive. Further, many people who do not smoke develop lung cancer. The purpose of this research is to develop a test that could predict which patients are at greatest genetic risk for developing lung cancer and would thus benefit from CT scans and from lifestyle modifications. We have found that an anticancer gene called Brahma (BRM) frequently stops functioning in those who develop lung cancer. This gene has alterations called polymorphisms that appear to be correlated with lung cancer risk. We will analyze blood samples, health history, and other information from healthy volunteers and from lung cancer patients to see if there is a difference in whether the BRM gene polymorphism is present. This work will determine whether it is feasible to develop BRM as a new biomarker test to predict lung cancer risk, a test that could make it practical and cost-effective to use CT scans and other methods to follow those at high risk for developing tobacco-related cancers.</p>
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Jianfeng Cai	University of South Florida	Design, synthesis, and evaluation of gamma-AApeptide-based protein tyrosine phosphatase inhibitors as novel anticancer agents	<p>Abnormal tyrosine phosphorylation is a frequent cause of human cancer and oncogene addiction required for the malignant state. Accumulating evidence suggest that some of protein tyrosine phosphatases (PTPs) are novel targets for developing anticancer drugs. The long-term objective of this project is to develop novel gamma-AApeptide-based compounds as inhibitors of specific PTPs that are targets for anticancer therapy. Building upon this initial success, the goal of the proposed research is to further develop gamma-AApeptide based PTP inhibitors focusing on Shp2 as the primary target. To achieve the goal, we have the following specific aims: 1. Design and synthesize novel gamma-AApeptides bearing phosphonate functionalities as potential PTP inhibitors. 2. Design and synthesize novel gamma-AApeptides bearing sulfonate functionalities as potential PTP inhibitors. 3. Determine the potency and selectivity of gamma-AApeptides for inhibition of protein tyrosine phosphatases in vitro and test potent and selective Shp2 inhibitors in cellular assays. The proposed project will lead to a new class of Shp2 inhibitors as novel anti-cancer therapeutics for cancer prevention, diagnosis, treatment and/or cure.</p>
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Alicja Copik	University of Central Florida	Generation of highly cytotoxic natural killer cells for cellular therapy of cancers using novel microparticle approach	<p>Stem cell transplantation (SCT) is the current core treatment for many types of blood cancers, including most types of leukemia. Unfortunately, challenges such as the lack of suitable donors for ethnically diverse patients, cancer relapse, and graft-versus-host disease limits their application and success. More than 70% of patients who could benefit from stem cell transplant do not have a matched sibling donor and the chances of finding a matched unrelated donor strongly correlates with ethnic background.</p> <p>Therefore, there is a great need for new and innovative approaches to enhance current therapies or to provide a completely different alternative to SCTs. The goal of this study is to establish a new cell therapy for AML using a type of immune cell called a natural killer (NK) cell. These NK cells will be generated by several different approaches to determine which approach yields a more potent anti-tumor product. Furthermore, a specific type of drug that may enhance the anti-tumor effect of these generated cells will be tested. Tumor cells will also be analyzed to determine how they are able to evade the immune system. In the end, this study is expected to lay foundations for a follow-up Phase-I/II clinical trial of an NK cell-based therapy for blood cancer patients at our institution. This therapy would provide a treatment alternative to disparate groups such as ethnic minorities who do not have a matched donor and elderly who require less rigorous treatments.</p>
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Scott Gilbert	Moffitt Cancer Center & Research Institute	Bladder Cancer Outcomes and Impact Study (BCOIS)	<p>Bladder cancer is the fifth most common cancer in the United States and accounts for nearly 70,000 new cases of cancer each year. Florida has the second highest number of bladder cancers diagnosed each year, following only California. Although most bladder cancers are detected at an early stage, about 25% of patients present with invasive disease for which bladder removal is recommended. In addition, 15-20% of patients originally diagnosed with a low-stage bladder cancer progress to higher stage tumors that prompt bladder removal at a later time. Approximately 10,000 bladder removals - called cystectomy in medical terminology - are performed each year in the US. Following bladder removal, urine is redirected out of the body in a reconstructive procedure called a urinary diversion. Cystectomy and urinary diversion are associated with long lasting and even permanent changes in physical appearance (most urinary diversions result in a bag worn by patients attached to the outside of their abdomen), body function (for example, incontinence), as well as increase the risk of developing kidney stones, urine infections or impairment in kidney function. To date, there has been relatively little research examining the effects of these changes. The objectives of this study are to assess how common and detrimental those complications are by tracking clinical outcomes as well as surveying patients and their spouses/partners regarding the impact of and adaptation to bladder removal.</p>
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Chen Ling	University of Florida	Treatment for human hepatocellular carcinoma based on genome- and capsid-optimized recombinant adeno-associated virus serotype 3 vectors	<p>Human hepatocellular carcinoma (HCC) is associated with ~695,900 deaths worldwide each year. Alternative therapies are still warranted to treat HCC. The main aim of this proposal is to develop novel recombinant adeno-associated virus (rAAV) vectors for the selective and highly efficient targeting of human HCC. rAAV vectors have been succeeded in a number of gene therapy clinical trials, including Leber's congenital amaurosis and hemophilia B. The lack of human disease associated with AAV and helper virus dependence are two major safety features for using rAAV as a gene therapy vector. In previous studies, we have shown that recombinant adeno-associated virus serotype 3 (rAAV3) vectors efficiently infect several HCC cell lines in vitro and HCC tumors in vivo. Meanwhile, the transgene expression can be restricted to malignant cells using human liver cancer specific promoter, such as alpha-fetoprotein (AFP) promoter. In clinic, it is important to target as many malignant cells as possible. To this end, we plan to modify both the viral capsid and viral genome to further enhance the infectivity of rAAV3 vectors in HCC cells.</p> <p>Secondly, the capsid- and genome-optimized rAAV3 vectors containing therapeutic genes will be tested for the potential gene therapy of human HCC tumors in murine models in vivo. The proposed studies will lead to a new method to treat human liver cancer patients.</p>
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Priyamvada Rai	University of Miami	Implications of Cellular Senescence as a Treatment Response in Prostate Cancer	<p>Prostate cancer is one of the most common cancers to afflict American men and a leading cause of cancer-related deaths. Unfortunately therapeutic options for prostate cancer treatment are limited once the tumors become non-responsive to androgen deprivation therapy (ADT). Development of novel treatment strategies is limited by the lack of knowledge regarding molecular mechanisms that give rise to these non-responsive or androgen-refractory tumors. ADT induces a proliferative arrest rather than cell death in the bulk prostate tumor. Our preliminary data, using cell culture models of prostate cancer, indicate these non-proliferating but viable cells resist cell death and eventually give rise to androgen-refractory cancer cells. Thus we hypothesize interventions that acutely promote cell death instead of non-proliferation under ADT in androgen-responsive prostate cancer cells will inhibit outgrowth of androgen-refractory tumors. Our proposed research addresses this issue by investigating how cell death can be activated by oxidative stresses produced during this initial ADT-induced proliferative arrest (termed cellular senescence), by defining the role of senescence-associated secreted inflammatory proteins in promoting androgen-refractory tumor growth, and by determining whether acquisition of chemo resistance to other clinically relevant senescence-inducing treatments also leads to androgen-refractory traits in prostate cancer cells.</p>
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<p>Tongyu Wikramanayake</p>	<p>University of Miami</p>	<p>Laser-accelerated Hair Regrowth after Chemotherapy-Induced Alopecia</p>	<p>In 2012, an estimated 1.6 million people will be diagnosed with cancer in the U.S. More than half of them will receive chemotherapy, and approximately 65% of those (~520,000) will develop chemotherapy-induced alopecia (CIA). CIA is one of the most common side effects of cancer treatment, and has significant negative impact on patients' quality of life, negatively affecting their perception of appearance, body image, sexuality, and self-esteem. Patients also worry about the loss of privacy of having cancer because of CIA, and some patients would even consider declining chemotherapy for fear of hair loss. To develop effective treatment for CIA, we recently observed that low-level laser (</p>
<p>James Wilson</p>	<p>University of Miami</p>	<p>FAST Probes: Reporters of Activation States in Cancer Relevant Signaling Pathways</p>	<p>While great strides have been made in detection and treatment of human cancers, there remain unanswered questions related origin, progression and resistance to treatment. Our goal is to develop a toolkit of chemical probes that enable detailed, molecular level investigations of the biomolecular changes associated with many cancers. Our tools, called FAST (Fluorescent Activation State) probes, will enable researchers to identify populations of cancer relevant signaling biomolecules. We will achieve this goal through 1) the design and chemical synthesis of new probes, 2) screening the probes for binding to cancer relevant biomolecular targets and 3) demonstrating their application in identifying these targets in tumor-derived cell lines. The knowledge gained through the application of these new chemical tools will aid in the development of new chemotherapies and provide better correlation between disease mechanisms and clinical outcomes.</p>



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Ravi Shridhar	Moffitt Cancer Center & Research Institute	Validation of a Radiation Response Signature in Borderline Resectable Pancreatic Cancer Patients Treated with Induction Chemotherapy followed by Stere	<p>Pancreatic cancer remains the fourth leading cause of cancer death in the United States. Cures occur with surgical resection leaving no microscopic disease behind (R0 resection) in only 20% of patients. Leaving disease behind (R1/R2 resection) is associated with poor outcome. Such patients do no better than those that are treated with chemotherapy only. Patients are classified as borderline resectable (BR) if the tumor involves the blood vessels running adjacent to the pancreas leaving no separation between which the surgeon can cut. In this setting preoperative chemotherapy and radiation can induce the death of part of the tumor and increase the likelihood of R0 resection. Conventional chemoradiation (CRT) is given in 28 fractions with chemotherapy as a radiosensitizer. High-dose radiation delivered in 5 treatments is stereotactic body radiotherapy (SBRT). We have found that SBRT is as effective as pre-operative CRT. Nevertheless, some patients are completely resistant to radiotherapy. We have developed a gene expression signature that predicts the sensitivity to conventional radiation in a variety of tumors. In this proposal our aim is to perform a clinical trial to validate this radiation signature in patients with BR pancreatic cancer which will allow us to predict which patients would most benefit from SBRT and avoid radiation in those who will be resistant. This is an essential first step in developing a personalized therapy for BR pancreatic cancer.</p>
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<p>Hendrik Leusch</p>	<p>University of Florida</p>	<p>Development of scale-up synthetic method for apratoxin S4, a novel drug for the treatment of colorectal cancer</p>	<p>Natural products show outstanding potential as starting points in drug discovery, especially in the quest for anticancer drugs. We have discovered that the marine natural products called apratoxins have anticancer properties; however, the original compound had some toxic side effects. We have generated a new apratoxin (apratoxin S4) that lacks the toxic side effects of the natural product. We aim to generate large quantities of this improved apratoxin, which is necessary for further drug development. Our goal is to demonstrate the feasibility of large-scale chemical synthesis to generate enough apratoxin S4 for extensive preclinical testing.</p>
<p>John Copland</p>	<p>Mayo Clinic</p>	<p>Stearoyl CoA as novel molecular target for treatment of kidney cancer</p>	<p>Kidney cancer remains on the increase in the United States with about 64,770 new cases of kidney cancer in 2012 and about 13,570 people will die from this metastatic disease. Current FDA approved drugs for metastatic disease give months of survival benefit but all patients develop drug resistance. There is a dire need for more effective treatment for metastatic kidney cancer. We have discovered a new gene, stearoyl CoA desaturase 1 (SCD1) that causes kidney tumors to grow. We have identified inhibitors of SCD1 and plan to develop a SCD1 inhibitor as a new treatment for kidney cancer. We have also discovered that an SCD1 inhibitor when combined with an FDA approved drug (a mTOR inhibitor) for kidney cancer results in increased tumor death and antitumor synergy. Thus, our goal is develop this new inhibitor as a combinatorial therapy for kidney cancer. We also will develop an assay which will detect SCD1 in kidney cancer tissues. This detection assay will be used as a diagnostic indicating that a patient should be treated with a SCD1 inhibitor. Our team includes an oncologist who specializes in treating kidney cancer and clinical trials. As a result of our research, we foresee clinical trials towards this new treatment strategy that should increase the survival benefit of patients diagnosed with the most common form of kidney cancer.</p>



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Branko Stefanovic	Florida State University	Controlling Fibrosis to Prevent Hepatocellular Carcinoma	<p>The major type of liver cancer is hepatocellular carcinoma (HCC). It is the 5th most common cancer and the 3rd leading cause of deaths among cancers. When diagnosed, patients have average survival of 9 months. There is no cure for HCC other than liver transplant. 90% of HCCs appear in cirrhotic livers, making cirrhosis essentially a precancerous state. Prevention or attenuation of liver cirrhosis can greatly decrease the incidence of HCC. However, there are no antifibrotic drugs to treat cirrhosis. Hepatic stellate cells (HSCs) produce type I collagen in liver fibrosis, and type I collagen is the protein responsible for development of liver fibrosis and cirrhosis. We have discovered one chemical compound (60D17) that can dramatically decrease type I collagen synthesis. The compound has been tested for inhibition of collagen synthesis by HSCs. 60D17 is a candidate antifibrotic drug that we want to bring to clinical trials. The first goal of this proposal is to test the efficacy of this compound in an animal model of liver fibrosis. We obtained 8 derivatives of the 60D17 compound with the similar core structure, this modifications may increase its potency. The second aim of the proposal is to test the 60D17 derivatives for collagen inhibition in HSCs and, if a more potent derivative is found, to test it in an animal model of hepatic fibrosis. The long-term goal is to develop a specific antifibrotic drug that is effective in reducing liver fibrosis and the incidence of HCC.</p>
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Pearlie Epling-Burnette	Moffitt Cancer Center & Research Institute	Verification of TERT assay for MDS diagnosis	<p>This application focuses on development and commercialization of a novel diagnostic assay for Myelodysplastic Syndromes (MDS), which is the most frequently occurring blood malignancy in the United States. The disease causes changes to the bone marrow, which is where blood cells are made. The diagnosis is based on subjective changes in cell shape and is complicated because multiple tests are needed. Our results have defined MDS to have a deficiency in a protein that maintains the ends of chromosomes called telomerase reverse transcriptase (TERT). Comparing cases and controls, we found a threshold that is able to differentiate between these two groups with 92% accuracy. Additional studies are needed to develop the assay and to attract investors. In this application, we propose specific aims necessary to advance the developmental potential of this product. Specific aim 1 will determine the sensitivity or the effectiveness of the test to differentiate patients with bone marrow biopsy-confirmed MDS from healthy controls. Specific aim 2 will determine the specificity, or the extent to which the test gives negative results in those that are free of the disease. With a team of experienced leaders in the field of commercial diagnostics, this proposal is sure to assist with advancing the marketability of the product within the funding period.</p>
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Barry Rosen	Florida International University	Development of High-throughput Assays to Identify Drugs to Prevent Arsenic Carcinogenesis	<p>The long term goal of this project is the discovery of drugs that can prevent arsenic-related cancer. According to the Environmental Protection Agency, arsenic is the most pervasive environmental toxic substance in nature and tops the EPA's Superfund List of Hazardous Chemicals. Arsenic is a Group I human carcinogen that causes bladder cancer, the 10th most common cancer worldwide, accounting for an estimated 261,000 new cases diagnosed and 115,000 deaths each year, as well as skin and lung cancer. Florida residents consume arsenic daily in their drinking water and food supply. Arsenic is used as an herbicide on Florida golf courses, and run-offs contaminate the water supply of Florida cities. Arsenic is used as an herbicide for rice, apples and tobacco. Rice grains and rice products such as baby food contain arsenic, and does apple juice and cigarette smoke. Arsenic is used as a growth promoter for chickens, turkeys and pigs. Their meat contain arsenic and their waste is used as fertilizer for crops. In humans inorganic arsenic is converted to the cancer-causing form by the liver enzyme As(III) S-adenosylmethionine methyltransferase (AS3MT). We are requesting funds to develop new methods to develop to drugs for the prevention of arsenic-related cancer.</p>
Jie Wu	Moffitt Cancer Center & Research Institute	Optimization and Characterization of Shp2 Inhibitors	<p>Activating Shp2 mutations are found in several types of human cancer and have been shown to cause leukemias. Furthermore, Shp2 is aberrantly activated in many cancer cells by oncogenic signals to promote tumor growth. The goal of this project is to optimize lead compounds of Shp2 inhibitors to develop them into a new class of anticancer drugs. Novel Shp2 inhibitors generated from this project should facilitate the development of a new treatment for human cancers.</p>



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Daiqing Liao	University of Florida	Development of a Novel Chemical Inhibitor of p300 for Treating Triple Negative Breast Cancer	Triple-negative breast cancer (TNBC) accounts for about 15%-20% of all breast cancers. It is defined by the lack of immunohistochemical detection of estrogen receptors, progesterone receptors and the epidermal growth factor receptor type 2 (Her2/Neu). Patients with TNBC exhibit a poorer prognosis than those with hormone receptor-positive BC subtypes due to lack of effective therapies and rapid disease relapse. Studies have shown the TNBC contains a large fraction of cancer stem cells that may be responsible for rapid metastatic progression and treatment resistance. Thus, factors that promote the survival and proliferation of cancer stem cells may be promising therapeutic targets for treating TNBC. P300 appears to be such a factor. This application is to determine the therapeutic potential of a novel chemical inhibitor that suppresses the enzymatic activity of p300 for treating TNBC using a preclinical mouse model. If proven effective in this project, this p300 inhibitor will be further tested in clinical trials, which may ultimately lead to a new therapy for treating patients with TNBC and other types of advanced cancer.
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Brian Law	University of Florida	Novel Anti-Metastasis Agents Targeting CDCP1	<p>Cancer morbidity and mortality could be significantly decreased if drugs were available that effectively block metastasis and kill metastatic cancer lesions. Such an approach requires developing drugs that target the key proteins that are involved in the detachment of cancer cells from their original site, and the survival of these cells in a detached state until they are able to establish colonies at distant sites. One such drug target that fits these criteria is the protein CDCP1. We have identified compounds that inhibit CDCP1 cellular functions resulting in the death of cancer cells that depend on CDCP1 for their survival. These CDCP1 inhibitors are termed iCDCP1. The proposed work involves 1) synthesizing derivatives of the current iCDCP1 compounds to optimize their effectiveness and specificity, 2) defining the subset of human cancers that would be most sensitive to iCDCP1 compounds to maximize the clinical benefit of these drugs, and 3) testing an optimized iCDCP1 compound in animal models for its ability to prevent cancer metastasis and to cooperate with existing molecularly targeted anticancer agents to synergistically kill tumor cells with minimal toxicity to the patient. These iCDCP1 agents represent the first efforts to develop CDCP1-targeted drugs and with further testing and optimization have significant potential to improve the lives of a wide array of patients suffering from advanced cancers.</p>
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Nasreen Najmunnisa	University of Florida	Micro-RNA Based Novel Targeted Therapy for Malignant Pleural Mesothelioma	<p>Malignant Pleural Mesothelioma (MPM) is an aggressive tumor of the pleura caused by asbestos exposure. Due to a long latency period the symptoms appear 30-40 years after asbestos exposure. More than 3,000 new mesothelioma cases are reported in the US annually, and 30% of cases are reported in Veterans. With an aging population, Florida is ranked 2nd in Mesothelioma deaths. According to government reports, there were 1,095 asbestosis deaths and 3,432 mesothelioma deaths in Florida between 1979 and 2000. Treatments such as surgery, radiation and chemotherapy failed to improve the survival. Chemotherapeutic drugs not only kill the cancer cells but severely damage the normal tissue. Hence, more effective and innovative therapies that target only cancer cells are desperately needed. Recently we reported MPM tumor cells overly express receptor EphA2 (a receptor tyrosine kinase) and normal cells do not express. Silencing receptor EphA2 or treatment with Ephrin-A1 attenuates MPM growth. However, the mechanisms are not clear. Ephrin-A1 induces microRNA-302b expression that targets receptor EphA2. We plan to study Ephrin-A1 conjugated and microRNA-302b encapsulated Liposomal nanoparticle (LNP) via intra-pleural delivery in a mouse model of MPM. Since, Florida is home to a large percentage of elderly and Veteran population suffering from mesothelioma; the knowledge obtained from these studies will help design new therapeutic strategies to improve the survival of MPM patients.</p>
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Prakash Chinnaiyan	Moffitt Cancer Center & Research Institute	Metabolomic Underpinnings of Malignant Glioma Tumorigenesis	<p>The established approach for both understanding and treating cancer has largely been genotype based. Unfortunately, clinical gains offered by this level of understanding have been limited, largely based on the complex nature of signaling networks associated with tumorigenesis and the inability to delineate the key “functional” signaling pathways actually driving growth in an individual tumor. While cancers have access to a wide variety of genetic and/or epigenetic modifications, there are a limited number of metabolic strategies that they can employ. The goal of this proposal is to identify specific metabolic programs allowing for brain tumors to grow, and determining if targeting these pathways can serve as a novel form a cancer therapy.</p>
Lung-Ji Chang	University of Floirda	T cell engineering targeting small cell lung cancer	<p>Small cell lung cancer (SCLC) accounts for 10-15% of all lung cancers. Risk of developing SCLC substantially increases with exposure to tobacco smoke. In contrast to early stage non-small cell lung cancer (NSCLC), surgical resection is rarely recommended due to the early spread of SCLC. The standard treatment is chemotherapy and concurrent radiotherapy. Patients with SCLC have a 70% chance of relapse within two years. The ability to cure even limited stages of SCLC remains rare (10%). Biological therapies including immunotherapy have reported substantial improvement in long-term survival and quality of life of cancer patients. Immunotherapy has been widely applied for NSCLC patients but little effort has been focused on SCLC. This proposal will target two highly expressed SCLC antigens using novel T cells with the following three specific aims: 1) engineer SCLC-specific T cells, 2) characterize the novel T cell functions, and 3) test these T cells along with chemotherapy in novel SCLC mouse models.</p> <p>These SCLC-specific T cells exert two different tumor-killing mechanisms to eliminate residual cancer cells systemically. A rational SCLC therapy strategy will be developed based on these novel T cell designs combined with chemotherapy. This project will build a research program with the goal of implementing a clinical trial in the near future.</p>



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David Meckes	Florida State University	Proteomic Analysis of Cancer Exosomes for Diagnostic and Therapeutic Targets	<p>Exosomes are small vesicles released at high levels from cancer cells that are thought to modulate the tumor environment and enhance disease progression. Exosomes are stable structures that can be isolated from many biological fluids including blood, urine, and saliva. Therefore, exosomes represent a rich source of potential biomarkers to better diagnose various cancers. Our laboratory seeks to utilize exosome purification strategies that we have developed together with advanced quantitative proteomics techniques to define the protein composition of exosomes secreted from a diverse set of human cancer cell lines (the National Cancer Institute's NCI-60 collection). The completion of this project will reveal a common set of proteins found in cancer exosomes that are likely important for their formation and function. Exosomal proteins differentially expressed in specific cancer types (e.g., breast, prostate and colon) will likely indicate disease-specific functions and reveal potential diagnostic biomarkers that will be further explored with patient samples.</p> <p>Overall, this project aims to understand the composition and function of exosomes secreted from cancer cells with the goal of discovering novel diagnostic targets for the early detection and treatment of cancer.</p>
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Bankhead-Coley Cancer Research Grants

Alicja Copik	University of Central Florida	Establishing Particle-Activated Natural Killer Cell Therapy For Treatment of AML In Preclinical NSG Mouse Model	<p>Stem cell transplantation (SCT) is the current core treatment for many types of blood cancers, including most types of leukemia and lymphoma. Unfortunately, challenges such as the lack of suitable donors for ethnically diverse patients, cancer relapse, and graft-versus-host disease significantly limits their application and success. More than 70% of patients who could benefit from stem cell transplant do not have a matched sibling donor and the chances of finding a matched unrelated donor strongly correlate with ethnic background (less than 10% for ethnic minorities).</p> <p>Therefore, there is a great need for new and innovative approaches to enhance current therapies or to provide a completely different alternative to SCTs. The goal of this study is to establish a new cancer cell therapy using a type of immune cell called a natural killer (NK) cell. Our research has designed a method for augmenting the amount of NK cell that could be injected or that potentially could increase the amount of NK cells in patients themselves. The current work is to test these methods in mice animal studies and devise the best treatment methodologies. In the end, this study is expected to lay foundations for a Phase-I/II clinical trial of an NK cell-based therapy for blood cancer patients at Florida Hospital. This therapy would provide a treatment alternative to disparate groups such as ethnic minorities who do not have a matched donor and elderly who require less rigorous treatments.</p>
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Bankhead-Coley Cancer Research Grants

Hendrik Luesch	University of Florida	Chemistry and Biology of Apratoxins	<p>Natural products show outstanding potential as starting points in drug discovery, especially in the quest for anticancer drugs. Over half of the currently approved anticancer drugs are derived from natural products but are directed against a small number of targets in the cancer cell. The objectives of the proposed research are the validation of a new mechanism of drug action for anticancer therapy and the assessment of the therapeutic potential of a class of marine natural products termed apratoxins which act via this unexplored mechanism. Our preliminary data indicate that apratoxins deplete cancer cells of several certain receptors and other proteins that are overexpressed or overactive in cancers. Through chemical modifications we have further improved on the natural product and increased the therapeutic index. Apratoxins interfere with the synthesis of these cancer-associated molecules, and we test the possibility that inhibition of their synthesis may be exploited for anticancer drug development. The research proposed here will characterize the mode of action, structure-activity relationship and anticancer drug potential of the apratoxins and, more generally, this mechanism, and identify targets for rational combination therapy.</p>
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Bankhead-Coley Cancer Research Grants

Derek Radisky	Mayo Clinic	Wnt mediators as breast cancer biomarkers and effectors of lobular involution	<p>The breast lobules are the structures that produce milk, but these lobules are also the primary site of breast cancer formation. As a woman ages beyond her childbearing years, her breast lobules are supposed to gradually disappear, reducing her cancer risk, in a process known as lobular involution. However, this doesn't always happen. By analyzing tissue samples from benign breast biopsies, we have found that more than 40% of postmenopausal women have incomplete lobular involution, and that these women are at substantially greater risk for subsequently developing cancer. Our project will provide insight into the previously unstudied mechanisms that control lobular involution and will define why postmenopausal women who have not completed the process of lobular involution are at greater risk for breast cancer development. From these experiments, we will identify biomarkers that can be used for better predicting who is at greatest risk for development of breast cancer. This research will be crucial for better guiding women who obtain breast biopsies toward the most appropriate strategies of surveillance, risk management, and treatment. This research will also point towards new physiologic strategies to reduce breast cancer incidence, including the induction of lobular involution in postmenopausal women for whom this process is incomplete.</p>
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Bankhead-Coley Cancer Research Grants

Clement Gwede	Moffitt Cancer Center	Latinos CARES (Colorectal cancer Awareness, Research, Education & Screening) Project	<p>Colorectal cancer (CRC) is the second leading cause of cancer-related deaths among Hispanic men and women in the US. As Latinos are one of the fastest growing groups in the country, and accounts for about 23% of the Florida population, we aim to take our recently developed English-language colorectal cancer materials (DVD + photonovella booklet), which are being tested in health clinics, and adapt (transcreate) them for Latinos. This process of adaptation involves a series of steps in which we get ideas and feedback from many Latinos in small groups and interviews rather than simple translation. This process helps to be sure that the new Spanish-language materials are easy-to-understand, motivating, and use just the right words, terms and visuals that are helpful and meaningful for Latinos. Next, we will carry out a study in health clinics to see if Latinos who get the newly created Spanish-language materials as compared to other Latinos who get a standard Spanish booklet complete their screening more. Both groups will get a stool blood test kit at no cost to collect a sample at home. The idea for this project is based on feedback from the community partners of the Tampa Bay Community Cancer Network (TBCCN) who identified this information need in our community. The study is important as it involves communities that have been working together in research for over 8 years and is expected to help reduce colorectal cancer health disparities among Latinos through screening.</p>
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Susan Vadaparampil	Moffitt Cancer Center	Developing Intervention Components to Support Physician Recommendation of HPV Vaccination in Males	<p>In 2011, a new vaccine against human papillomavirus (HPV) was recommended for all adolescent males ages 9-21 and young adult males ages 22-26 at increased risk of HPV-related cancers. Vaccination may be especially beneficial for males from racial/ethnic and sexual minority groups who are more likely to develop HPV-related cancers. The Centers for Disease Control and Prevention strongly supports increasing physician recommendation as a main way to increase adolescent HPV vaccination rates. Yet, little is known about whether physicians actually recommend vaccination and their reasons for doing (or not doing) so. This information is greatly needed to develop interventions to increase physicians' HPV vaccine recommendations to males. In order to address this important gap in knowledge, our study begins by surveying 500 pediatric and family physicians in Florida at two time points. The first survey will assess their current knowledge, attitudes, and clinical practices (Year 1) and the second survey will use that information to develop and then assess what kinds of interventions (e.g., messages, visuals, graphics) physicians prefer (Year 2). While it is tempting to develop interventions based on "common sense" or "expert opinion," asking physicians about what they prefer is most likely to result in interventions that they will feel are both relevant and usable in their clinical practice.</p>
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Jeffrey Weber	Moffitt Cancer Center & Research Institute	Tumor Biomarkers for Outcome with Checkpoint Protein Inhibitors	<p>Drugs that release the “brakes” on the immune system have shown promise in treating melanoma and other cancers. Only a minority of patients show shrinkage of tumor after treatment with antibodies that block substances on immune cells called CTLA-4 or PD-1 which act as the brakes on T cells. We wish to perform a clinical trial in which those two antibodies are given to patients with melanoma one after the other, and tumor biopsy samples will be collected before and after the treatment. The tumor will be analyzed to find out what pattern of genes are expressed prior to and after therapy from patients that respond to the treatment. We also wish to find out what factors are impacted by treatment with one antibody that increase the chance that the tumor will shrink after receiving the other antibody in sequence. This information will help direct us to how these antibodies work in patients so we may improve the treatment and chose patients most likely to benefit. We also wish to find out which type of immune cells in the tumor are responsible for shrinkage of tumor with those antibodies, and what molecules identify the immune T cells important for tumor shrinkage. The pattern of genes and the identity of molecules expressed by the immune cells within tumors will be measured.</p> <p>We wish to understand how those antibodies to immune checkpoint proteins work in patients whose tumors shrink after the therapy, and to allow the patients most likely to benefit to receive the treatment.</p>
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Bankhead-Coley Cancer Research Grants

Tan Ince	University of Miami/Interdisciplinary Stem Cell Institute/Sylvester Cancer Center	Analysis of Heat Shock Factors in Tumor Stem Cell Regulation	<p>Tumor stem cells (TSCs) are a small subset of cells within the tumor that are able to self renew and differentiate into other tumor cells. Developing new treatments that target TSCs is important because TSCs are believed to cause chemo-resistance, tumor relapse and distant metastasis, which remain to be critical clinic problems. In preliminary studies we discovered that heat shock factor 1, 2 and 4 (HSFs) are over expressed in human breast tumor stem cells. These factors protect tumor cells from various internal and external stressors; for example, it has been shown that high expression of HFSs makes TSCs resistant to deleterious metabolic and genomic alterations. Thus, we hypothesize that high HSF expression in TSCs is partly responsible for the drug resistance and metastasis. In this project we will attempt to establish the association between HSFs and TSCs by studying a comprehensive panel of standard and primary tumor cell lines and tumor tissues. Next, we will examine whether HSFs over-expression can create TSCs, and HSF inhibition can kill TSCs. Lastly, we will test whether inhibition of HSFs can make the TSCs more sensitive to standard treatments. If successful, the results of these experiments can provide the basis for clinical studies that target HSFs/TSCs as an alternative breast and ovarian cancer treatment strategy.</p>
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Bankhead-Coley Cancer Research Grants

Alexander Parker	Mayo Clinic Jacksonville	Exploration of serum and urine-based biomarkers of benign versus malignant renal masses	<p>The increased use of imaging technologies in medical practice has led to a dramatic rise in the number of individuals who are told that they have a “suspicious mass” in their kidney. Specifically, more and more individuals are undergoing exploratory CT imaging of their abdomen only to be told that the radiologist happened to notice a “suspicious mass” in their kidney while looking at the scan. The majority of these masses are less than 4cm in diameter and are collectively referred to as small renal masses (SRM). Currently, the standard of care for SRM patients remains partial or complete removal of the affected kidney. After surgery most of these SRMs are found to be cancerous; however, roughly 20% are actually benign tumors that could have been managed with either watchful waiting or less invasive approaches than open surgery (i.e. cryoablation). The inability to determine which SRMs are benign versus cancerous prior to surgery highlights the need for the development of prediction tools to help guide the best treatment choice for this growing population of patients. In this proposal, we will explore for the first time whether the presence of specific biological markers within the blood and urine (called microRNAs) can help predict which SRMs are benign and which are cancerous. The development of such tests has the potential to reduce the number of unnecessary surgeries, lower healthcare costs and enhance overall patient quality of life.</p>
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Bankhead-Coley Cancer Research Grants

Jiandong Chen	Moffitt Cancer Center	Investigation of novel MDM2 and MDMX intra-molecular interactions	<p>The p53 tumor suppressor is mutated or functionally incapacitated in nearly all types of human tumors. In lung cancer, p53 is a direct target of mutagens derived from tobacco smoke. Nearly 70% of lung cancer contain mutations of p53 that result in loss of function. Furthermore, tumors accumulate mutant p53 proteins that have abnormal functions that promote metastasis. In breast cancer, p53 mutations are less frequent (~30%) but its function is compromised due to overexpression of MDM2 and MDMX. The MDM2 and MDMX proteins also interact with mutant p53. Inactivation of MDM2 is an important mechanism of mutant p53 accumulation in tumors. Therefore, understanding how wild type and mutant p53 are regulated by MDM2 and MDMX-mediated ubiquitination is critical for the development of novel drugs for the treatment of tobacco-related cancers and many other tumor types. This proposal will elucidate new mechanisms by which MDM2 and MDMX employ to inhibit p53. The knowledge gained from these experiments will be essential for the development of novel drugs that target MDM2 and MDMX through different mechanisms from the current generation of MDM2 drugs, providing alternatives to address potential limitations of current drugs in areas such as efficacy and side effects. Because the p53 pathway is universally inactivated in cancer, our proposed research will benefit all types of cancer, particularly tobacco-related lung and breast tumors with frequent p53 mutation or MDM2/MDMX amplification.</p>
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Bankhead-Coley Cancer Research Grants

Tuya Pal	Moffitt Cancer Center and Research Institute	Investigation of Genetic Risk Assessment for Inherited Breast Cancer (IGRAB)	<p>The discovery of the BRCA genes almost 15 years ago, allows us to identify people who have changes in these genes. A woman with a gene change has a high chance to develop breast and ovarian cancer. Yet, it is still difficult to spot people with these changes due to the small number of medical experts familiar with the BRCA genes. As such, many practitioners and patients in the community are not aware of these genes. Roughly 10% of all people with the BRCA gene change know that they carry this change. In Florida, we have the second highest number of new cancer cases yet very limited expertise in the topic of Clinical Cancer Genetics. Because of this, many providers and patients are less aware about the topic of BRCA mutations, which could possibly lead to misinformed healthcare decisions. We plan to better understand how BRCA testing is being done and how BRCA carriers are being managed throughout Florida by networking with providers and patients across the state thereby boosting access of information about BRCA gene changes. In order to achieve our goals, we will seek information from women who have a BRCA mutation, breast cancer patients, and healthcare providers who perform BRCA testing. The eventual goal of our efforts is to improve the care given to those with BRCA gene changes in Florida.</p>
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Bankhead-Coley Cancer Research Grants

Krishna Komanduri	University of Miami Miller School of Medicine	Selective Inhibition of GVHD for Allogeneic Transplantation for Cancer	<p>Allogeneic stem cell transplantation (SCT), where bone marrow cells from a donor are given to patient after chemotherapy, is the preferred therapy for many cancers. A major complication occurs when cells from the donor attack the patient, called graft-versus-host disease (GVHD). Current treatment for GVHD shuts down all immune cells including the beneficial ones which prevent life-threatening infections in patients after SCT. The research we propose will test a new strategy to prevent GVHD while sparing the immune cells that protect patients from infections. We have promising preliminary results that suggest that this will be possible using a drug that is very safe and already used in humans. The proposed work will test this concept by determining the exact drug among the available drugs in this new class that has the best potential to be used to treat patients. This will be based on experiments we perform in the laboratory on cells from healthy donors and in animal experiments funded by the proposed research. The goal of the research is to design a clinical trial to test this treatment in humans at the end of the 2 year grant period.</p>
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Bankhead-Coley Cancer Research Grants

Masanobu Komatsu	Sanford-Burnham Medical Research Institute	microRNA regulation of vascular functions in colorectal cancer	<p>It is well known that blood vessels grow extensively in malignant tumors: a process called tumor angiogenesis. However, the network of tumor blood vessels (tumor vasculature) is abnormal and defective. Through the improvement of vessel functionality, the normalization of tumor vasculature will provide an opportunity to better deliver chemotherapeutic agents and other anti-cancer drugs, and reduce the chance of cancer spreading. The long-term goal of our study is to find a way to induce vascular normalization in tumors. A cellular protein called R-Ras promotes normalization of abnormal vasculature. The ability to control R-Ras protein could therefore provide a therapeutic advantage in cancer. MicroRNAs (miRNAs) are thought to be involved in most biological processes including angiogenesis. We hypothesize that there exist specific miRNAs that regulate tumor vessel normalization process through regulation of R-Ras. In this research project, we will identify R-Ras-regulating miRNAs in the vasculature of malignant colorectal tumors (Aim 1) and determine their roles in endothelial cell and pericyte regulations (Aim 2). The identification of R-Ras-targeting miRNAs could lead to the discovery of a network of collective pathways that governs tumor vascular normalization. Such miRNAs could be exploited therapeutically to control multiple vessel normalization pathways simultaneously.</p>
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Bankhead-Coley Cancer Research Grants

Rakesh Singal	University of Miami	Methylation Profiling in Free Circulating DNA as a Biomarker for Risk Stratification of Prostate Cancer	<p>A large proportion of newly diagnosed prostate cancer patients have 'indolent' disease that would not impair the quality or quantity of life. These patients are suitable for active surveillance, in which patients are carefully observed and when they show signs of disease progression, they are offered active treatment. However, active surveillance is not widely accepted at present. The major reason is the absence of tests that can distinguish indolent from aggressive prostate cancer. Our study will result in a simple blood test that can classify the aggressiveness of prostate cancer and thereby help determine the appropriate management option. This will improve the acceptance of active surveillance in prostate cancer management. Our project addresses the Bankhead-Coley program goals as follows – 1. If successful, this project will provide a basis for follow up studies to bring this test into clinical practice. Also, the information gained about aggressive prostate cancer will form the basis of other studies and therefore help significantly expand cancer research capacity in the State. 2. A recent study from Johns Hopkins indicates that 'active surveillance' may miss aggressive cancer in black men. Our project will help identify those with aggressive cancer in black men and thereby reduce the impact of cancer on disparate groups.</p>
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Bankhead-Coley Cancer Research Grants

Robert Hromas	University of Florida	Targeting Histone Methylation for Triple-Negative Breast Cancer Therapy	<p>Enormous strides have been made in the treatment of most types of breast cancer in the last two decades. However, these treatment advances have not extended to triple negative breast cancers. These triple negative breast cancers lack estrogen receptors, progesterone receptors, and the Her2/Neu receptor. The presence of these three receptors not only defines a more treatable form of breast cancer, they are also targets for highly effective therapy themselves. Thus, there are fewer options to treat triple negative breast cancer than for other types of breast cancer. There are certainly many other drugs that can be used to treat breast cancer besides estrogen/progesterone receptor inhibition and targeting Her2/Neu. Most of the other therapies used for treating triple negative breast cancers function by damaging DNA. However, triple negative breast cancers often resist such DNA damaging chemotherapy. Thus, triple negative breast cancer represents the most difficult single problem in breast cancer currently. We have identified a DNA repair component termed Metnase that triple negative breast cancers use to resist chemotherapy. We have shown that repressing Metnase restores the sensitivity of triple negative breast cancer cells to DNA damaging chemotherapy. This project will generate novel and specific Metnase inhibitors and test whether they can overcome resistance of triple negative breast cancers to chemotherapy</p>
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Bankhead-Coley Cancer Research Grants

Elizabeth Franzmann	University of Miami	Early Detection for Smoking-Associated HNSCC	<p>Head and neck cancer (HNC) is a deadly disease that includes cancers of the mouth, throat and voice box. Blacks suffering from this disease have worse outcomes than whites. The main risk factors are smoking, drinking and human papillomavirus infection.</p> <p>Since the disease is curable if detected early, our group has developed a simple and inexpensive diagnostic test that measures markers in oral rinse samples. The markers, solCD44 and protein, are expressed at higher levels in cancer patients, carry a poor prognosis and abnormalities in their expression are detectable before cancers are visible. We began investigating this test in Liberty City, a minority-rich, economically disadvantaged community in Miami-Dade County. Preliminary data indicates that the test is accurate in this population. To continue this work, in Aim 1 we will evaluate how oral rinse marker levels vary over time to determine whether levels change as disease progresses.</p> <p>Since marker levels seem to be elevated before tumors are detectable, smoking cessation may reverse the disease process. In Aim 2 we will determine changes in oral rinse marker status with smoking cessation. To determine the link between marker levels and disease burden, in Aim 3 we will examine solCD44 and protein levels in oral rinses from HNC patients before and after treatment. These efforts are critically important because they aim to develop a useful early detection test that will help communities suffering disproportionately from HNC.</p>
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