bankheadcoley
Florida Biomedical Research Program

2009 Annual Report

The Bankhead-Coley Cancer Research Program

As established in section (s.) 381.922, *Florida Statutes* (F.S.), the purpose of the Bankhead-Coley Cancer Research Program is to advance progress towards cures for cancer by awarding research grants using a peer-reviewed, competitive process (see Appendix A).

Specifically, the Program seeks to:

- Expand research capacity in the state
- Improve participation in clinical trials
- Reduce the impact of cancer on disparate groups
- Foster collaborations among institutions, researchers, and community practitioners

For more information about the Program, visit www.floridabiomed.com or contact the Office of Public Health Research, (850) 245-4585. Additional print copies of this report are available upon request.

William G. “Bill” Bankhead Jr. and David Coley Cancer Research Program

Annual Report

January – December 2009

Submitted to

The Governor
The President of the Senate
The Speaker of the House of Representatives

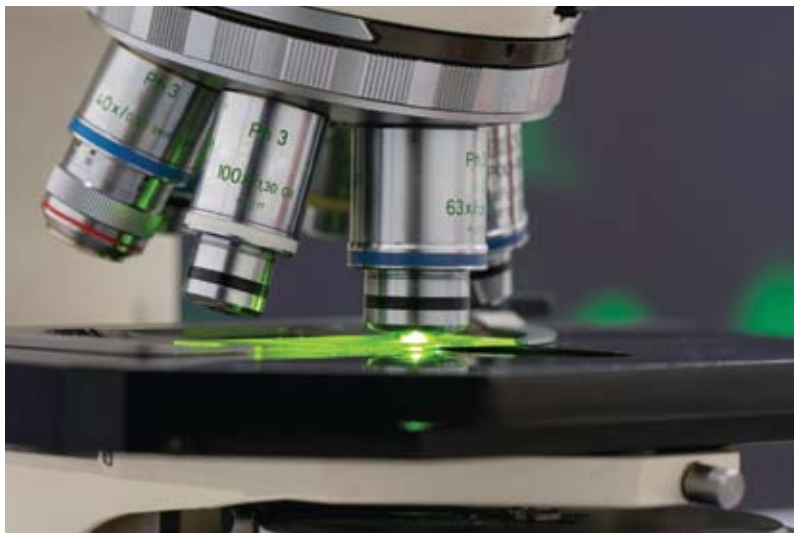
and

The Florida Center for Universal Research to Eradicate Disease

by

The State Surgeon General
State of Florida

December 15, 2009



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Executive Summary

For the Bankhead-Coley Cancer Research Program (the Program), 2009 was a year marked by significant change. Shortly after the year began, the downturn in Florida's economic cycle forced a 25 percent reduction in the Program's fiscal year (FY) 2008-2009 obligations. The Program responded by trimming administrative expenses and reducing or terminating grants. At mid-year, the Program budget increased more than two-fold from a share of the newly increased state cigarette surcharge. As a result of the increase, 39 research grants totaling nearly $11.4 million were awarded in a first round of funding and grants impacted by earlier reductions were restored. As the year drew to a close, the Program was in the process of awarding a second round of FY 2009-2010 grants made possible by this additional funding.

The following highlights of the year's accomplishments show the Bankhead-Coley Program's role in helping the state's cancer research community accelerate its capacity to address Florida's extraordinary cancer burden.

By the end of 2009, Florida's investment of more than $36 million in the Program has already helped Bankhead-Coley grantees attract an additional $72 million in funding to the state, based on the high quality of their cancer research.

Program grants have provided teams of scientists with seven leading-edge instruments for shared use that would otherwise have been too expensive for a single researcher to purchase.

Thirty-five new investigators have launched independent careers in cancer research in Florida with Bankhead-Coley grants.

Program-funded investigators have employed and trained more than 70 post-doctoral researchers, 29 undergraduate science majors, and 106 other lab workers, including research associates, lab technicians, nurses, and biostatisticians.

Articles published in peer-reviewed journals based on Bankhead-Coley research climbed to 76 this year—evidence of the national and international importance of the findings.

In addition to this progress, Bankhead-Coley grants are helping Florida's emerging cancer centers as well. Since the National Cancer Institute (NCI) has endorsed the peer review and funding decision processes used to select Bankhead-Coley awards, these grants are accelerating the ability of at least three emerging cancer centers in Florida to achieve NCI Cancer Center designation.

The Bankhead-Coley Program is currently undergoing a Legislative sunset review. This summer Senate professional staff reviewed the Program's performance, outcomes, and financial management. Senate staff published their findings in a September 2009 report recommending re-enactment. The Legislature will take up the review during the 2010 Regular Legislative Session.

The Office of Public Health Research continues to ensure accountability for the use of public funds by putting processes in place to track, monitor, and report scientific progress against the research aims of grants. The Program also monitors grantees' fiscal responsibilities and compliance with grant terms and conditions. The Biomedical Research Advisory Council has followed best practices in scientific peer review and avoided conflict-of-interest in recommending Program awards.

During the last quarter of the year, the Department of Health and the Biomedical Research Advisory Council laid the foundation for a five-year strategic plan that will guide the Program's future toward more rapid translation of research into widespread clinical practice.

Program at a Glance

The Bankhead-Coley Program offers competitive cancer research grants to Florida institutions based on scientific merit. The Program is funded annually with 2.5 percent of proceeds from a state cigarette surcharge up to $25 million and is managed by the Florida Department of Health and 11-member advisory council.

First awards made:	January 2007
Total awards made:	124
Total Florida institutions supported:	12
Total value of awards:	$36.1 million
Additional funding leveraged:	$72.3 million
Publications generated:	76
Presentations at scientific meetings:	129

Through October 2009

Program Background

Florida's Cancer Position

A recent study estimated that over the next 20 years, the number of new U.S. cancer cases will increase by 45 percent, cases among minorities will double, and cancer among seniors will increase by 67 percent. According to National Cancer Institute (NCI) Director Dr. John Niederhuber, "Unless our investment in science has a significant impact on these numbers, the impact on healthcare will be enormous."

Florida's demographic make-up, with a large senior population coupled with a large minority population, makes it particularly vulnerable to such increases. The state has one of the highest foreign-born populations in the United States.[2] Florida also leads the country in the number of residents 65 years of age and older, and more than half of all new cancer cases occur in this age group.[3] This may partially explain why Florida trails only California in the estimated number of new cancer cases and cancer deaths for 2009.[4]

Because cancer is such a complex disease and the time needed to go from basic science research to introducing new discoveries into widespread clinical practice is decades long, it will be years before Florida's cancer research infrastructure overtakes its demand. However, there is reason for optimism.

Florida's academic research institutions and cancer centers are steadily increasing their capacity to provide Floridians with state-of-the-art cancer research and patient care. This growth is largely being fueled by external funding, most notably from the NCI and other federal and national grant programs.

In its strategic planning efforts, the Biomedical Research Advisory Council (Advisory Council) is considering ways for the Bankhead-Coley Program to accelerate Florida's cancer research capacity.

The Role of the Bankhead-Coley Cancer Research Program

As a statewide competitive, peer-reviewed grant program, the Bankhead-Coley Program is an important resource benefiting Florida's entire cancer research community, and a strategic component of the state's overall cancer research effort.

- It is guided by an advisory council drawn from a cross-section of Florida's academic institutions, medical centers, and voluntary health organizations for their complementary expertise.
- It channels the available dollars through grant types designed to meet Florida's greatest needs in building cancer research capacity.
- It uses an unbiased, merit-based process to fund the best science proposed from anywhere in the state.
- It helps Florida researchers compete more successfully for external funding.
- It holds grant recipients accountable for using the money wisely.

Bankhead-Coley Program Funding History

In 2006, the Legislature authorized funding to support grants for biomedical research in Florida. Specifically, they appropriated $9 million annually for four years to support cancer research and established the Bankhead-Coley Program. This addition to Florida's research portfolio signified the state's commitment to join with the Florida Dialogue on Cancer and the American Cancer Society to reduce the state's cancer incidence and mortality rates.

Within six months, the Program crafted specific grant types (referred to as grant mechanisms), conducted a statewide competition for awards, implemented a peer review of applications, and awarded its first grants in January of 2007.

In fiscal year (FY) 2008-2009, the Bankhead-Coley Program, like the rest of Florida and the nation, made sacrifices due to the economic recession. In late January 2009, the Program's budget was reduced by 25 percent. After reducing administrative expenses and 2008 grants as much as possible, it was still necessary for the Program to end four grants prematurely. In May, as the Legislature wrestled with record revenue deficits, they chose to give the Program a 2.5 percent share of the new $1 per pack tobacco surcharge for FY 2009-2010, with an upper limit of $25 million. Figure 1 provides an overview of Program funding history.

Revenue to the Program for the first quarter of FY 2009-2010 was $12.5. Assuming no change in spending habits for the remainder of the year, the Program's projected share of the tobacco surcharge revenue for FY 2009-2010 is $25 million.

With an increase in funding, the Program reinstated the 2008 grants to full funding and announced in August a second competition for FY 2009-2010 grant awards, releasing a set of Special Calls for Applications for awards to begin in January 2010.

The 2010 Legislature will determine the most appropriate funding source and level of funding for the Bankhead-Coley Program beyond the current fiscal year.

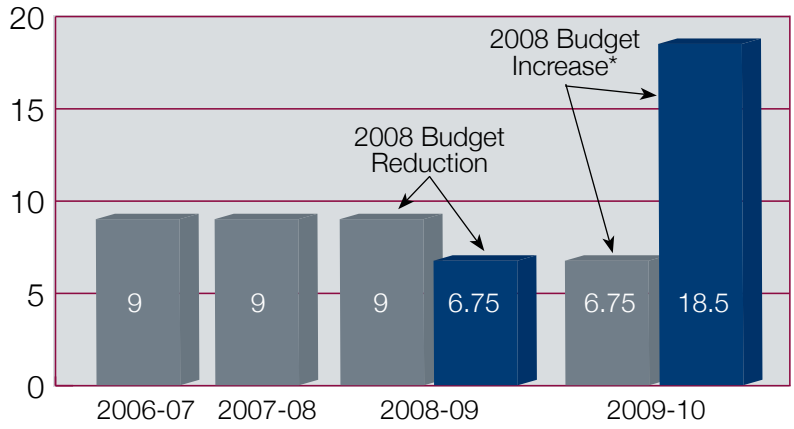


Figure 1 – Program Funding History (Millions)

**Estimated budget based on July revenue from cigarette surcharge*

Program Accomplishments

Highlights of Award Activity

Through October 2009, the Bankhead-Coley Program has extended 124 grants totaling $36.1 million in funding commitments.

As illustrated in Figure 2, the beneficiaries of these grants include 12 research institutions throughout Florida. Each has put forward cancer research projects that have earned high merit ratings from panels of experts from outside Florida.

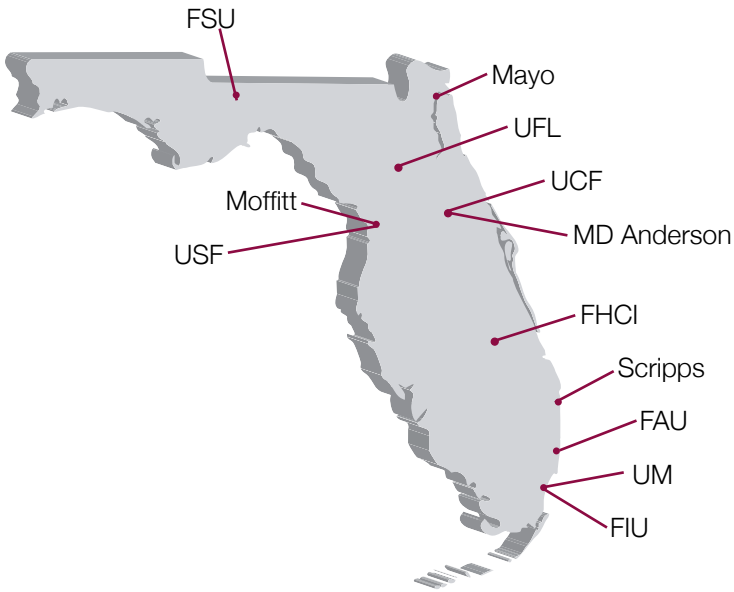


Figure 2 – Institutions Awarded Bankhead-Coley Grants Since Program Inception

Florida Atlantic University (FAU)
Florida Hospital Cancer Institute (FHCI)
Florida International University (FIU)
Florida State University (FSU)
Mayo Clinic Jacksonville (Mayo)
M.D. Anderson Cancer Center (MD Anderson)
Moffitt Cancer Center & Research Institute (Moffitt)
Scripps Institute (Scripps)
University of Central Florida (UCF)
University of Florida (UFL)
University of Miami (UM)
University of South Florida (USF)

These grants strategically target specific Program goals and the needs of Florida's cancer research community:

- Support for new investigators as they launch independent research careers (New Investigator Research Grants)
- Interim funding for promising cancer research projects that remained unfunded due to a lack of federal research dollars (Bridge Grants)
- Assistance in creating the foundations for large-scale, multidisciplinary collaborations in researching organ-specific cancers (Specialized Programs of Research Excellence Planning Grants)
- Understanding the barriers to patient participation in Florida's clinical trials (Special Emphasis Projects)
- Encouraging collaboration between small businesses and institutions in Florida (Technology Transfer/Commercialization Partnership Grants)
- Supporting promising high-risk, high-reward cancer research proposals (Florida Research Challenge Grants)
- Shared access to new, state-of-the-art instruments for cancer research (Shared Instrument Grants)

"Initiatives like Bankhead-Coley are critical. Our researchers get very close to winning national funding. Bankhead-Coley allows us to get better data, gain recognition, re-submit applications, and win national funding. People go to other places when they don't find that kind of support."

Dr. Eduardo Sotomayor
H. Lee Moffitt Cancer Center & Research Institute, 2009 Bridge Grant

Progress Toward Program Goals

The Program is charged with meeting ambitious goals and after only three years, there is encouraging progress to report.

Expanding Research Capacity

- Bankhead-Coley grants are being leveraged by grantees to attract additional funding to Florida. By mid 2009, the amount of this additional funding surpassed the state's total investment, and this trend should accelerate in future years. See Appendix B for a list of awards reported by Bankhead-Coley grantees in 2009.

- Presentations and publications serve as a benchmark for progress in the scientific community. While the number of completed Bankhead-Coley research projects is still few, significant findings produced by these grants are already being published in peer-reviewed journals and presented at scientific meetings. Appendix C contains the list of this year's publications, as reported by Bankhead-Coley awardees.

- Mentored research opportunities are helping 15 new investigators establish independent research careers in 2009 at seven Florida institutions, bringing the total number of such awards to 35 since Program inception.

Fostering Collaborations

- Grants intended to build new collaborations have launched six multi-disciplinary teams of researchers, each focused on a single organ-specific cancer, positioning them to compete successfully for multi-million dollar Specialized Programs for Research Excellence (SPORE) grants from the NCI.

- Among its very first grants, the Bankhead-Coley Program provided seven state-of-the-art instruments to five Florida institutions. Each of these instruments could only be justified by shared use, bringing teams of researchers together around the application of new technology. This offering was so successful that it was offered again for the Special Call for Applications in 2009.

Improving Participation in Clinical Trials

- In 2007, the Program funded two different, two-year studies aimed at identifying the barriers to participation in clinical trials by Florida cancer patients. These studies were intended to inform the Advisory Council regarding potential future grant mechanisms that would fund effective interventions. The Advisory Council was pleased with preliminary findings presented by the two project leaders at the January 2009 meeting. Since receiving Program funding, both research teams have earned additional federal funding to extend their work.

- In an attempt to address common patient recruitment difficulties in projects involving clinical trials, the Program offered a Clinical Research Planning (CRP) Grant in both 2008 and 2009. The results were disappointing, with no awards made in either competition. However, the Program is offering new grant mechanisms for 2010 that target translational research, which moves scientific discovery closer to human applications and clinical trials.

- Low patient participation rates in clinical trials is a global problem currently attracting much attention as it slows down the translation of research into clinical practice. Developing new strategies for addressing this problem was part of the 2009 strategic planning effort.

Reducing Health Disparities

- Projects involving health disparities have been explicitly encouraged in each of the Program's Calls for Grant Applications. Prior to the second round of 2009 awards, four projects specifically related to reducing health disparities were funded.

- The FY 2010-2011 Calls for Grant Applications released as this report goes to press includes solicitations that more directly target research in meeting the needs of Florida's disparate populations.

- Developing new strategies for addressing this goal was a major emphasis of the 2009 strategic planning work.

The following pages provide more information on the early outcomes of Bankhead-Coley Program grants in four specific areas:

- Leveraging funding to win new awards
- Accelerating research through collaboration
- Expanding research knowledge and capacity
- Increasing innovation

Leveraging Funding to Win New Awards

From January 2007 through October of 2009, the Bankhead-Coley Program has committed over $36 million in 124 grant awards to cancer researchers working at 12 different public and private research institutions throughout Florida.

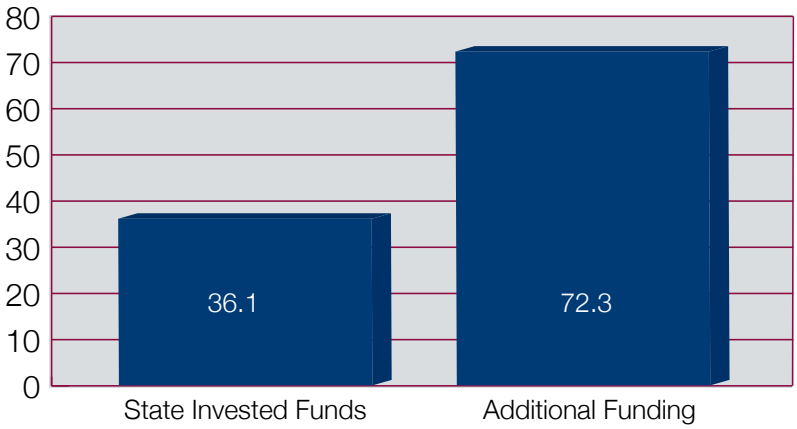


Figure 3 – State Invested Funds versus Additional Funding

The Program sponsors meaningful projects in their own right, but also leverages the state's investment by helping researchers compete nationally for Florida's share of the billions of dollars available in federal grants and other sources of cancer research funding.

Program investments have begun to yield high returns in attracting additional funding from outside Florida. Between June of 2007 and October of 2009, Bankhead-Coley awardees have already leveraged their grants to win $72.3 million in additional cancer research funding as shown in Figure 3.

Refer to Appendix B for a list of follow-on awards reported in 2009 by Bankhead-Coley researchers.

One particular grant mechanism, the **Bridge Grant**, has been a lifeline for Florida scientists and their cancer research. These awards help experienced investigators continue research initiatives during gaps in their federal funding, and provide time to collect more data and prepare winning federal grant applications. In

William Harrington, M.D.
Izidore Lossos, M.D.
Glen Barber, Ph.D.

University of Miami

2007 Specialized Programs of Research Excellence Grant

Nine years ago, a team of Florida's top researchers started testing a potential treatment for viral lymphomas and leukemia. "Viral lymphomas are very common in the Florida region, especially in Southern Florida, so we've tried to tailor our treatment to our patients' needs," explained team member, Dr. Glen Barber. In 2007, the team, consisting of Drs. Harrington, Lossos, and Barber, won a multi-project Bankhead-Coley grant to accelerate progress and increase their chances of obtaining further data to procure national funding.

The momentum shot to the next level early this year with the award of a $7 million prestigious P01 (Program Project) international grant from the National Institutes of Health. Clinical trials are pending approval, anticipated by year's end.

The team's principal investigator, Dr. Harrington, initiated the team's international partnerships with Brazil and sought to understand antiviral resistance in Adult T-cell leukemia/lymphoma. Dr. Lossos focused on developing a model for HIV-associated large cell lymphoma to predict which treatments will work best for individual patients based on gene expression profiles, thus providing targeted, less toxic treatment plans for patients. Dr. Barber's research centered on the use of vesicular stomatitis virus (VSV) as an anti-cancer agent to fight lymphomas and leukemia. He detailed the timeline of moving advances from his lab to patients: "It's taken nine years of basic research with

the first two years these grants were offered, 73 percent of Bridge recipients collectively received over $10.5 million in additional federal funding. As of October 2009, Bridge grant awardees have secured over $47 million toward cancer-related research.

Since the Program's inception three years ago, the first round of grantees that did not bridge to national grant programs have only recently completed their research projects so the potential for follow-on funding has yet to be realized. As more multi-year grants mature and the research results unfold, the financial rate of return for Bankhead-Coley grants will accelerate and so will the pace of cancer research for the benefit of Floridians.

"We used the data from this project to kick-start our next proposal and grant application, and we won a very, very competitive grant. We were able to leverage the $999,999 from Bankhead-Coley funding into a $7 million award."

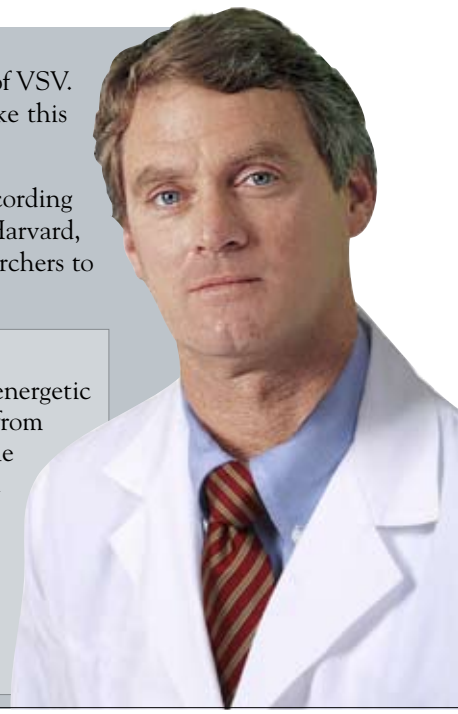
Glen Barber, Ph.D.
University of Miami, 2007 SPORE Planning Grant

funding from sources including the Bankhead-Coley Program to test the efficacy and safety of VSV. The data we generated in the Bankhead-Coley grant will be evaluated to see if we can take this into a variety of clinical trials."

Program funding provides a critical, competitive edge for success at the national level. According to Dr. Lossos, "When Florida researchers compete at the federal level, we are up against Harvard, Stanford, and very established research institutions. Bankhead-Coley funding allows researchers to breach gaps in support and is invaluable."

In Memoriam: William J. Harrington, Jr., M.D.

On January 29, 2009, the Bankhead-Coley Program and Florida's medical community lost an energetic and dedicated physician-scientist when Dr. Harrington (pictured at right) died suddenly from a cerebral hemorrhage at the age of 54. Dr. Barber described Dr. Harrington's invaluable leadership. "Dr. Harrington focused on how these viral malignancies are caused and concentrated on our disparate patient populations in Southern Florida, the Caribbean, and Latin American countries. Among his many contributions, he increased our research base by developing collaborations with Brazilian groups, which increased the number of tumors we can examine, as well as opened up novel clinical trials to help treat these countries' patients." As the work continues, Dr. Harrington's passion and unselfish service for those with viral malignancies will be greatly missed.



Accelerating Research Through Collaboration

The Program has designed multiple strategies to recognize the importance of collaboration in moving cancer research forward.

One strategy has been to provide shared, leading-edge instruments through the **Shared Instrument Grant (SIG)** mechanism that might otherwise be too expensive or impractical for a single scientist, department, or even a single institution to purchase. This strategy was endorsed in August by the state Task Force on the Study of Biotech Competitiveness, which highlighted the value of scientific collaboration, recommending more of it between universities and research centers, including the creation of shared databases and equipment.[5]

One example of a shared resource that the Bankhead-Coley Program has funded is the Illumina® Beadstation 500, an instrument that allows researchers to conduct genetic analysis studies at the rate of one million genetic variations at a time by using synthetic beads. Awarded to Dr. Jennifer Hu, University of Miami, seven different programs within the cancer center use the instrument for cancer research. To date, 20 researchers have used the Beadstation to collect data and prepare grant applications. Currently, eight grants totaling $1.7 million have resulted from data generated through shared use of this new instrument.

W. Jarrard Goodwin, M.D.

Sylvester Cancer Center
University of Miami

2009 Specialized Programs of Research Excellence Planning Grant

Dr. Jarrard Goodwin, head and neck cancer (HNC) surgeon, has initiated a project uniting many of the state's best researchers in an unprecedented HNC project in Florida. A cadre of 13 lab personnel and eight researchers including HNC surgeons/scientists, a medical oncologist, pathologists, epidemiologists, and basic scientists with combined decades of experience are working on four projects. An advisory team, which is a requirement of the SPORE Planning grant, provides another valuable source of input to this work as scientists from Johns Hopkins, University of Pittsburgh, and M.D. Anderson contribute perspective, expertise, and insight to this Florida grant.

As scientists join years of research knowledge with new approaches, Dr. Goodwin says the team "brings a new power" that enables the acceleration of progress. Together, they are exploring the genetic basis for disparities, testing new methods that detect cancer earlier (which is the key in any cancer battle), and using their findings to develop more effective treatments. In particular, Dr. Goodwin's team will study a virus that destroys cancer cells but is harmless to normal cells.

One particularly troubling aspect of this disease the team plans to address is the racial disparities found among HNC patients.

"Although harder to quantify, an additional benefit of shared equipment is collaboration. This Leica Confocal microscope has become a focal point to launch a number of interesting collaborative efforts. Dr. Alexander Ishov, an expert in its use, is frequently sought by other researchers for technical advice. Intrigued by others' research, he has assisted many scientists with their research."

Stephen Sugrue, M.D.
University of Florida, 2006 Shared Instrument Grant

Another Program strategy has been to offer **Specialized Programs of Research Excellence (SPORE) Planning Grants** that drive faster translation of research findings between basic researchers and healthcare providers. These grants require the participation of multi-disciplinary teams, often focusing on a single organ-specific cancer. To date, such efforts have focused on T-cell leukemia/lymphoma; non-Hodgkin's and Hodgkin lymphomas; colon cancer; prostate cancer; melanoma; breast cancer; and head and neck cancer—including the racial disparities seen in this cancer type.

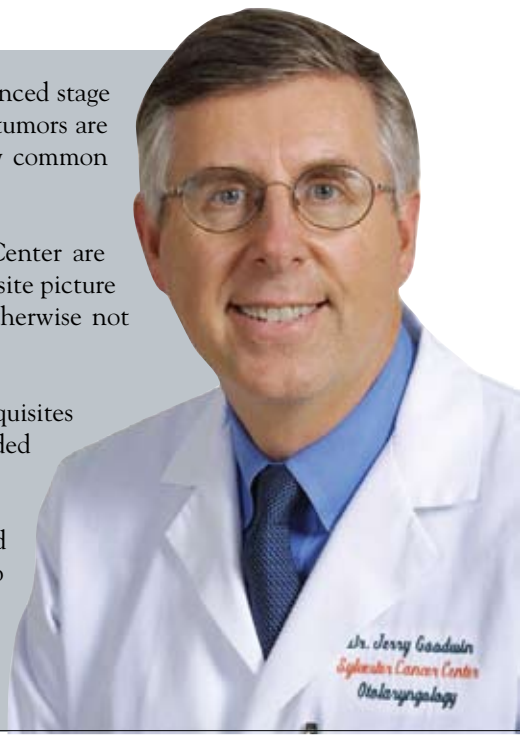
Finally, the newest strategy introduced in the 2009 Special Call is the **Technology Transfer/ Commercialization Partnership (TTCP) Grant**. Patterned after a successful grant mechanism offered by the James & Esther King Biomedical Research Program since 2004, the TTCP is designed to encourage collaboration between academic researchers and small business entrepreneurs. The goal is to stimulate technology transfer activities for research discoveries that could lead to innovative commercialization prospects for cancer treatment, diagnosis, cure, or prevention.

"We know that African Americans are diagnosed at a younger age with a more advanced stage of the disease, in general, and have poorer survival than others. Is this because the tumors are different in genetic make-up? How do genetic factors play a role in this relatively common cancer?"

Both H. Lee Moffitt Cancer Center & Research Institute and Sylvester Cancer Center are contributing tissue samples for the research. This combined effort will bring a composite picture of both Caucasian and African American tumors, enabling study and discovery otherwise not occurring.

The experience and data gained through this project will allow the team to meet prerequisites and apply for large (up to $12.5 million) NCI SPORE grants. Last year, the NCI awarded two HNC SPORE grants nationwide.

According to Dr. Goodwin, "If we didn't have this SPORE Planning grant, we would have to look to private funding sources, and there's just never enough money to go round. We wouldn't be applying for an NCI SPORE, and the work just wouldn't get done . . ."



Expanding Research Knowledge and Capacity

The promise of finding a cure for cancer grows as the number of scientists attacking the problem increases. The Program has provided funds to 89 senior researchers to continue their pursuit of cancer knowledge and awarded grants to 35 new investigators embarking on independent careers in cancer research.

"The Program is enabling Florida science and biotechnology to develop and catch up with some of the states that have had more mature scientific infrastructures. The impetus behind the Program was the Florida Dialogue on Cancer wanting to bring Florida science on a par with states that have many Principal Investigators. The Program is absolutely critical to building Sylvester and other cancer infrastructure."

W. Jarrard Goodwin, M.D.
University of Miami and Director, Sylvester Cancer Center
2009 SPORE Planning Grant

For new investigators, a Bankhead-Coley Program grant allows them to launch independent research labs – hire staff, acquire tools and small equipment, and, most importantly, begin generating preliminary data. According to a report from the National Academies: "The receipt of an [NIH] R01 award is crucial in the career of an early-career researcher and unmatched by any other awards…R01 applications require submission of preliminary data that would predict the success of the proposed project, but new investigators who wish to do something original have difficulty obtaining such preliminary data."[6]

Once established, these new investigators are more likely to stay at their institutions, pursue a research career, and remain in Florida. For example, Dr. Akash Gunjan, 2007 New Investigator Grant (NIR) recipient from Florida State University (FSU), started his lab from scratch at FSU and explained it like this: "My research is very technically and physically challenging. Now that I have hired and trained the right kind of people, I will stay. It's not that easy to start over somewhere else."

According to the Florida Biotech Competitiveness Task Force 2009 report,[7] investing in university science creates a stable academic

Eduardo Sotomayor, M.D.

H. Lee Moffitt Cancer Center & Research Institute

2009 Bridge Grant

The goal of every cancer researcher is to extend life. Dr. Sotomayor has been privileged to see his patients having very good responses, with minimal side effects, to cancer vaccines for two B-cell lymphomas: follicular and Mantle Cell Lymphoma (MCL).

"We are developing vaccines to harness the immune system, educating them to kill certain targets. Patients with follicular lymphomas who are treated with vaccines are living longer. In patients with MCL, a very aggressive and incurable B-cell tumor, we are converting an aggressive disease into a more indolent one. However, vaccines are not the panacea. In this grant, we are looking at specific molecules in the malignant cells that if properly manipulated might allow us to improve the effectiveness of vaccines and make them work in more patients." Dr. Sotomayor envisions a clinical trial in two to three years.

Dr. Sotomayor's group was part of a vaccine trial for patients with follicular lymphomas conducted in selected institutions in the United States. This work was presented as a plenary paper at the 2009 American Society of Clinical Oncology conference, which means it was one of eight featured research stories out of 4,500 submitted abstracts.

environment that helps attract and retain top researchers throughout the state.

The impact of funding 124 principal investigators grows exponentially as they dedicate themselves to training lab professionals and students in research methods and lab techniques and procedures. To date, Program-funded investigators have employed and trained 70 post-doctoral researchers, 29 undergraduate science majors, and 106 other lab workers, including research associates, lab technicians, nurses, and biostatisticians. Additionally, grantees who are new investigators receive mentoring themselves from established researchers in methods and techniques, lab management, and grantsmanship. By expanding and training the life science workforce, the Program attracts more outside research dollars and creates even more high-paying jobs at Florida's universities and in its biomedical industry.

As the Program awards more grants, the number of different organ specific cancers being studied in Florida also grows. (See Figure 4 for a list of cancers studied by Program researchers.) From prevention to basic research to early detection and beyond, the expansion of Florida's cancer research effort produces new, important findings and accelerates the pace of discovery.

Ultimately, the Bankhead-Coley Program is an investment, not just in Florida's knowledge economy, but also in a cancer-free future.

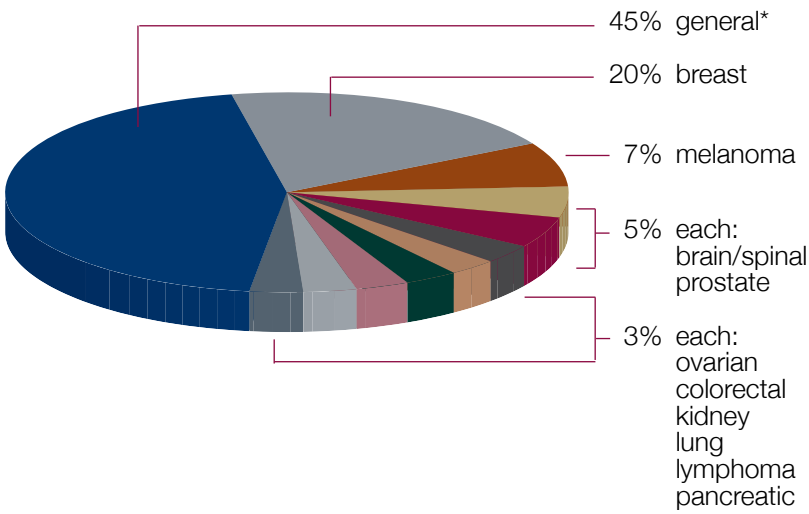


Figure 4 – Types of Cancer Studied by Bankhead-Coley Researchers

**General Cancer includes all cancer that is not organ-specific.*

When the work from a Florida lab is recognized by peers and experts in the field, such recognition speaks of quality research and helps attract more talent to the state.

What drew a researcher like Dr. Sotomayor to Florida? "I came to Florida because I saw opportunities here. I trained at Johns Hopkins and had opportunities around the country. But here I knew I could say 'I built something.' Florida gave me that opportunity."

"Because of my Bankhead-Coley grant, I have been able to add 4 more people to my lab. When I moved here 10 years ago, it was very difficult to recruit scientists to Florida. It is much easier now that we have several high-profile academic institutions in the state. People nationwide are noticing. It gives us momentum."

Beyond continued training, this grant has accelerated progress in the lab. "My federal application scored very well. If I did not have Bankhead-Coley funds, the project would be on hold. Thanks to this grant, I have time now to go back and address the questions from my study section and re-submit my application because I have people working to help me improve it. I am very optimistic about future funding."

Increasing Innovation

An important indicator of the level of innovation of the entire Bankhead-Coley Program is the recognition it earns within the larger scientific community. This recognition takes the form of acceptance of scientific articles for publication in peer-reviewed journals and invitations to present research findings at conferences. Journal articles and presentations offer one way of measuring performance because they must report significant innovation through new findings or breakthroughs to merit dissemination.

Like the attraction of additional funding, performance against these measures will grow as Program-funded research matures. Already, after only three years, Bankhead-Coley researchers have published at least 76 peer-reviewed journal articles and been invited to deliver 129 presentations at scientific meetings. A list of articles published in 2009 based on Program-funded research is included in Appendix C.

In recent years, many have criticized the National Institutes of Health and other granting organizations of reluctance to fund truly new ideas in favor of incremental progress.[8] Faced with many more worthwhile proposals than they can support, federal agencies and private funders tend to choose projects certain to produce favorable findings. In many cases, scientists say, those findings break little new ground. In June, the chief medical officer of the American Cancer Society told *The New York Times*, "the way to get ahead in science [as a career] is staying within narrow parameters and doing what other people are doing …. No one wants to fund wild new ideas."[9]

Omar Zeidan, M.D.

M.D. Anderson Cancer Center Orlando

2008 New Investigator Research Grant

Dr. Omar Zeidan, a medical physicist, is at the leading edge of an innovative new type of cancer treatment called proton radiotherapy. The treatment, which uses a beam of protons to eradicate tumor cells, offers several advantages over traditional radiation.

"In proton therapy, we deliver the dose to the cancerous region while sparing surrounding healthy tissue. Proton therapy requires fewer beams to deliver dose to tumors in comparison to conventional radiation, which requires multiple beams to achieve similar tumor dose coverage."

Reducing damage to surrounding tissue is especially critical in cancers of the brain, spine, eye, and prostate. Above all, children stand to benefit because regardless of cancer type, they are particularly vulnerable to healthy tissue damage from radiation. This therapy holds great promise of improved long-term prognosis and quality of life for cancer patients, more than 50 percent of whom receive radiation.

In an effort to ensure that the Bankhead-Coley portfolio includes a reasonable number of high-risk, high-reward cancer research projects, the Department of Health and the Advisory Council took advantage of a unique opportunity during 2009.

When the NIH chose to use a portion of its American Recovery and Reinvestment Act funding to solicit highly innovative Research Challenge (RC1) projects, the agency received more than 20,000 proposals for approximately 200 available grants. Among the unfunded applications were numerous potentially paradigm-shifting cancer projects from Florida researchers that were very highly rated during the federal review process.

With increased funding made available in 2009, the Program issued a Special Call for Grant Applications specifically asking for RC1 cancer research projects from Florida researchers. The Program will be able to fund some of the best of these projects, which are expected to start in January 2010.

As the work of Bankhead-Coley researchers is recognized for its innovation by the community of scientists both within and beyond Florida, it also enhances the growing reputation of the State's institutions as leaders in cancer research.

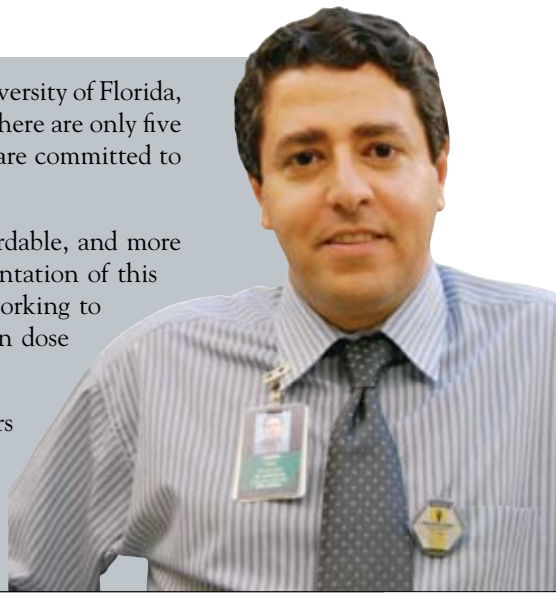
"Continued support of this Program is essential not just for Florida's researchers, but to make the state a major player in medical research at the national level. It is one of the most important factors in attracting scientists and establishing a strong base for medical research."

Omar Zeidan, M.D.
M.D. Anderson Cancer Center, Orlando, 2008 NIR Grant

Today there is one place in the entire Southeast with a clinical proton facility–University of Florida, Jacksonville. (Dr. Zeidan initiated a collaboration with UF for instrument use.) There are only five proton facilities nationwide. According to Dr. Zeidan, several centers in Florida are committed to building proton facilities over the next few years.

"Proton treatment is the hottest topic in cancer therapy. It is getting more affordable, and more people want to acquire it. We have a responsibility to ensure accurate implementation of this technology. We need appropriate quality assurance tools, and that's what I'm working to develop with my Bankhead-Coley grant–a radiation dosimeter to validate proton dose delivery."

"Florida's Biomedical Research Program is a great mechanism for young investigators like me to launch a successful research career," explained Dr. Zeidan. "It is very hard for young investigators to compete at the national level against experienced investigators. I believe new findings from this project will greatly enhance my chances to get NIH type funding in the near future."



Program Evaluation

Program evaluation has occurred at the national and state level. In 2007, at the Program's request, the NCI evaluated the Program's peer review and funding processes. In 2009, the Department of Health began an internal evaluation; in the summer of 2009, the Florida Senate conducted a statutorily mandated review.

National Program Evaluation and Recognition

Together with the James & Esther King Biomedical Research Program, the Bankhead-Coley Program has earned national recognition.

In late 2007, the NCI added these two programs, under the umbrella of the Florida Biomedical Research Programs, to its list of only 17 funding programs in the country meeting its rigorous standards for peer review.[10] Of these 17 programs, only one other is a state-level program. This means that cancer centers in Florida can count research grants from the Bankhead-Coley or James & Esther King Program toward their required research base in qualifying for and maintaining multi-million dollar NCI Cancer Center Support Grants (CCSG).

Florida is significantly underrepresented in the nation's NCI-designated cancer centers, with only two in 2009 (H. Lee Moffitt Cancer Center & Research Institute in Tampa and Mayo Clinic in Jacksonville). Refer to Table 1 for national cancer rankings and corresponding NCI-designated centers. At the time this report was prepared, three other Florida institutions were seeking NCI designation: M.D. Anderson Cancer Center in Orlando, University of Florida's Shands Cancer Center in Gainesville, and University of Miami's Sylvester Cancer Center in Miami.

Table 1 – Cancer Statistics and Number of NCI Cancer Centers

	Estimated New Cancer Cases in 2009[11]	Estimated Cancer Deaths in 2009[12]	Number of NCI Cancer Centers[13]
California	152,170	54,600	10
Florida	102,210	41,270	2
New York	101,500	34,190	6
North Carolina	42,270	18,550	3
Tennessee	32,570	13,340	2

By earning this important NCI recognition, the Bankhead-Coley Program is helping close this gap by providing all five of Florida's cancer centers with an important advantage in competing for and retaining NCI Cancer Center designation,[14] along with the accompanying multi-million dollar federal awards.

State Program Evaluation

When the Bankhead-Coley Program was established in 2006, the Legislature required a review of its performance, outcomes, and financial management during the 2010 Regular Session of the Legislature. The statute establishing the program expires January 1, 2011, unless reviewed and reenacted by the Legislature before that date (see Appendix A).

External Program Evaluation

Interim Report 2010-219 entitled *"Biomedical Research Programs–Performance, Outcomes and Financial Management,"* published in September 2009 by the Senate Committee on Health Regulation, reports the results of its evaluation of the Bankhead-Coley Program and the James & Esther King Biomedical Research Program.

The Recommendations section of this report contains the following statements:

> Senate professional staff recommends that the Legislature re-enact the King Program and the Bankhead-Coley Program. These programs are achieving the goals established in statute and are benefiting the state in a variety of tangible and intangible ways. The Bankhead-Coley Program is expanding cancer research capacity in this state, improving research and treatment through clinical trials, and undertaking activities to reduce the impact of cancer on disparate groups.
>
> The 2009 Legislature identified a recurring source of funding for these two programs that will provide stability and solidify the state's commitment to invest in biomedical research. This will enhance Florida's competitive position for external funding opportunities and attracting additional biomedical and biotechnology industry to the state.

Internal Program Evaluation

The Department has begun an internal assessment of the Bankhead-Coley Program that is patterned after its comprehensive internal program evaluation of the James & Esther King Biomedical Research Program. These internal program evaluations are multi-pronged, long-term endeavors and include:

- Customer satisfaction surveys of applicants, grantees, research institute administrative personnel, and other customer groups
- Creation of a database and processes for the systematic collection, storage, and reporting of grant outcome data such as presentations, publications, invention disclosures, and patents
- Periodic collection, storage, and reporting of program performance information including deadlines met, number of customers served, and milestones reached

The internal program evaluation will be used to improve operations and service as well as monitor progress towards Program goals.

Planning for the Future

The recent increase in state funding is an important endorsement of the Bankhead-Coley Program's ability to identify and capitalize on strategic opportunities to enhance Florida's cancer research capabilities.

In recognition of this fact, the Advisory Council and Program staff dedicated substantial effort in the 4th quarter of 2009 to developing a five-year strategic plan. To assist with the process, the Program engaged AltshulerGray LLC, a nationally-recognized firm with expertise in strategy consulting for biomedical research enterprises.

The Program began the planning process in September by conducting a series of three 90-minute conference calls for Program staff, the Advisory Council, and interested members of the public. Topics for these initial planning meetings included:

- Funding basic science for overcoming research challenges in applying laboratory findings and preclinical studies to the development of trials and studies in humans
- Funding research aimed at overcoming barriers to the adoption of best practices in the community, especially as it relates to research in implementation of practices and health disparities
- Learning from other states' efforts to facilitate research

Meetings included brief presentations from one or more invited speakers and a discussion among call participants on implications to the Program. With the benefit of this background work, the planning effort continued in a two-day working session in Orlando in mid-November.

While the results of these efforts are still being documented as this report goes to press, more information can be found on the Program website, www.floridabiomed.com.

Recommendation to Further the Program's Purpose

According to (s.) 381.922(2) (a), *F.S.*, the Program is scheduled to expire January 1, 2011, unless reenacted by the Legislature before that date. The 2010 Legislature will determine the most appropriate funding source and means of funding these programs.

Based on the Program goals, benefits, and accomplishments evidenced in this Annual Report, the Biomedical Research Advisory Council strongly recommends the re-enactment of the Bankhead-Coley Program, with funding to be maintained at 2.5 percent of the revenue generated from the cigarette surcharge enacted in 2009, not to exceed $25 million per year.

2009 Grant Awards

Planning for the FY 2009-2010 awards began with the assumption that the funding cycle would be similar to the previous year, and the Program anticipated awarding $5-$8 million based on prior year appropriations. However, the Program experienced two significant changes in funding levels during 2009 that affected the grant award cycle.

Early in the year, Florida's budget challenges necessitated a 25 percent budget reduction. Then, during the 2009 Regular Session of the Legislature, Florida lawmakers approved a cigarette surcharge and allocated part of those revenues to the Program, more than doubling Program funding for FY 2009-2010.

The Program took quick action to put the additional funding to work by restoring prior grant reductions and cancellations on multi-year grants. The Advisory Council then recommended $11 million in funding for projects for FY 2009-2010 from the applications submitted in February and peer reviewed in March and April. Historically, the Program has received more qualified grant applications than it could fund, so the Advisory Council was able to recommend more grants for funding without compromising its high standards for scientific merit. Finally, the Advisory Council recommended a second funding competition to make additional FY 2009-2010 awards. The 2009-2010 Special Call for Applications, issued in August 2009, offered different grant mechanisms than the regular Call in order to meet additional Florida cancer research needs.

This report includes an account of applications received in response to the Special Call; however, as this report goes to press, the Program had not yet made Special Call award announcements. These grants are expected to start January 1, 2010.

Results for the Regular Annual FY 2009-2010 Call for Grant Applications

Table 2 - Grant Mechanisms Offered in Regular Annual Call

Grant Type	Purpose	Maximum Amount & Duration
Bridge Grant	To provide interim support for promising cancer research projects that have been highly rated by national panels of scientific peer reviewers in recent federal competitions but were not funded due to budgetary constraints. Researchers use the Bridge grant to collect preliminary data and improve their national applications based on peer review feedback.	$200,000 for one year
New Investigator Research (NIR) Grant	To foster development of new investigators so they can undertake independent research that will be competitive for national research funding. New investigators are those who have been full-time faculty for less than six years and have not received a large (over $100,000) peer-reviewed national grant. A senior researcher serves as a mentor.	Up to $125,000 per year for three years
Clinical Research Planning (CRP) Grant	To increase the likelihood of success in research projects involving clinical investigations (clinical trials) of new drugs, biologics, and devices intended for licensure by the Food and Drug Administration, and behavioral studies.	$100,000 for one year
Specialized Program of Research Excellence (SPORE) Planning Grant	To assemble and prepare strong interdisciplinary teams of Florida researchers to plan and compete successfully for NCI SPORE grants. Teams collect preliminary data and conduct and translate basic research findings from the laboratory to a clinical/patient setting.	Up to three years and a maximum of $1,000,000

In the regular FY 2009-2010 Call released on December 1, 2008, the Program solicited applications for the grant mechanisms described in Table 2 above.

In response, the Program received 65 proposals requesting a total of $21.8 million. Over half of all the applications were for New Investigator Research Grants, 37 percent sought Bridge Grants, and 6 percent applied for SPORE Planning Grants. As anticipated, the Program received only a small number of applications for the SPORE Planning Grant due to the magnitude of the work and the high degree of collaboration and interdisciplinary research involved.

While disappointed by the lack of applications for the CRP Grant, the Program is continuing to explore effective grant mechanisms that will produce better outcomes in clinical trials research.

The Program completed the application review and award process in June 2009, and the Advisory Council recommended funding 39 research grants totaling nearly $11.4 million to begin July 1, 2009. This action resulted in an overall award-to-proposal ratio of 60 percent, compared to success rates of fewer than 20 percent for NIH. Table 3 summarizes applications received and awarded.

Table 3 – 2009 Grant Applications Received/Awarded in Annual Call

Grant Mechanism	Applications Received	Applications Awarded	Percent of Applications Awarded	Awarded Funding Amounts
Bridge Grant	24	22	92%	$ 3,773,358
New Investigator Research	37	15	41%	$ 5,606,114
Clinical Research Planning Grant	0	0	0%	$ 0
Specialized Program of Research Excellence	4	2	50%	$ 2,000,000
Total	**65**	**39**	**60%**	**$ 11,379,472**

Of the 2009 awards, 49 percent of grant funds were allocated for New Investigator Research Grants, and 33 percent were for Bridge Grants. The remaining 18 percent of the available funding was dedicated to two SPORE Planning Grants.

Public and private research institutes throughout Florida are benefiting from these awards. This year the Program awarded grants to 12 Florida research institutions as shown in Figure 5.

Refer to Appendix D for the FY 2009-2010 grantee information including principal investigator, institution, award amount, project title, and abbreviated abstract.

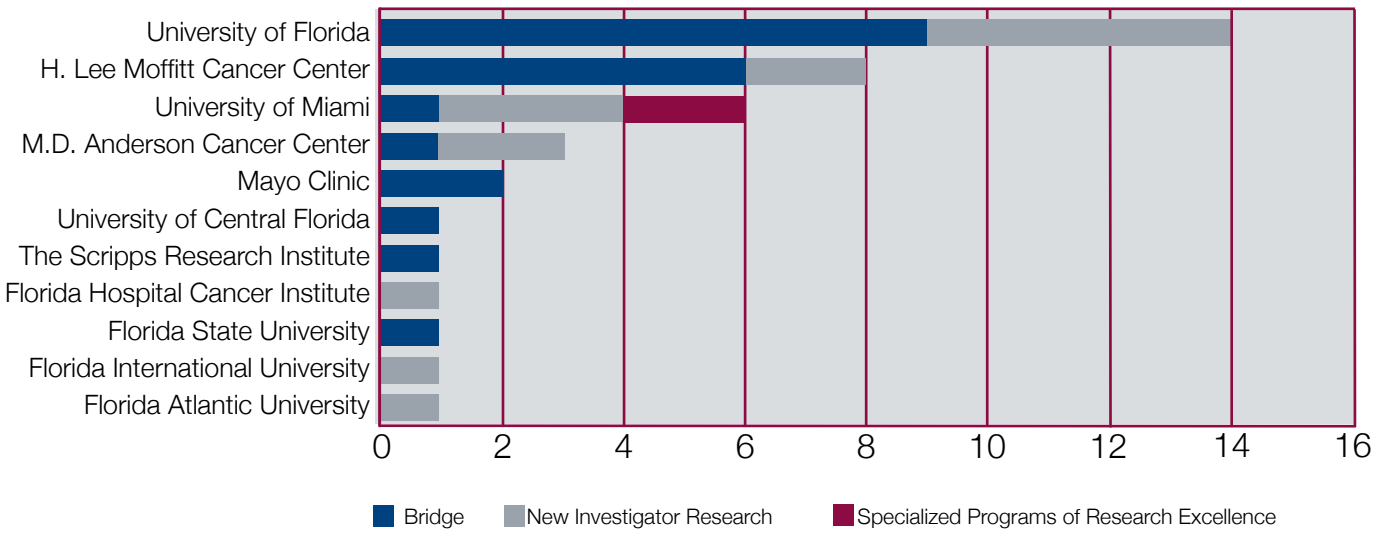


Figure 5 – 2009 Annual Grants Awarded by Institution

Preliminary Results for the 2009-2010 Special Calls for Grant Applications

Table 4 - Grant Mechanisms Offered in Special Call

Grant Type	Purpose	Maximum Amount & Duration
Florida Research Challenge (RC1) Grant	To provide support for promising high-risk, high-reward cancer research proposals submitted by Florida investigators to the NIH in response to its "2009 Challenge Grants in Health and Science," seeking highly innovative research projects.	Not to exceed $1,000,000 in two years
Shared Instrument Grant (SIG)	To support Florida investigators who are conducting cancer research by improving access to state-of-the-art research instruments that can only be justified on a shared-use basis and for which meritorious cancer research projects are described.	Range $100,000 to $500,000 for a single instrument
Technology Transfer/ Commercialization Partnership (TTCP) Grant	To encourage the collaboration of investigators at eligible institutions and small businesses; stimulate technology transfer activities for promising research discoveries that could lead to innovations in the prevention, diagnosis, treatment, or cure of cancer; and strengthen a project's economic feasibility and commercialization prospects.	$100,000 for one year

In August, the Program released a second set of "Special" Calls for Applications, offering grant mechanisms described in Table 4 above.

While a form of the TTCP grant has been offered by the James & Esther King Biomedical Research Program since 2004, this was the first year the Bankhead-Coley Program offered this type of grant. In order to be responsive to time-sensitive market opportunities, the TTCP Call for Applications invited applications at any time up to February 2010, with funding decisions announced within 60 days of application receipt. To facilitate this quick response, the Advisory Council recommended a pre-established peer review merit threshold for Department use in making final award decisions.

In this second competition round, 35 eligible applications have requested a total of $20 million. Table 5 provides a breakdown of the requests across the offered grant mechanisms.

The Advisory Council considered the results of the peer review of Florida Research Challenge Grant and Shared Instrument Grant applications and made funding recommendations during a public meeting held in late November. After final approval by the State Surgeon General, awards were announced in early December, as this report was in press. These projects will begin in January 2010.

For information about the research projects funded in this second round, please visit the website, www.floridabiomed.com.

Table 5 - Grant Applications Received in Special Call

Grant Mechanism	Applications Received	Requested Funding Amount
Research Challenge Grant	19	$ 13,239,033
Shared Instruments Grant	15	$ 6,723,712
Technology Transfer Commercialization Grant	1*	$ 99,745
Total	**34**	**$ 20,062,490**

** As of 10/30/2009*

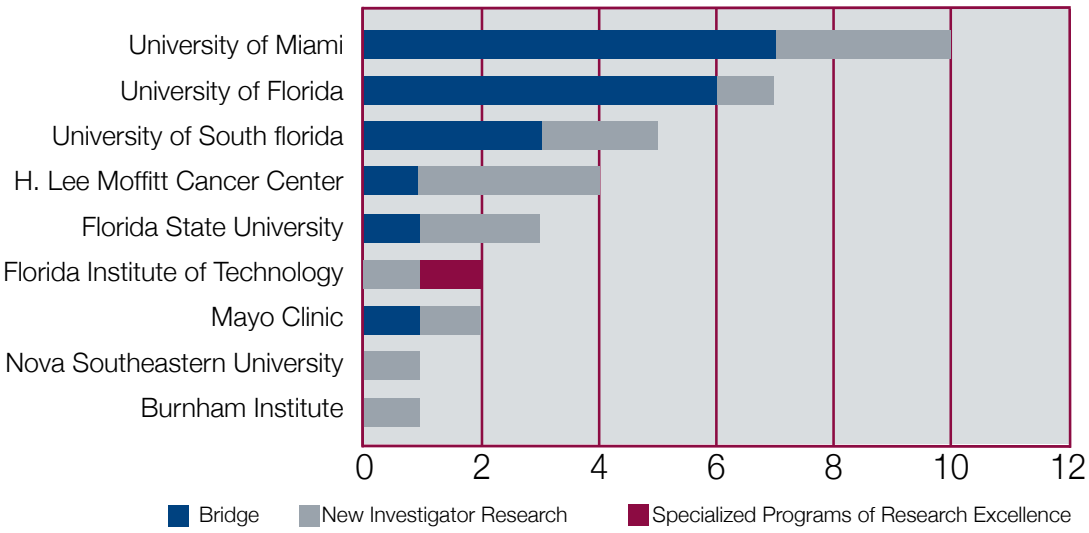


Figure 6 - Grant Applications Received by Institution

Biomedical Research Advisory Council

Section 381.922, *F.S.*, charges the Program with awarding grants for cancer research through the Bankhead-Coley Cancer Research Program (included in Appendix A). The Advisory Council meets this directive by advising the Office of Public Health Research at the Department of Health and the Florida State Surgeon General regarding the direction and scope of the Program and assists in developing guidelines to ensure fairness, neutrality, and adherence to the principles of merit and quality in the conduct of the Program. The Advisory Council also functions in the same role for the James & Esther King Biomedical Research Program.

Veena Antony, M.D.
Chief of Pulmonary, Critical Care and Sleep Medicine
Professor
College of Medicine
University of Florida
Seat: American Lung Association
Appointed: July 1, 2007

Albert Latimer, B.B.A.
Senior Vice President
External Affairs & Investor Relations
Enterprise Florida, Inc.
Seat: General Public
Appointed: February 27, 2006

Richard J. Bookman, Ph.D.
Executive Dean for Research & Research Training and Vice Provost for Research
Miller School of Medicine
University of Miami
Seat: Advisory Council Chair and American Heart Association
Appointed: July 1, 2000

Daniel Morris, M.D.
Medical Physician
Medical Oncology and Hematology
Naples Medical Center
Seat: Senate-Cancer Program (ACoS)
Appointed: July 17, 2006

Randal Henderson, M.D., MBA
Associate Medical Director of Proton Therapy Institute
Professor/Medical Director
Department of Radiation Oncology
University of Florida
Seat: House – Cancer Program (ACoS)
Appointed: April 20, 2007

Sigurd Normann, M.D., Ph.D.
Professor
College of Medicine
Department of Pathology, Immunology, and Laboratory Medicine
University of Florida
Seat: American Cancer Society
Appointed: July 1, 2000

Myra Hurt, Ph.D.
Associate Dean, Research and Graduate Programs
Professor
Department of Biomedical Sciences
College of Medicine
Florida State University
Seat: Research University
Appointed: February 27, 2006

Edith Perez, M.D.
Professor of Medicine
Hematology/Oncology
Mayo Clinic
Seat: Senate-Cancer Program (ACoS)
Appointed: August 12, 2009

Among the significant contributions of the Advisory Council are the recommendations of specific grant mechanisms and eligibility requirements to achieve the statutory goals of the Program. The Advisory Council follows strict measures to avoid conflicts-of-interest in making funding recommendations to the State Surgeon General, relying primarily upon the outcome of the independent scientific peer review process.

Notable changes to the Advisory Council membership in 2009 were a rotation in designated representatives of a cancer program approved by the American College of Surgeons appointed by the President of the Senate from Daniel Morris, M.D., to Edith Perez, M.D., and the reappointments of Myra Hurt, Ph.D. and Albert Latimer. A sincere thank you is also given to Clarence Brown III, M.D. and Paul Hull for serving as alternates in the American Cancer Society seat during the absence of Sigurd Normann, M.D., Ph.D.

Penny Ralston, Ph.D.
Dean Emeritus and Professor
College of Human Sciences
Florida State University
Seat: Senate-Behavioral/Social Research
Appointed: July 17, 2006

Herbert Weissbach, Ph.D.
Distinguished Research Professor and Director
Center for Molecular Biology and Biotechnology
Department of Biological Sciences
Florida Atlantic University
Seat: Advisory Council Vice-Chair and Biomedical Research
Appointed: February 27, 2006

Mary Lou Sole, R.N., Ph.D., CCNS, FAAN
Professor
College of Nursing
University of Central Florida
Seat: House – Professional Medical Organization
Appointed: April 19, 2007

The 11 appointees to the Biomedical Research Advisory Council:

- One representative of the Florida Division of the American Cancer Society
- One representative of the Greater Southeast Affiliate of the American Heart Association
- One representative of the American Lung Association of Florida
- Four members appointed by the Governor, two with expertise in biomedical research
- One from a Florida research university
- One representing the Florida general population
- Two members appointed by the President of the Florida Senate: One with expertise in behavioral or social research and one from a cancer program approved by the American College of Surgeons (ACoS)
- Two members appointed by the Speaker of the Florida House of Representatives: One from a professional medical organization and one from a cancer program approved by ACoS

Program Operations

For reasons of timing in publishing this report, the information reported in Table 6 only includes those grants awarded prior to October 2009, and therefore does not include the grants from the Special Call.

Through July 2009, the Bankhead-Coley Program has awarded 124 grants since inception, representing $36.1 million in research funding. The following table outlines the number of grant applications received and the number, type, and total value of grant awards extended for each of the Program's four years to date.

Table 6 - Program Award History

Award History

	FY 2006-07		FY 2007-08		FY 2008-09		FY 2009-10*	
Applicants	47		35		57		65	
Awards	No.	Million	No.	Million	No.	Million	No.	Million
Bridge 1 yr.	23	3.8	11	2.0	15	2.5	22	3.8
Bridge 2 yr.**	3	0.9	n/a	n/a	n/a	n/a	n/a	n/a
NIR	n/a	n/a	10	3.6	10	3.7	15	5.6
SEP	n/a	n/a	2	0.9	n/a	n/a	n/a	n/a
SIG	7	3.4	n/a	n/a	n/a	n/a	n/a	n/a
SPORE	n/a	n/a	2	2.0	2	1.9	2	2.0
Total	**33**	**$8.10**	**25**	**$8.50**	**27**	**$8.10**	**39**	**$11.40**

**Results of the Special Call were not available at time of press*
***Only offered to new investigators in 2006-07*

Program Management

The Office of Public Health Research, within the Department of Health, manages the Bankhead-Coley Program. In addition to the support from the Advisory Council, the Department of Health relies on the assistance of a contracting partner, Lytmos Group, Inc., to assist in matters of program oversight and administration.

Jointly, the Office of Public Health Research and the Lytmos Group team fulfill a number of behind-the-scenes responsibilities, providing a seamless interface to support applicants, grantees, and the Advisory Council. See Table 7 for key activities that support Program operations.

Table 7 - Key Program Operation Activities

Program Area	Activities
Program Planning and Development	• Plan and implement Program logistics and funding cycles • Prepare and release the Call for Grant Applications • Develop and refine Program policies and procedures and Program materials
Application Processing	• Prepare for, accept, and process online applications and provide technical assistance • Complete an administrative review of applications, checking compliance with all requirements
Peer Review Management	• Develop evaluation materials • Recruit, assign, and manage peer reviewers for scientific reviews of applications and progress reports • Maintain confidentiality agreements and monitor peer reviewer conflicts of interest • Monitor peer reviewer performance to ensure quality reviews
Decision Support	• Analyze and report competition statistics and data • Provide funding decision aids • Provide Advisory Council support
Applicant and Grantee Support	• Provide ongoing Program and technical support from application through project work to grant completion
Administrative and Programmatic Monitoring	• Evaluate financial reports and budget changes; monitor grants for financial and scientific concerns • Review scientific and technical progress, conduct independent progress assessments, conduct site visits, and process project protocol change requests • Ensure compliance with human and animal use regulations • Process continuation and no-cost extension requests
Program Evaluation and Improvements	• Monitor and implement process and technology improvements • Work with the Advisory Council to compare the Program against benchmarks, review and update long-term goals, and assist with strategic planning
Technical Support	• Provide automated application processing, grant management systems support, and website development and maintenance (www.floridabiomed.com)

How Grants are Awarded

The Program typically follows an annual cycle for soliciting applications and making awards, as illustrated in Figure 7 below. The 2009 Special Call followed the same steps outlined in the annual funding cycle but was performed on an accelerated schedule with funding recommendations by the council made in November. In evaluating proposals, the Program draws on the expertise of more than one hundred independent subject matter experts from outside Florida. These peer reviewers evaluate grant applications that match their specific expertise, rating scientific and technical merit and fit with programmatic goals. Unlike other peer review processes in which reviewers consult with each other, these reviews are performed independently and average scores compiled. To highlight the validity of this approach, the Program sought and received recognition from the NCI as having an approved peer review process.

In making funding recommendations, the Advisory Council considers a number of factors about each application without knowing the names of the researchers, their institutions, or the proposal titles in order to avoid conflicts-of-interest. They consider the peer review scores for scientific merit, cancer relatedness, and degree of collaboration, along with categories of research to develop a funding plan across all grant types, within budget constraints.

After awards are announced, the Program obtains signed contracts, final budgets, and human subject and animal study approvals from grantees.

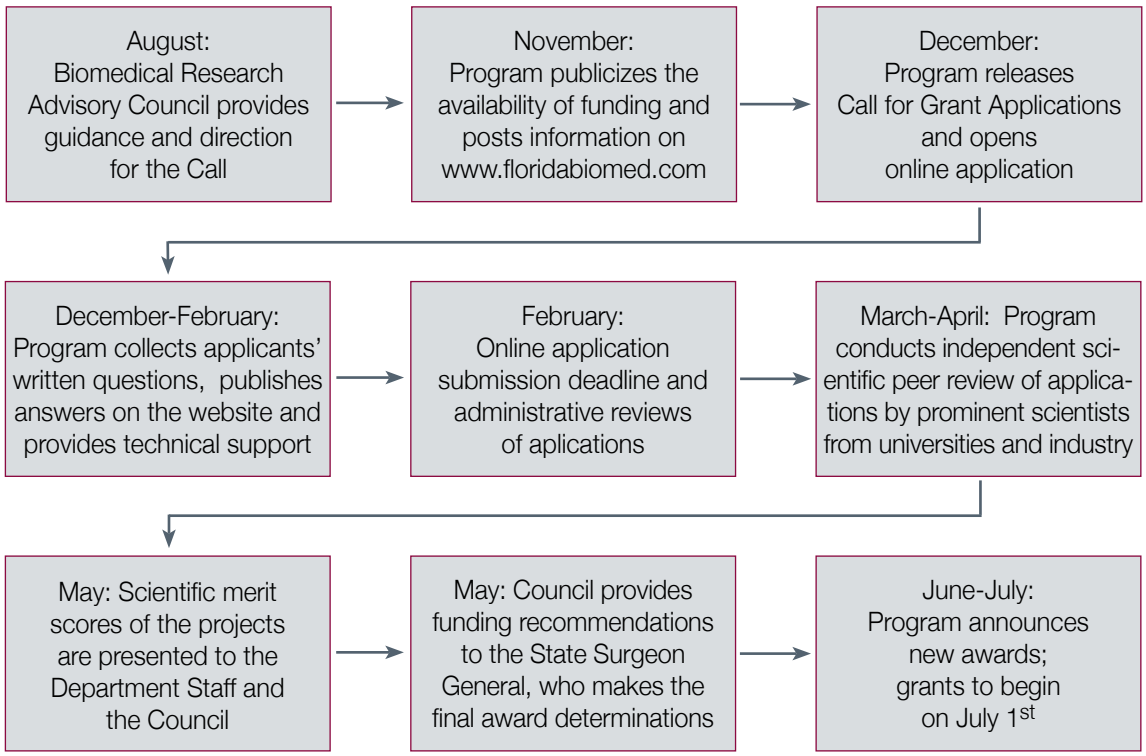


Figure 7 - The Annual Funding Cycle

Table 8 - Grant Management Processes and Tools

	Process or Tool	Value
Internal Controls	Signed terms and conditions (contract) with schedule of deliverables	• Defines expectations
	Grant Administration Manual	• Clarifies policies and procedures • Helps grantees comply with requirements
	Web-based system	• Provides grantees with convenient report submission • Serves as central data center • Provides efficient review of post-award deliverables
Financial Management	Regular review of budgets, financial reports, and expenditure changes	• Assures fiscal accountability
	Analysis of spending patterns	• Identifies potential accounting problems or project delays
Performance Management	Project work plans and research milestone charts	• Provides measurement framework
	Peer review of annual progress reports for multi-year grants	• Obtains informed progress assessment • Provides additional mentoring to grantees
	Periodic site visits	• Validates project progress • Checks institutional controls • Solicits stakeholder feedback • Promotes the Program to increase applicant pool

How Grants are Managed

The Program uses tools and processes to ensure financial and research accountability, to support grantees, and to maintain compliance with grant terms and conditions, as illustrated in Table 8. Reporting requirements are intended to ensure progress rather than add administrative burden.

Annual renewal of multi-year grants is dependent on satisfactory performance as well as the availability of funds.

Feedback from stakeholders—including potential applicants, principal investigators, sponsored research office officials, and technology transfer offices, among many others—is highly valued and drives the Program's emphasis on making continuous improvement.

Impacts of FY 2008-2009 Budget Reduction

As an outcome of the special legislative session to address the State's revenue shortfall, the Program's FY 2008-2009 budget was cut by

$2.25 million in January 2009. In response, the Program first reduced its remaining administrative expenses by canceling all remaining grantee site visits for the year and scaling back on the number of peer reviews of Bridge Grant applications in the FY 2009-2010 spring competition. The Department negotiated a corresponding reduction in its contract with Lytmos Group.

Then, to address the balance of the reduction, the Program reduced its commitment to four New Investigator Research grants from three years to one, and reduced all other FY 2008-2009 grants by up to 10 percent.

Impacts of FY 2009-2010 Budget Increase

During the regular session in 2009, the Legislature eliminated the general revenue appropriation and provided that 2.5 percent of the revenue generated from the cigarette surcharge enacted in 2009, not to exceed $25 million per year, was to be transferred into the Biomedical Research Trust Fund for the Bankhead-Coley Program.

Prior to awarding any new grants to begin July 1, the Program elected to restore its original funding commitments to the four cancelled FY 2008-2009 grants as well as all other FY 2008-2009 multi-year grants whose budgets had been reduced. In addition, the Program resumed making grantee site visits and released a set of Special Calls for Applications in August, with awards announced in December. These research projects are expected to begin January 1, 2010.

Program Administrative Costs

The Program by statute can use up to 10 percent of the appropriated funds for administrative expenses. As shown in Table 9 below, Program staff has held administrative costs below this statutory limit.

Grant money that is obligated but not disbursed by the end of the fiscal year is carried forward to pay out multi-year grants in subsequent years.

Table 9 - Program Expenditures (Millions)

Fiscal Year	Appropriation	Grant Expenses	Percent	Administrative Expenses	Percent*
FY 09-10	24.98[a]	12.3[b]	n/a[c]	1.4[d]	6%
FY 08-09[e]	6.75	6.08	90%	0.66	10%
FY 08-09[f]	9.00	8.10	90%	0.81	9%
FY 07-08	9.00	8.15	91%	0.73	8%
FY 06-07	9.00	8.10	90%	0.82	9%
Total (excluding FY 09-10)	**24.75**	**22.33**	**90%**	**2.21**	**9%**

[a] *Annualized based on revenues collected for July, August, and September 2009.*
[b] *As of October 2009.*
[c] *At press time, a second round of funding was underway which will result in additional awards expected to begin January 2010.*
[d] *Projected expenses.*
[e] *Mid-year revision due to budget reduction.*
[f] *Original grant awards and projected expenses prior to mid-year budget reduction.*

Appendix A. Section 381.922, *Florida Statutes* – William G. "Bill" Bankhead, Jr., and David Coley

(1) The William G. "Bill" Bankhead, Jr., and David Coley Cancer Research Program, which may be otherwise cited as the "Bankhead-Coley Program," is created within the Department of Health. The purpose of the Program shall be to advance progress towards cures for cancer through grants awarded through a peer-reviewed, competitive process.

(2) The Program shall provide grants for cancer research to further the search for cures for cancer.

(a) Emphasis shall be given to the goals enumerated in s. 381.921, as those goals support the advancement of such cures.

(b) Preference may be given to grant proposals that foster collaborations among institutions, investigators, and community practitioners; as such, proposals support the advancement of cures through basic or applied research, including clinical trials involving cancer patients and related networks. (3)(a) Applications for funding for cancer research may be submitted by any university or established research institute in the state. All qualified investigators in the state, regardless of institutional affiliation, shall have equal access and opportunity to compete for the research funding. Collaborative proposals, including those that advance the Program's goals enumerated in subsection (2), may be given preference. Grants shall be awarded by the 1State Surgeon General, after consultation with the Biomedical Research Advisory Council, on the basis of scientific merit, as determined by an open, competitive peer review process that ensures objectivity, consistency, and high quality. The following types of applications shall be considered for funding:

1. Investigator-initiated research grants.
2. Institutional research grants.
3. Collaborative research grants, including those that advance the finding of cures through basic or applied research.

(b) In order to ensure that all proposals for research funding are appropriate and are evaluated fairly on the basis of scientific merit, the 1State Surgeon General, in consultation with the council, shall appoint a peer review panel of independent, scientifically qualified individuals to review the scientific content of each proposal and establish its priority score. The priority scores shall be forwarded to the council and must be considered in determining which proposals shall be recommended for funding.

(c) The council and the peer review panel shall establish and follow rigorous guidelines for ethical conduct and adhere to a strict policy with regard to conflicts of interest. A member of the council or panel may not participate in any discussion or decision with respect to a research proposal by any firm, entity, or agency with which the member is associated as a member of the governing body or as an employee or with which the member has entered into a contractual arrangement. Meetings of the council and the peer review panels are subject to chapter 119, s. 286.011, and s. 24, Art. I of the State Constitution.

(4) By December 15 of each year, the Department of Health shall submit to the Governor, the President of the Senate, and the Speaker of the House of Representatives a report indicating progress towards the Program's mission and making recommendations that further its purpose.

(5) Beginning in fiscal year 2006-2007, the sum of $9 million is appropriated annually from recurring funds in the General Revenue Fund to the Biomedical Research Trust Fund within the Department of Health for purposes of the William G. "Bill" Bankhead, Jr., and David Coley Cancer Research Program and shall be distributed pursuant to this section to provide grants to investigators seeking cures for cancer, with emphasis given to the goals enumerated in s. 381.921. From the total funds appropriated, an amount of up to 10 percent may be used for administrative expenses.

(6) By June 1, 2009, the Division of Statutory Revision of the Office of Legislative Services shall certify to the President of the Senate and the Speaker of the House of Representatives the language and statutory citation of this section, which is scheduled to expire January 1, 2011.

(7) The Legislature shall review the performance, the outcomes, and the financial management of the William G. "Bill" Bankhead, Jr., and David Coley Cancer Research Program during the 2010 Regular Session of the Legislature and shall determine the most appropriate funding source and means of funding the Program based on its review.
(8) This section expires January 1, 2011, unless reviewed and reenacted by the Legislature before that date.

History.--s. 8, ch. 2006-182; s. 32, ch. 2008-6; s. 2, ch. 2009-5; s. 4, ch. 2009-58.

Section 381.921, *Florida Statutes* – Florida Cancer Council Mission and Duties

The council, which shall work in concert with the Florida Center for Universal Research to Eradicate Disease to ensure that the goals of the center are advanced, shall endeavor to dramatically improve cancer research and treatment in this state through:

(1) Efforts to significantly expand cancer research capacity in the state by:
  (a) Identifying ways to attract new research talent and attendant national grant-producing researchers to cancer research facilities in this state;
  (b) Implementing a peer-reviewed, competitive process to identify and fund the best proposals to expand cancer research institutes in this state;
  (c) Funding through available resources for those proposals that demonstrate the greatest opportunity to attract federal research grants and private financial support;
  (d) Encouraging the employment of bioinformatics in order to create a cancer informatics infrastructure that enhances information and resource exchange and integration through researchers working in diverse disciplines, to facilitate the full spectrum of cancer investigations;
  (e) Facilitating the technical coordination, business development, and support of intellectual property as it relates to the advancement of cancer research; and
  (f) Aiding in other multidisciplinary research-support activities as they inure to the advancement of cancer research.
(2) Efforts to improve both research and treatment through greater participation in clinical trials networks by:
  (a) Identifying ways to increase adult enrollment in cancer clinical trials;
  (b) Supporting public and private professional education programs designed to increase the awareness and knowledge about cancer clinical trials;
  (c) Providing tools to cancer patients and community-based oncologists to aid in the identification of cancer clinical trials available in the state; and
  (d) Creating opportunities for the state's academic cancer centers to collaborate with community-based oncologists in cancer clinical trials networks.
(3) Efforts to reduce the impact of cancer on disparate groups by:
  (a) Identifying those cancers that disproportionately impact certain demographic groups; and
  (b) Building collaborations designed to reduce health disparities as they relate to cancer.

History.--s. 11, ch. 2004-2; s. 7, ch. 2006-182.

Appendix B.
Related Awards Reported by Grantees in 2009

Harrington, W., Barber G. (2007 SPORE Planning),"Host defense regulation and viral oncogenesis." National Cancer Institute, $7,308,476.

Hu, J. (2006 SIG), "Comprehensive and alternative medicine in preventing radiotherapy-induced adverse skin reactions." Department of Defense, $114,750.

Ishov, A. (2006 SIG), "Function of Daxx in mitosis that determines paclitaxel sensitivity in breast cancer." National Cancer Institute, $1,391,750.

Lampidis, T. (2006 SIG), "Targeting glycolysis and glycosylation to improve treatment efficacy in various tumor types." SCCC, $200,000.

Lokeshwar, V. (2008 Bridge), "Mechanisms of bladder cancer progression." National Cancer Institute, $1,333,095.

Pearl, S. (2006 SIG), "PPARgamma: Biomarker for breast cancer in older women." National Institute on Aging, $519,859.

Pereira, D. (2009 Bridge), "Cognitive behavioral effects on sleep, pain and cytokines in gynecologic cancer." National Cancer Institute, $1,677,592.

Radisky, E. (2007 NIR), "Targeting mesotrypsin-induced prostate cancer cell invasion." National Cancer Institute, $71,754.

Siemann, D. (2008 Bridge), "Enhancing radiation therapy: vascular targeting agents." National Cancer Institute, $1,001,944.

Weber, J. (2008 Bridge), "PD-1 abrogation and immunity in melanoma." National Cancer Institute, $1,313,260.

Zhang, Y. (2008 NIR), "Measuring strand discontinuity-directed mismatch repair in yeast Saccharomyces cerevisiae by cell-free nuclear extracts." Stanley J. Glaser Foundation, $26,000.

Zimmer, T. (2006 SIG), Manipulating STAT3 signaling for muscle preservation in cancer cachexia." American Cancer Society, $720,000.

Appendix C.
Grantee Publications Reported in 2009

The following list represents new publications in peer-reviewed journals and books based on funded research that current Program grantees have reported since October 2008. This list does not include works submitted or in preparation. Publications are presented in alphabetic order by last name of the principal investigator, shown in **bold** type.

Li Z, Chen L, Kabra N, Wang C, Fang J, **Chen J**. Inhibition of SUV39H1 methyltransferase activity by DBC1. J Biol Chem. 2009; 284(16):10361-6. Epub 2009 Feb 13.

Zhang Y, Zhang M, Dong H, Yong S, Li X, Olashaw N, Kruk PA, **Cheng JQ**, Bai W, Chen J, Nicosia SV, Zhang X. Deacetylation of cortactin by SIRT1 promotes cell migration. Oncogene 2009; 28(3):445-60. Epub 2008 Oct 13.

Sun Y and **Goodison S**. Optimizing molecular signature for predicting prostate cancer reoccurrence. Prostate. 2009 (pre-print available on PubMed).

Singh RK, Paik J, and **Gunjan A**. Generation and management of excess histones during the cell cycle. Front Biosci. 2009; 14:3145-58.

Singh RK, Miguel Kabbaj M, Paik J, and **Gunjan A**. Histone levels are regulated by phosphorylation and ubiquitylation dependent proteolysis. Nat Cell Biol. 2009; 11(8):925-33. Epub 2009 Jul 5.

Sakai Y, Goodison S, **Kusmartsev S**, Fletcher B, Eruslanov E, Cao W, Porvasnik S, Namiki K, Anai S, and Rosser C. Bci-2 mediated modulation of vascularization in prostate cancer Xenografts, Prostate. 2009; 549: 69(5).

Lustria, MLA, Cortese J, Noar SM, & Glueckauf RL. Computer-Tailored health interventions delivered over the web: review and analysis of key components. Patient Educ and Couns. 2009; 74(2),156-73.

Glueckauf R and **Lustria MLA**. (2008) E-Health self-care interventions for persons with chronic illnesses: review and future directions (In J.C. Parker & E. Thorson (Eds.) "Health Communication in the New Media Landscape," NY: Springer Publishing Company; 151-241.

Redman BG, Chang AE, Whitfield J, Esper P, Jiang G, Braun T, Roessler B, **Mulé JJ**. Phase Ib trial assessing autologous, tumor-pulsed dendritic cells as a vaccine administered with or without IL-2 in patients with metastatic melanoma. J of Immunother. 2008; 31:591–98.

Coppola D, **Mulé JJ**. Ectopic lymph nodes within human solid tumors. J Clin Oncol. 2008; 26: 4369–70.

Hu X, Li X, Li H, Valverde K, Fu X, Noguchi C, **Qiu Y**, Huang S. LSD1-mediated epigenetic modification is required for TAL1 function in hematopoiesis. Proc Natl Acad Sci 2009; 23:106(25):10141-6. Epub 2009 Jun 3.

Litt M, **Qiu Y**, and Huang S. Histone arginine methylation: their roles in chromatin dynamic and transcriptional regulation. Biosci. 2009; 29(2):131-141.

Sondak VK, Messina JL. Lymphangiogenesis: host and tumor factors in nodal metastasis. Archives of Dermatology. 2008; 144(4): 536–37.

Lien MH, **Sondak VK**. Diagnostic techniques for primary cutaneous melanoma. Italian Journal of Dermatology and Venereology. 2009;144(2):187-94.

Tornaletti, S. Transcriptional processing of G4 DNA. Mol. Carcinog. 2009; 48(4):326-35.

Su Z, Frye C, Bae K-M, Kelley V, and **Vieweg J**. Differentiation of human embryonic stem cells into immunostimulatory dendritic cells under feeder-free culture conditions. Clin Cancer Res. 2008; 14(19):6207-17.

Kusmartsev S, Eruslanov E., Kubler H., S Sakai Y, Su Z, Rosser C., Dahm P, Siemann D, **Vieweg J**. Oxidative stress up-regulates expression of VEGFR1 in myeloid cells: link to tumor-induced immune suppression in renal cell carcinoma. J Immunol. 2008; 181(1):346-53.

Weber J, Boswell W, Smith J, Hersh E, Snively J, Diaz M, Miles S, Liu X, Obrocea M, Qiu Z, Bot A. Phase 1 trial of intranodal injection of a Melan-A/MART-1 DNA plasmid vaccine in patients with stage IV melanoma. J Immunother. 2008; 31(2):215–32.

Lopatiuk-Tirpak O, Langen K, Meeks S, Kupelian P, Maryanski M, Hsi WH, Palta J, and **Zeidan OA**. Evaluation of a novel 3-D polymer gel dosimetry system for proton radiotherapy. Med. Phys. 2008; 35:2787.

Kabra N, Li Z, Chen L, Li B, **Zhang X**, Wang C, Yeatman T, Coppola D and Chen J. SirT1 is an inhibitior of proliferation and tumor formation in colon cancer. J Biol Chem. 2009; 284(27):18210-17. Epub 2009 May 11.

Yuan F, El Hokayem J, Zhou W, and **Zhang Y**. FANCI proteins binds to DNA and interacts with FANCD2 to recognize branched structures. J. Biol. Chem. Epub 2009 June 27.

Yuan F, Lai F, Gu L, Zhou W, El Hokayem J, and **Zhang Y**. Measuring strand discontinuity-directed mismatch repair in yeast Saccharomyces cerevisiae by cell-free nuclear extracts. Methods. 2009; 48(1):14-18.

Appendix D
Abbreviated Abstracts of Grant Awards

The following is a list of grants awarded by the Program in the first funding round of 2009.

Arlen, Philip
2009 Bridge
M.D. Anderson Cancer Center Orlando
$75,677

The Role of Extracellular Cytokeratin 8 in Prostate Cancer

Prostate cancer is the most common male cancer by incidence and the second most common cause of male cancer death in the U.S. Prostate cancer is a complex problem; not all prostate cancers behave similarly, and there is a need to design methods and strategies that identify and exploit differences in types of prostate cancer. Cytokeratin 8 (CK8) is a protein that is normally contained within prostate cells. However, some prostate cancer cells display parts of this protein externally on the surface of the cell. When CK8 is on the cell surface, it can participate in the growth and spread of cancer cells. Interestingly, some prostate cancer cells display CK8 on the external surface of the cell, but some do not. This finding has important implications in designing treatment strategies that are specific to the type of prostate cancer present in a particular patient. The objective of our research is to define the role CK8 plays in prostate cancer and to identify how CK8 locates to the external surface of prostate cancer cells. Understanding the changes that occur in prostate cancer and how these changes alter the behavior of the disease may lead to individualized treatments for patients and improved patient survival and quality of life.

Baker, Cheryl
2009 NIR
M.D. Anderson Cancer Center Orlando
$373,325

Nanoceria: A Novel Nanoparticle Adjuvant Therapy to Increase the Efficacy of Radiotherapy for Lung Cancer Patients

The main treatment option for lung cancer is surgery. However, in patients with locally advanced disease or in patients who are not candidates for surgery, radiation therapy plays an important treatment role. Unfortunately, radiation can cause significant injury to surrounding normal lung tissue, and therefore, the amount of radiation that can be used may not be sufficient to eradicate the tumor. In previous reports, we demonstrate that cerium oxide nanoparticles (nanoceria) protect normal lung tissue from radiation without protecting the tumor tissue. In this grant, we will monitor the uptake and distribution of nanoceria using mice and profile the changes to proteins and the expression levels of proteins induced by nanoceria in lung tumors and normal lung tissue. We will also investigate the role of TGF-b, a key pathway involved in the adverse changes to normal lung tissue in response to radiation therapy. These studies will provide a better understanding of the distribution of nanoceria in tissue, the changes in protein expression caused by nanoceria, and how nanoceria protects normal tissue from radiation. Our ultimate goal is to apply nanoceria in conjunction with radiation for the treatment of lung cancer to maximize the effectiveness of radiation therapy and to increase the survival and quality of life of lung cancer patients.

Blaydes Ingersoll, Susan, 2009 NIR,
Florida Hospital Cancer Institute
$374,049

Cellular Therapy in Combination with Cytokines as Treatment of Ovarian Cancer

While chemotherapy has impressive response rates in treating ovarian cancer, its impact on long-term survival is modest. Therefore, there is a compelling need to develop new strategies to treat this disease. Cellular therapy, in which the patient is treated with adult blood stem cells to elicit an immune response against the tumor, is being explored. The aim of our grant is to test the use of cellular therapy in combination with cytokines (signaling proteins) to treat ovarian cancer. We have shown that when the cytokines interferon alpha-2b and interleukin-2 are combined with cells from the immune system, we can achieve up to 70 percent killing of the tumor cells. In addition, we have developed ovarian cancer cells that when injected in mice develop tumors; this model is used to test which combinations of cytokines and immune cells have the greatest impact on the tumor. First, we will test the effects of cytokines in combination with cellular therapy on ovarian cancer cells from patients to identify which combination(s) have the greatest impact on tumor cells. Second, we will characterize tumors from patients to determine which tumor types respond best to treatments. Finally, we will test these combinations in our mouse model to determine which combination(s) have the greatest effect. These studies may open avenues for new treatments for ovarian cancer patients.

Brown, Kevin
2009 Bridge
University of Florida
$137,500

Defining Molecular Alterations in Chromatin Structure During Gene Silencing in Breast Cancer

Cancer is a disease of the genome. Genomic alterations that cause cancer are changes in DNA sequence (genetic changes) and DNA structure (epigenetic changes). Among the epigenetic changes, occurring in cancer cells is epigenetic silencing, which results in decreased expression of anti-cancer tumor-suppressor genes (TSGs). We are using cutting-edge molecular genetics approaches to study multiple molecular events that occur during epigenetic silencing in both cultured breast cancer cells and mammary tumors. In Aim 1, we are studying silencing of the TG2 gene, a TSG silenced in breast cancer. In addition to this study, we plan to treat human breast cancer cells with 5-azadC, a drug that reverses gene silencing, and monitor molecular events that occur during TSG re-silencing following the removal of 5-azadC. In Aim 2, we are studying epigenetic events during tumor development. Since this work is not feasibly conducted in humans, we will use an engineered mouse line that is highly prone to developing mammary tumors. We will dissect mammary glands from these mice at various time points and examine epigenetic changes within several TSGs prior to and during the development of mammary tumors. Defining early epigenetic events has promise in providing patients with better prognostic and diagnostic cancer markers.

Regulatory Immunologic Mechanisms in Hepatocellular Carcinoma

Liver cancer (HCC) is the fifth most common cancer worldwide, and the fastest growing GI malignancy. The majority of patients with HCC present in the latter stages of the disease and conventional chemotherapy has failed to impact survival. As such, new treatment strategies are urgently needed. Preliminary studies have shown that patients with HCC have ineffective immune responses, which are characterized by elevation of suppressive CD4+CD25+ regulatory T cells (Treg), poor effector T cell (Teff) responses, and significant elevations in soluble CD25 (sCD25). The impaired Teff responses, elevated Treg frequency, and higher levels of sCD25 correlate with tumor stage and patient survival. This grant consists of two specific aims that explore the hypothesis that HCC promotes the release of sCD25, which impairs tumor immunity by suppressing Teff responses and enhancing Tregs, thereby promoting HCC development and progression. Aim 1 determines the cellular sources of sCD25 and seeks to identify a functional role for sCD25 on Teff responses as well as Treg function. Aim 2 directly evaluates the immune profile of HCC patients as novel immune biomarkers that correlate with prognosis and treatment response. This grant is designed to identify novel prognostic and treatment monitoring tools as well as targets for immune-based therapy for patients with HCC.

Cabrera, Roniel
2009 NIR
University of Florida
$375,000

Role of Alpha-B-Crystallin (CRYAB) and the Unfolded Protein Response in Tumor Vascularization

The integration of host blood vessels into a developing tumor is critical for tumor survival, growth, and metastasis of cancer to other tissues and organs. Tumor cells secrete a number of factors, including vascular endothelial growth factor (VEGF) that stimulates blood vessel growth and expansion within the tumor. We have recently identified alpha-B-crystallin (CRYAB), a chaperone protein, as a critical component in tumor-induced angiogenesis. We have observed that a) CRYAB is upregulated by factors released by tumor cells, b) breast tumors' biopsies exhibit elevated levels of CRYAB, c) CRYAB is strongly associated with intracellular VEGF, and d) inhibition of CRYAB blocks in vitro angiogenesis. Our data suggests that CRYAB sustains tumor angiogenesis by activating the internal autocrine VEGF signaling loop, which is unresponsive to current anti-angiogenesis therapies. This project will characterize the pathways that upregulate CRYAB, identify potential inhibitors of CRYAB, and then translate these inhibitors into animal tumor models to determine their efficacy in slowing or halting tumor progression. The results of our research will provide an alternative intervention strategy in the treatment of a range of cancers including breast cancer.

Cai, Jun
2009 NIR
University of Florida
$359,178

Mechanisms of Tumor-Induced Local Immunosuppression

Advances in cellular and molecular immunology have brought various concepts and ideas to cancer immunology, leading to breakthroughs in cancer immunotherapies that are being tested in an expansion of clinical trials. These trials have generated promising results that may lead to the goal of curing cancers, but have also revealed many challenges that are difficult to address. As exemplified in cancer immunotherapy trials by blocking the cytotoxic T lymphocyte antigen 4 (CTLA4), a prominent issue that has emerged is the entangling of autoimmunity toxicity and antitumor immunity. We propose to use new mouse models to dissect the autoimmunity implications in antitumor immunity. Our focus is on the quantitative interactions among CTLA4, regulatory T (Treg) cells, and the tryptophan-degrading enzyme indoleamine 2,3-dioxygenase (IDO) since these elements may present a major hurdle for immune destruction of tumors. The quantitative variation of CTLA4 is associated with human autoimmunity, cancer occurrence, and both the autoimmune toxicity and therapeutic efficacy in cancer immunotherapy. A better understanding of the CTLA4-mediated local immunosuppressive mechanisms at the tumor site will help therapeutic targeting to overcome the local immunosuppression at the tumor sites while minimizing off-target autoimmune adverse effect.

Chen, Zhibin
2009 NIR
University of Miami
$375,000

MicroRNAs Regulated by TGFbeta-dependent and -independent Pathways in Breast Cancer-initiating Cell and Metastasis

Metastasis, the process by which cancer cells move away from the primary tumor and establish new tumors in distant locations, accounts for 90 percent of all cancer death in breast cancer patients. In order to address this life-threatening problem, it is crucial to understand the molecular and cellular mechanisms that cause primary tumor to metastasize. It has been well documented that breast cancer stem cells underlie the relapsing nature of advanced disease and that transforming growth factor (TGF) beta plays a key role in regulating breast cancer stem cell self-renewal and promoting breast cancer metastasis. In addition, inhibition of the TGFbeta pathway resulted in a reversal of the breast cancer stem cells. We have recently established three breast cancer stem cell lines and shown differential expression of microRNAs (which regulate gene expression) between breast cancer stem cells and their parental cells. Because a single microRNA could regulate hundreds and even thousands of protein-coding genes, we hypothesize that the microRNAs have a critical role in regulation of cancer stem cell and metastasis. To test this, we will 1) Perform microRNA microarray analysis in all three breast cancer stem cell lines treated with/without TGFbeta inhibitor and 2) Determine whether modulation of key microRNAs reverses breast cancer stem cell phenotype, including growth in mammosphere, chemoresistance, tumorigenesis, and metastasis. These investigations will significantly enhance our understanding of the role of microRNAs in breast cancer stem cell and metastasis and provide potential therapeutic targets for treatment of this disease.

Cheng, Jin
2009 Bridge
H. Lee Moffitt Cancer Center & Research Institute
$137,500

Felty, Quentin
2009 NIR
Florida International University
$375,000

Metastases and Promotion of Aggressive Angiogenic Phenotype in Breast Cancer

Breast cancer progression is dependent on robust formation of blood vessels, a process called angiogenesis. Our research targets the ability of breast cancer cells to attract a new blood supply that will ultimately exacerbate breast tumor growth and invasiveness. We have provided evidence for a paracrine signaling mechanism by which high reactive oxygen species (ROS) production by environmental estrogen-exposed, metastatic breast cancer cells stimulate an aggressive angiogenic phenotype. More specifically, we hypothesize that ROS from metastatic breast cancer cells exposed to environmental estrogens mediate an aggressive angiogenic phenotype in neighboring endothelial cells by Pyk2 signaling. The findings from this grant will contribute to a more profound understanding of how estrogenic environmental chemicals mediate breast tumor angiogenesis. This, in turn, will lead to biomarkers for identifying individuals susceptible to estrogen-induced neovascularization and ultimately improve public health. In summary, the findings of this study will: (i) provide a novel paradigm for understanding the molecular mechanism by which environmental estrogenic chemical exposure increases the risk of an aggressive angiogenic phenotype in breast cancer; and (ii) lead to the discovery of novel drug therapies or biomarkers.

Goldberg, John
2009 NIR
University of Miami
$375,000

Dendritic Cell Vaccine for Malignant Glioma and Glioblastoma Multiforme in Adult and Pediatric Subjects

This project aims to develop a new treatment for brain tumors that has been started in Europe, but to add Florida-specific research changes to it that should benefit both the citizens of our state as well as patients globally. We are studying dendritic cell (DC) vaccination in patients with high grade glioma and glioblastoma multiforme. These brain tumors strike both children and adults, are lethal, and take these patients quickly. DCs are naturally occurring blood cells that trigger the immune system by showing foreign protein to T cells. Many researchers have used DCs as a vaccine to "show" that cancer cells are foreign to the immune system in hopes that this action will cause the immune system to destroy the tumor. By taking DCs through blood draws, we are able to add protein from brain tumors that have been cut out, and then give the vaccine back to the patient as a way to trigger immune attack on the brain tumor. Although DC vaccination has been tried for patients with brain tumors elsewhere in the United States, no other investigators have used this strategy, which has shown amazing preliminary results in patients in Europe. The special step for this protocol is to use imiquimod, a skin medication, to help make the vaccination more effective. Researchers in Miami are experts at DC vaccines so we will be able to start this complex treatment and make improvements upon it. We will be the only center in the United States doing this work.

Goodison, Steve
2009 Bridge
University of Florida
$199,733

Cell Surface Factors in Cancer Progression

Despite successful first line therapies, breast cancer relapse can often occur many years after the initial diagnosis. Hence, successful treatment of breast cancers depends upon the early detection of primary tumors with the highest potential to metastasize, followed by the initiation of aggressive, rational, and preferably targeted therapy as quickly as possible. Key to achieving this goal is the identification of reliable molecular signatures and reagents that target these molecules for imaging and therapeutic delivery. The goal of our grant is to use innovative approaches to create molecular probes for the detection of aggressively metastatic breast cancer cells. We will utilize the advantages of DNA aptamers as specific protein-binding reagents. (DNA aptamers are molecular biosensors that can bind to specific targets.) DNA aptamers bind to their specific targets in a similar manner to antibodies, but unlike antibodies, aptamers can be generated rapidly and cheaply. When modified with fluorescent tags or joined to nanomaterials, cell-targeting aptamers can be used as molecular probes for cancer detection, as carriers of drugs for targeted drug delivery, or as function-inhibiting reagents. Furthermore, aptamers can be used to discover new biomarkers on the cancer cell surface.

Goodwin, W. Jarrard
2009 SPORE
University of Miami
$1,000,000

Racial Disparities and Potential New Therapeutic Strategies in Head and Neck Squamous Cell Carcinoma

This SPORE grant combines experienced investigators and diverse patient populations at the Sylvester and Moffitt Cancer Centers to develop translational research focusing on tumor genetics and new therapeutic strategies in Head and Neck Cancer (HNC). Four research projects, two cores (teams that provide support to researchers), and programs in career and research development are planned. Projects are led by scientists conducting both basic laboratory research and clinical research (patient applications). Project 1 will focus on the late preclinical development of VSV-IFN-based therapy. VSV-IFN-based therapy will utilize a customized variant of vesicular stomatis virus (VSV), which is harmless to normal cells and destroys the cancer cells it infects. Project 2 will focus on cancer stem cell marker CD44 as the therapeutic target for HNC. Project 3 will develop genetic prediction models of HNC clinical outcome. Project 4 will evaluate epigenetic changes in HNC survival. The Career Development Program fosters the emergence of new investigators, and the Developmental Projects Program provides rapid funding of innovative ideas. This research program will develop targeted diagnostic and treatment strategies to improve survival of medically underserved Floridians suffering from HNC. This grant is also designed to promote collaboration in the preparation of a National Cancer Institute SPORE application.

Image Guided Hyperthermic Anti-Angiogenenic Therapy for Breast Cancer

Breast cancer is a major health problem in Florida. Innovative, more effective, less invasive, and less toxic treatments for breast cancer are needed to reduce suffering. Cancer nanotechnology, which is a new field where very small, biocompatible objects with unique anticancer properties are engineered, has tremendous potential for revolutionizing breast cancer care. As breast cancer grows, it develops its own blood supply, which is required for its survival and ultimate spread. If this blood supply can be eradicated, then the cancer can be destroyed. In this interdisciplinary grant, we will design, create, and test novel biocompatible nanoparticles that are engineered to seek out and destroy tumor blood vessels. These tumor vessel-targeting nanoparticles (which can be imaged inside a living organism) will specifically destroy tumor vessels and not damage normal vessels or normal tissue. If successful, this will represent a new non-invasive, image-guided paradigm for breast cancer treatment. These concepts could then be rapidly translated into new treatments for patients with breast cancer providing hope to patients who previously had none. Moreover, we anticipate that these efforts will result in simpler medical procedures that will translate into lower costs for the patients and will enable greater access to highly effective methods for the detection and treatment of breast cancer for all Floridians, including underserved minorities and elderly populations.

Grobmyer, Stephen
2009 Bridge
University of Florida
$137,500

Discovery of Novel Anti-Inflammatory Compounds for Use as Chemopreventatives of Pancreatic Cancer

The overall objective of this grant is to identify bioactive marine samples that inhibit inflammation as potential novel chemo-preventatives of pancreatic cancer. Patients with pancreatitis have a much higher risk to develop pancreatic cancer than the general population. Thus, compounds that inhibit inflammation have the potential to prevent the development of pancreatic cancer. To this purpose, pancreatic cancer cells will be treated with samples from the Harbor Branch Oceanographic Institution (HBOI) library of marine-derived natural products to find inhibitors of three key proteins: NFkB, STAT3, and IL-8. These three molecules are important inflammatory regulators and have been implicated with the aggressiveness of pancreatic cancer. Once the activity is identified in pancreatic cancer cells, the most active samples will be further validated by determining if they help stop the uncontrolled growth of pancreatic cancer cells or promote their death. The successful completion of this grant is expected to lead to the identification of novel inhibitors of inflammation that may aid in the fight against pancreatic cancer. The data obtained from this project will be used to secure funding to perform the next steps necessary to bring any of the identified compounds closer to the clinic.

Guzmán, Esther
2009 NIR
Florida Atlantic University
$374,999

Development of a Homogeneous, One-Step Immunoassay for Cancer Marker Detection

Millions of people around the world face the risk of cancer, which has been one of the leading causes of mortality. Early detection of cancer can significantly improve the treatment and survival rate of cancer patients. As a tumor develops, the cells, tissues, and organs can release, increase, or decrease the release of certain chemicals in the circulating blood system. These specific chemicals are called biomarkers. New techniques and tools that enable routine monitoring of cancer biomarkers will allow doctors to track the biomarker level change in each individual more closely and specifically. In this grant, we are developing an extremely simple and highly sensitive immunoassay for prostate cancer biomarker research and detection. (An immunoassay is a biochemical test that measures the concentration of a substance in a biological liquid such as urine or serum.) The successful development of this technology will significantly expand our capability in the discovery and validation of unique biomarkers associated with prostate cancer, allow much earlier detection of prostate cancer, increase the accuracy of cancer diagnosis, and improve the cancer treatment.

Huo, Qun
2009 Bridge
University of Central Florida
$175,000

Role of NF kappa B and Foxo in the Regulation of Muscle Atrophy Genes and Muscle Atrophy During Experimental Cancer Cachexia

One of the most serious consequences of cancer is cachexia – a condition characterized by a progressive and inexorable loss of lean body mass, which is a result of significant wasting of skeletal muscles. This muscle wasting leads to a pronounced loss of body weight, energy depletion, weakness, loss of functional independence, and reduced quality of life. Significantly, cachexia correlates inversely with the patient survival time and cachexia may be responsible for up to 20 percent of cancer-related deaths. Therefore, preventing cancer cachexia-associated muscle wasting is of significant clinical importance, yet there are currently no routinely used therapies to counteract muscle wasting. The long-term goal of our research program is to develop a specific and effective countermeasure to the muscle wasting associated with cancer cachexia. However, we must first understand the signaling pathways and target genes that regulate skeletal muscle mass during cancer cachexia. Therefore, the proposed work will use an experimental model of lung cancer to study muscle atrophy genes known to be up-regulated during cancer cachexia and determine if they are regulated by specific signaling pathways. We will further determine if inhibition of these pathways can prevent cancer cachexia-associated muscle wasting. Understanding the regulation of these atrophy genes is essential in making progress towards fulfilling the pressing need to develop therapies for the treatment of cancer cachexia.

Judge, Andrew
2009 NIR
University of Florida
$375,000

Konduri, Santhi
2009 NIR
M.D. Anderson Cancer Center Orlando
$374,563

Novel Insights in Tamoxifen Regulation of MGMT Expression in Human Breast Cancers and Its Therapeutic Relevance

With more than 200,000 new cases per year, breast cancer is the most commonly diagnosed cancer and second leading cause of cancer-related deaths among women in the United States. The most commonly used hormonal therapies for breast cancer have brought about positive outcomes for many patients; however, after years of treatment, most patients develop drug resistance to these treatment options. Therefore, there is an urgent need for innovative/improved therapeutic strategies that avoid/overcome drug-related resistance and increase the overall survival of breast cancer patients. Recent reports show that cancer cells recognize and efficiently repair the therapy-induced DNA damage. This repair mechanism plays a major role in drug resistance to cancer cells, thereby having the potential to negatively impact the therapeutic efficacy. Human breast cancers are known to possess higher levels of a unique DNA repair protein called MGMT than normal breast. We identified that prolonged treatment with tamoxifen (commonly used anti-estrogen therapeutic agent for breast cancer) also induces MGMT expression. Therefore, we propose that the observed MGMT activity in breast tumors may cause resistance to therapies and usage of anti-estrogens along with MGMT blockers will not only overcome drug resistance but will also increase the efficacy of anti-estrogen drugs, ultimately decrease tumor burden, and increase the overall survival of breast cancer patients.

Law, Brian
2009 Bridge
University of Florida
$137,500

Cdk Activation Specifies Breast Tumor Subtype and Initiates Genetic Instability

Cancer is a disease of uncontrolled cell proliferation. A family of proteins called the Cdks stimulates cell proliferation and these proteins are over-activated in most breast cancers. Interestingly, different members of the Cdk family are over-activated in different types of breast cancer. This suggests that excessive activation of different Cdks may cause alternate types of breast cancer. This is significant because some types of breast cancer are associated with high survival rates whereas patients with other breast tumor types fare poorly. The first goal of this grant is to test the idea that different members of the Cdk family cause distinct types of breast cancer that differ in their aggressiveness. In addition to causing cell proliferation, Cdks can also cause mistakes during cell division. This leads to permanent genetic damage to the breast cell. Thus, Cdks contribute to cancer in two ways: first by promoting cell division and second by causing mistakes during cell division. The second major goal of this grant is to determine whether Cdk stimulation of cell division, or mistakes in cell division caused by Cdks, are more important to the ability of this family of proteins to promote breast cancer formation and growth. The ultimate goal of these studies is to determine whether inhibiting the activity of the Cdk proteins is an effective strategy for suppressing breast tumor growth and for preventing the formation of specific types of breast cancer.

Liao, Daiqing
2009 Bridge
University of Florida
$137,500

Mechanism of Antagonizing Mdm2 and Mdm4 by Adenovirus Type 12 E1B 55-kDa Protein

The p53 gene is one of the most frequently mutated genes in cancers. In tumors that do not carry p53 mutations, it is inactivated by oncogenes (genes that contribute to the production of a cancer) called Mdm2 and Mdm4 that are implicated in cancer etiology and progression. The consequence of disabled p53 is transformation of normal cells, leading to malignant tumors. In addition, functional p53 is critical for the beneficial responses of anticancer chemotherapies and radiotherapies. Thus, lack of functional p53 also contributes to therapeutic resistance. Therefore, restoration of functional p53 pathway is a focal point of anticancer drug discovery. We have been studying the interaction between p53 and the E1B 55-kDa protein (E1B) from adenovirus, a harmless virus that is widely used in gene therapy. We found that E1B interacts with Mdm2 and Mdm4 and promotes their degradation. This mechanism is expected to stabilize p53 and increase its anticancer activities. Our objective is to evaluate the effects of E1B in restricting proliferation of breast cancer cells with known genetic status of p53 and on tumor regression using a mouse cancer model. The outcome may guide future clinical applications for treating patients based on precise knowledge of molecular abnormalities of specific patients. Our immediate goal is to establish feasibility of this innovative anticancer strategy to attract long-term federal funding for this project in Florida.

Liu, Zhao-Jun
2009 NIR
University of Miami
$375,000

The NOTCH Signaling in Melanoma

Arising from pigmented epidermal melanocytes, melanoma is the most lethal skin cancer and its incidence rate has been rising rapidly in the last several decades. Melanoma is highly metastatic and resistant to current therapeutic regimens. The identification of novel, critical molecular pathways involved in melanoma development and progression will lead to more effective targeted therapies. Involvements of NOTCH signaling in melanoma have recently been highlighted. (NOTCH is a protein spanning the cell membrane and is important for cell-cell communication.) We and others have demonstrated that the NOTCH pathway is activated in human melanoma. Moreover, we have observed that activated NOTCH signaling is oncogenic in promoting melanocytic transformation and facilitating progression of primary melanoma. Our working hypothesis is that aberrant NOTCH signaling is a crucial oncogenic promoter in driving melanoma development and progression. In this grant, we are aiming at elucidation of the precise molecular and signaling mechanisms underlying the oncogenic NOTCH signaling in promoting melanoma development. Findings from our study will provide guidance for developing therapeutic strategy to combat this deadly skin cancer.

Snail-mediated Epigenetic Regulations in Cancer Metastasis

The most deadly aspect of cancer is its ability to spread, or metastasize. Most human cancer cells are derived from epithelial cells. Through a process termed epithelial-mesenchymal transition or EMT, epithelial cancer cells quickly lose epithelial features and acquire increased capability of invasion and migration. Snail, a DNA-binding protein, is known as a master regulator of EMT. Snail promotes tumor invasion and metastasis, and its expression in human cancer is associated with poor clinical outcome. Snail can inhibit expression of epithelial genes; however, the mechanism underlying Snail's action is unclear. The goal of this grant is to define the biochemical basis by which Snail inhibits epithelial genes and drives EMT. Human DNA is wrapped around proteins to form chromatin, whose modification and structure are critical for gene expression. It was found in the grantee's laboratory that Snail physically interacts with LSD1, an enzyme capable of modifying chromatin. We hypothesize that Snail may induce multiple chromatin modifications during EMT. Here we plan 1) to characterize Snail-induced chromatin modifications at its target genes; and 2) to determine the function of Snail-induced chromatin modifications in cancer metastasis. This grant will shed light on how a specific combination of multiple chromatin modifications is achieved and its contribution to cancer metastasis. Since chromatin modifications are reversible and many key regulators are enzymatic proteins that can be targeted by small molecule drugs, the study may identify therapeutic targets for cancer treatment.

Lu, Jianrong
2009 NIR
University of Florida
$375,000

The Kinase-Independent Function of IKKalpha Protein in Breast Cancer

The dramatic differences between loss of Ikka protein and inactive Ikka kinase on tumorigenesis suggest that the enzyme-dependent and independent functions of IKKa play opposite roles in breast cancer development. Inhibition of IKKa kinase activity suppresses breast cancer development whilst inhibition of IKKa protein expression augments tumorigenesis. Given the widespread involvement of this pathway in breast cancer, it is very important to confirm that selective inhibition of IKKa kinase activity, rather than complete ablation of IKKa protein, is a safe and effective means of blocking breast tumor development. To accomplish this work, we plan to first address the following questions: Does IKKa loss affect mammary gland development. Does IKKa loss augment carcinogen-induced transformation of mammary epithelial cells? How do IKKa kinase- dependent and independent functions regulate breast cancer stem cells (CSCs) self-renewal and differentiation? Are IKKa expression and kinase activity augmented in human breast cancer? We believe these experiments will help us to achieve the research goals that will lead to the development of IKKa agents that selectively inhibit its kinase activity as cancer therapeutics.

Luo, Jun-Li
2009 Bridge
The Scripps Research Institute
$137,500

Photodynamic Therapy Development Using NF1 Tumor Xenografts

Photodynamic therapy (PDT) is an established cancer therapy that involves the selective uptake of a photosensitizer by tumor cells that when activated with light results in selective tumor destruction. Neurofibromatosis (NF1) is a genetic disease associated with a high risk of tumors that affect peripheral nerves. To our knowledge, no experimental or clinical evaluation of PDT for NF1 or other peripheral nerve tumors has been conducted. The objective of this project is to develop PDT for eradication of NF1 tumors. We hypothesize that the unique anatomic properties of peripheral nerve and vascular permeability of nerve sheath tumors allow for highly effective tumor destruction using PDT without incurring collateral nerve damage. Specific aims are: 1) To test the uptake and accumulation of photosensitizers in numerous human NF1 tumor cell lines and other cultures of normal nerve cells. 2) To determine the mode of action and efficacy of PDT using different classes of photosensitizers when applied to NF1 tumors grown in the nerves of mice. These studies will provide essential foundation information to develop an optimal PDT protocol and conduct a preclinical, federally funded study for eradication of NF1 tumor xenografts in mice. Our goal is to discover and develop PDT's potential for better tumor control without sacrificing normal nerve function and, ultimately, to provide a safe therapy for better clinical outcomes and quality of life for patients with peripheral nerve sheath tumors.

Muir, David
2009 Bridge
University of Florida
$199,993

The RCET System: An Information Technology Infrastructure for Advanced Radiotherapy

The primary goal of the Resource Center for Emerging Technologies (RCET) is to provide technical infrastructure necessary to improve radiotherapy patient outcomes. The advanced medical informatics technology used in the design of the RCET infrastructure can facilitate education, collaboration, and peer review, as well as provide an environment in which researchers can receive, share, and analyze anonymized voluminous multimodality diagnostic images, treatment planning images, radiotherapy plan data, and demographic information instantaneously via World Wide Web. The confluence of these endeavors will lead to improved patient care. The RCET will provide resources that will facilitate inter-institutional collaborative research in advanced-technology radiation therapy while maintaining patient confidentiality, timeliness of data submission, and optimal utilization of resources. A broader yet germane objective is to make these resources available to radiation oncologists in the community and at remote sites to get expert advice from their clinical peers. This is likely to improve the quality of care for a broad spectrum of often underserved radiotherapy patients around the world.

Palta, Jatinder
2009 Bridge
University of Florida
$197,363

Pereira, Deidre
2009 Bridge
University of Florida
$200,000

Cognitive Behavioral Effects on Sleep, Pain, and Cytokines in Gynecologic Cancer

Gynecologic cancers cause substantial morbidity and mortality among women. Developing, implementing, and disseminating interventions that reduce morbidity and mortality secondary to gynecologic cancers are a public health priority. In spite of this, there is a paucity of research examining the effects of psychosocial interventions on patient-centered and physiological outcomes in this population. To the extent that psychological factors may influence quality of life and tumor biology among women with gynecologic cancers, psychological interventions may represent an important addition to standard clinical care in this population. This Bridge Grant will examine the effects of a cognitive behavioral therapy (CBT) intervention on patient-centered (insomnia, pain, and distress) and physiological outcomes (cortisol, i.e., a stress hormone; proinflammatory/proangiogenic cytokines, i.e., immune factors associated with inflammation and tumor growth) among women with gynecologic malignancies for which adjuvant chemotherapy is the standard-of-care. If hypothesized relationships emerge, they will guide future research examining the extent to which CBT may impact long-term quality of life, response to cancer treatment, length of disease-free intervals, and length of disease-free survival in women with gynecologic cancer.

Radisky, Evette
2009 Bridge
Mayo Clinic
$130,000

Development of Highly Selective MMP-9 Inhibitors for Breast Cancer Therapy

We aim to develop a new anticancer drug for selectively blocking MMP-9, an enzyme that facilitates the growth and metastasis of breast cancer, using as a prototype a natural inhibitor of MMPs produced within our bodies called TIMP-1. In many studies TIMP-1 has shown an ability to slow cancer growth and spread by blocking MMP-9 and related enzymes, but under some circumstances, TIMP-1 can exhibit an opposite effect by interfering with apoptosis, a natural mechanism of programmed cell death. Apoptosis plays a vital role in maintaining breast function by balancing cell division with cell death; acquiring the ability to escape apoptosis is a key step in the development of breast cancer. Previous investigations of how TIMP-1 interferes with apoptosis suggest that it will likely be possible to separate the MMP-blocking function from the apoptosis-blocking function, to produce an altered TIMP-1 that can still inhibit MMPs, while having no effect on apoptosis. In this Bridge Grant application, we propose to determine the specific component of TIMP-1 that is responsible for blocking apoptosis in breast cancer cells and to construct an altered TIMP-1 that is devoid of any apoptosis-blocking function but that retains its antitumor properties. This altered TIMP-1 will then serve as a prototype for further optimization toward development of a novel and effective therapy for treatment of breast cancer.

Siegel, Erin
2009 NIR
H. Lee Moffitt Cancer Center & Research Institute
$375,000

Insulin-like Growth Factor Biomarkers and Colorectal Cancer

People who do not exercise, eat unhealthy diets, and are extremely overweight have been shown to be at an increased risk of both developing and dying from colorectal cancer (CRC). Insulin and several members of the insulin-like growth factor (IGF) hormone family are generally kept at low-levels in the blood but may be higher among overweight people that do not exercise and have poor diets. The high levels of insulin and IGFs may be the link between these unhealthy factors and the risk of developing colorectal cancer. This study plans to enroll 300 CRC patients and follow them both during and after treatment for 12 months. We will measure the levels of insulin and of three members of the IGF; family in blood samples and have patients fill out questionnaires on their quality of life and health behaviors at study entry, 6 and 12 months. We will measure insulin and IGFs in the blood and see if different levels are linked not only to changes in the molecular characteristics of the cancer tissue but also to patient quality of life. This study is taking a holistic approach to understanding how insulin and IGFs in the blood are related to tumor biology and to patient quality of life during the first 12 months after diagnosis. Our long-term goals are to identify blood tests and health behaviors that can help doctors predict which patients will have longer survival with good quality of life after treatment of their cancer.

Slingerland, Joyce
2009 SPORE
University of Miami
$1,000,000

Novel Experimental Therapeutic Approaches to Breast Cancer Therapy

Basic scientists and medical doctors join forces in this grant to find new ways of blocking growth-promoting effects of estrogen, growth factor signaling pathways, and the tumor's blood supply, all of which are key to a breast cancer's survival and growth. We will test new smart bombs that can specifically block pathways activated in cancers and not in normal cells, killing the cancer but leaving normal cells unharmed. Four research groups will tackle molecular causes underlying different forms of breast cancer. Projects 1 and 2 investigate causes of aggressive estrogen receptor (ER) negative breast cancers that often affect young women and test if blocking pathways that degrade the ER might allow ER negative to become ER positive, thus making them susceptible to antiestrogen therapies. HER2 is a growth promoting receptor that is overexpressed in up to 30 percent of breast cancers and can be targeted by antibodies to block tumor growth. Project 3 will develop and test a new drug that combines antibody blockade of HER2 with a drug that blocks tumor blood vessel growth. This drug may prove to be better than trastuzumab (Herceptin), not only blocking HER2 in cancers that have high HER2 levels but also in cancers that only weakly express HER2 or have become trastuzumab resistant. Finally, Project 4 tests how estrogen causes breast cancer growth by turning on a transcription factor, GREB1, and will find and test new small molecule drugs that could turn off GREB1 and shut off growth of the most common form of breast cancer, namely ER positive cancer. These teams aim to define molecular patterns in the tumor that predict who will respond to treatment so that treatment can be individualized for maximum efficacy.

Defining the Signaling Network of NRAS-Mutated Melanomas

Melanoma remains a great challenge. Despite over 30 years of research, we are currently unable to prolong the survival of patients whose melanoma has spread to other organ sites. It is now known that melanomas can be divided up into smaller groups, depending upon the genetic changes that initiate them. It is hoped that a greater understanding of these molecular changes will allow us to develop "personalized therapies" that selectively kill the melanoma cells while leaving normal cells unharmed. One group of melanomas that has been relatively ignored by the research community is those that activate mutations in a gene called NRAS. Mutations in the NRAS gene activate signaling pathways leading to the uncontrolled growth and survival of the melanoma cells. Little is currently known about the underlying biology of the NRAS-mutated melanomas, making it difficult to develop new therapy strategies. This grant aims to redress this balance by defining the nature of the molecular signals found in NRAS-mutated melanomas. Initially, this study will focus upon two pathways that are downstream of NRAS activity, the CRAF pathway and the PI3K pathway. We will use molecular tools, such as shRNA, to dissect the exact mechanisms the melanoma cells use to grow and survive. This information will then be used to develop new therapeutic strategies with the aim of improving treatment and survival of patients whose melanomas are activated by NRAS.

Smalley, Keiran
2009 NIR
H. Lee Moffitt Cancer Center & Research Institute
$375,000

Light-Triggered Carrier Drug Release for Treatment of Disseminated Cancer

Chemotherapy is standard treatment for metastatic cancer; however, drug toxicity limits the dosage that can safely be used thus reducing treatment efficacy. Drug carrier particles can help reduce toxicity by shielding normal tissue from drug and selectively depositing drug in tumors. Most drug carriers release drug passively by slow leakage, but this uncontrolled, passive drug release can limit treatment efficacy, as it can be difficult to achieve therapeutic concentrations of drug at tumor sites even with tumor accumulation of the carriers. Controlled rapid drug release can be more effective due to higher achievable peak drug concentrations. The long-term objective this research is to harness a photochemical technique called delayed photolysis as a new light-based method for rapid controlled drug release from carriers to improve the treatment of metastatic cancer. The objective of this grant is the first demonstration of delayed photolysis in an animal model. This project represents the first attempt to demonstrate delayed photolysis in a live animal and the first attempt to harness this technique for therapeutic benefit. The results of this project will provide a basis for further development of the technique for targeting tumors to improve treatment of metastatic cancer lesions. This technology will have potential positive impacts in chemotherapy of advanced metastatic cancer.

Sorg, Brian
2009 NIR
University of Florida
$375,000

Targeting Negative Regulatory Pathways for Immunotherapy of B-cell Lymphomas

B-cell lymphomas are cancers that arise in lymphoid organs. They grow in the very same compartment where important cells of the immune system (T-lymphocytes) are located, indicating that B-cell lymphomas have developed mechanism(s) to avoid immune attack. As lymphoma expands, they further impair the function of immune cells, diminishing their ability to respond to immunotherapeutic strategies. Recently, we have identified two targets (Stat3 and Histone deacetylases) that by restraining inflammatory responses impose a significant barrier to our efforts to harness immune responses against B-cell lymphomas. In this grant, we aim to understand these barriers better in a particular type of lymphoma, named Mantle Cell Lymphoma (MCL). In addition, we will evaluate novel therapeutic strategies to overcome these barriers in MCL, an incurable B-cell malignancy. Key experiments include in vitro and in vivo studies in mouse models (Aims 1 and 2) and in human MCL cells (Aim 3) are proposed within this mechanistically-oriented and translational project that would result in innovative treatments for MCL and other B-cell malignancies.

Sotomayor, Eduardo
2009 Bridge
H. Lee Moffitt Cancer Center & Research Institute
$200,000

Cyclosporine, Cyclophilins, and HCV Replication

The long-term goal of our research program is to advance the knowledge of virus' host cell interactions that are relevant for liver cancer. Hepatitis C virus (HCV) infects 3 percent of the world's population and causes fibrosis, liver cirrhosis, and hepatocellular carcinoma (HCC), which is a malignant liver cancer that kills most patients within a year. There is no vaccine to prevent HCV infection, and the only FDA-approved treatment, interferon combined with ribavirin, faces serious drug-resistance issues. New classes of anti-HCV drugs are urgently needed. Cyclosporine A (CsA) and its derivatives represent promising candidates of such drugs and can be combined with the current interferon-based therapy. Despite the potent antiviral effects, exactly how CsA functions to inhibit HCV replication remains unknown. In addition, drug resistance to CsA has not been studied systematically. Both of these issues need to be addressed for CsA or any of its derivatives to be developed into a successful drug. The experimental goals are to illustrate the mechanisms that determine the antiviral effect of CsA and the related drug resistance using comprehensive virology and structural biology techniques. Our results may reveal additional targets for therapeutic intervention. Given the medical importance of HCV infection and HCC, knowledge that can be gained from the grant will also have direct implications for both antiviral and anticancer drug development.

Tang, Hengli
2009 Bridge
Florida State University
$198,000

Torres-Roca, Javier
2009 Bridge
H. Lee Moffitt Cancer Center & Research Institute
$173,602

Development of an Assay to Predict Radiosensitivity in Prostate Cancer

Prostate cancer is the most common cancer diagnosed in men and the second leading cause of cancer death in men. In this grant, we are adapting a technology that predicts the likelihood that a tumor will respond to radiation therapy. This technology, which is still in development, has already been shown successful in preliminary unpublished studies in esophageal, rectal, and head and neck cancer patients. It is logical, to test it in prostate cancer since radiation therapy is one of the principal treatments for patients with this disease, thus, the potential clinical impact of this technology is of great significance. Finally, we think this technology will be central in moving forward personalized medicine in cancer. The purpose of personalized medicine is to select clinical therapies based on the likelihood of benefit to a specific individual. Thus, the aim is to select the right therapy for the right patient. Personalized medicine, if successful, would improve overall healthcare by individualizing care and avoiding unnecessary and toxic therapies, resulting in public healthcare improvement and health cost savings.

Endnotes

1 John E. Niederhuber, M.D., Director NCI, "President Obama's 2010 Budget, posted May 13, 2009, http://www.cancer.gov/directorsnotes/051309, accessed October 6, 2009.

2 http://www.migrationinformation.org/datahub/state.cfm?ID=FL, accessed 9/4/2009.

3 American Cancer Society, "Surveillance Research 2009, Estimated New Cancer Cases by Sex- and Age, 2009", available for download at http://www.cancer.org/downloads/PRO/2009_cases_deaths_by_age.pdf. Accessed 9/30/09.

4 American Cancer Society, Inc., Surveillance and Health Policy Research, in "Estimated New-Cancer Cases for Selected Cancer Sites by State, US, 2009" available for download at http://www.cancer.org/downloads/stt/CFF2009_EstCSt_4.pdf , and "Estimated Cancer Deaths for Selected Cancer Sites by State, US, 2009", available for download at http://www.cancer.org/downloads/stt/CFF2009_EstDSt_5.pdf. Both documents accessed 9/30/2009.

5 "Task Force on the Study of Biotech Competitiveness, Final Report and Recommendations," August 12, 2009. For a link to the report, visit the Governor's Office of Tourism, Trade and Economic Development at http://www.flgov.com/otted_home.

6 The National Academies Board on Life Sciences, Bridges to Independence: Fostering the Independence of New Investigators in Biomedical Research, 2005, available for download at http://books.nap.edu/openbook.php?record_id=11249, accessed 10/26/2009.

7 "Task Force on the Study of Biotech Competitiveness, Final Report and Recommendations," August 12, 2009. For a link to the report, visit the Governor's Office of Tourism, Trade and Economic Development at http://www.flgov.com/otted_home.

8 "Grant System Leads Cancer Researchers to Play It Safe," Gina Kolata. The New York Times, June 28, 2009. Available at http://topics.nytimes.com/top/news/science/series/forty_years_war/index.html, accessed 9/4/2009.

9 Ibid.

10 "The Cancer Centers Branch of the National Cancer Institute Policies and Guidelines Relating to the Cancer Center Support Grant," September 2008, p.26. Available for download at http://cancercenters.cancer.gov/documents/CCSG_IGuide9_08r1.pdf. Accessed 10/2/09.

11 http://www.cancer.org/downloads/STT/500809web.pdf, accessed 10/7/2009.

12 Ibid.

13 http://cancercenters.cancer.gov/cancer_centers/cancer-centers-list.html, accessed 10/7/2009.

14 "The Cancer Centers Branch of the National Cancer Institute Policies and Guidelines Relating to the Cancer Center Support Grant," September 2008, p.26. Available for download at http://cancercenters.cancer.gov/documents/CCSG_IGuide9_08r1.pdf. Accessed 10/2/09.

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