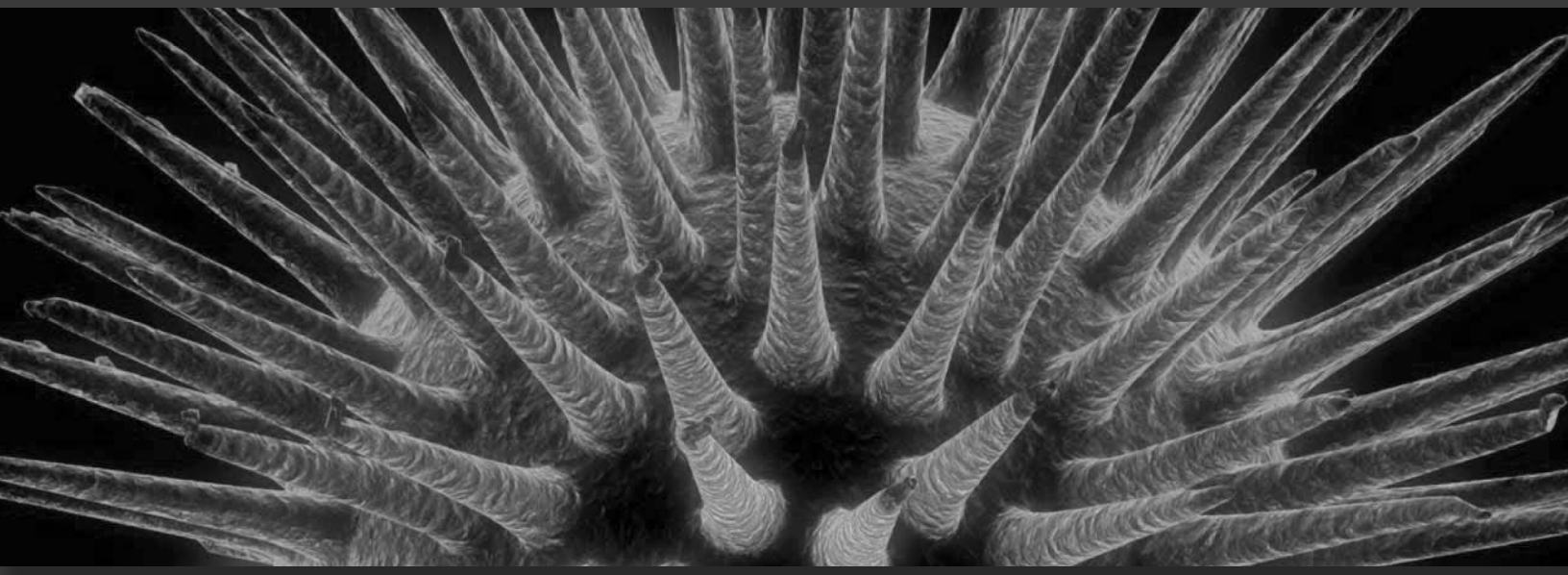
2010 ANNUAL REPORT



bankheadcoley
Florida Cancer Research Program

The Bankhead-Coley Cancer Research Program

As established in Section 381.922, *Florida Statutes*, 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 cancer research capacity in the state
- Improve research and treatment through greater participation in cancer clinical trials networks
- 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. Print copies of this report are available upon request.

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

Annual Report

January – December 2010

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
of Florida

December 15, 2010

The high quality of science in Florida maintained by this outstanding Program allows new discoveries that lead to novel therapies for cancer, with a direct benefit for Floridians in clinical trials. This will also attract biotech companies.

- Dr. Peter Storz
Mayo Clinic
2007 NIR Grant

Co-investigator Evette Radisky and Principal Investigator, Peter Storz, 2010 RPG, Mayo Clinic

The Florida Biomedical Research Program has been incredible for Florida science and scientists. We are grateful for these opportunities to be funded and work towards more NIH funds. This Program has been incredible for our research growth and reputation.

- Respondent 59804764
DOH Grantee Satisfaction Survey Results
February 2010

Joshua Lentz, laboratory member on 2009 TTCP led by Mike Buffa, Nano Discovery, Inc.

Table of Contents

Executive Summary

After four full years of operation, the Bankhead-Coley Cancer Research Program (the Program) has many successes to relate in this year's annual report.

Prominent on the list is the **re-enactment of the Program** in the 2010 regular Legislative session after last year's favorable review of Program performance by Senate professional staff. Other notable accomplishments:

- **The portfolio of active Bankhead-Coley grants ballooned to 97**, more than twice the number in December 2009. Florida lawmakers made this growth possible with a substantial increase in annual funding, beginning in 2009.
- **Additional funding attracted from outside the state reached nearly $109 million** as of October 2010, more than three times the value of all awards made through mid-2009. Major factors contributing to this accomplishment are the Biomedical Research Advisory Council's (Advisory Council) careful design of grant types to capitalize on federal funding trends and the Program's practice of funding the best science, regardless of origin within the state.
- The escalating numbers of **grantee publications in peer-reviewed journals and presentations at scientific meetings** are helping to solidify Florida's reputation as a leader in cancer research.
- The Program successfully managed an annual competition for grants that produced **three times the number of applications received in any previous round**, completing peer reviews and announcing awards within the normal funding schedule.

Bridget Riggs, laboratory member on 2009 NIR led by Erin Siegel, Moffitt Cancer Center & Research Institute

- **The Advisory Council and staff reached out to key stakeholders** in order to better understand research sponsorship needs and respond with suitable grant mechanisms. Working with a team of university-based technology transfer manager, the Program refined a long-standing grant type and introduced a complementary new one. Partnering with the Department of Health Office of Minority Health, FL CURED, and BioFlorida, the Program drew upon the outcome of an invitational summit to begin defining a statewide health disparities research agenda that can be supported with future Bankhead-Coley grants.

Program at a Glance

The Bankhead-Coley Program offers competitive cancer research grants to Florida institutions based on scientific merit.

Annual funding: A share of the proceeds of the state cigarette and tobacco product surcharge, $20.0 million for 2010

Management: Florida Department of Health and 11-member Biomedical Research Advisory Council

First awards made: January 2007

- The Advisory Council and staff **continued the strategic planning work** begun in late 2009 by articulating a vision for the future of the Bankhead-Coley Program, with five priorities to shape its investments for the coming years:

    1) Target biomedical research workforce recruitment, retention, and training
    2) Provide equipment and resources to support research discovery and emerging technologies
    3) Increase investment in clinical and translational research and health disparities research
    4) Accelerate technology transfer
    5) Improve key processes

The Program is continuing to implement these priorities with its preparations for 2011 awards. In 2008 there were only seven health disparate projects, that number has reached 37 in 2010. Factored into the set of grant types offered is a strong concern that Florida's cancer researchers will face sharply greater competition for federal funding as American Recovery and Reinvestment Act (ARRA) funds are depleted.

The goal of my research is to foster collaboration between major academic centers and medical practitioners in improving radiation oncology in Florida.

- Dr. Jatinder Palta
  University of Florida
  2009 RC1 Grant

- Consistent with its statutory responsibilities, the **Advisory Council made the following primary recommendations** to the Department of Health this year to advance the Program's mission:

    - Advocate for stable state funding with adequate administrative funding;
    - Obtain an exemption from Florida open meeting law for the scientific peer review of grant proposals to align with best practices and enable frank reviewer communication regarding scoring variations; and
    - Obtain authority to extend the maximum carry-forward period for grant funds from three years to five years to enable longer grant projects.

The Department of Health continues to ensure accountability to the citizens of Florida for the use of public funds with disciplined processes for tracking, monitoring, and reporting scientific progress and compliance with award terms and conditions. The balance of this report explains the outcome of the 2009 Special Call for Applications and introduces 53 new grants awarded in 2010. It aggregates the impact of Program awards in building Florida's capacity for cancer research and bolstering the state's technology-based economy. It details the accomplishments of individual grantees in securing additional funding and publishing findings in peer-reviewed journals. And perhaps most importantly, it provides glimpses into some of the many laboratories across Florida, "where the rubber meets the road," and talented research teams are turning Bankhead-Coley grants into important cancer discoveries.

Total awards made: 177
Florida institutions supported: 15
Total value of awards: $61.4M
Additional funding leveraged: $109M
Estimated number of jobs supported: 1837

Mass spectrometer purchased by Gregory Roth, 2009 SIG, Sanford-Burnham Medical Research Institute

Program Background

Program Created to Accelerate Cancer Research in Florida

Florida continues to record the second-highest numbers of new cancer diagnoses and cancer deaths in the nation, a disproportionate cancer burden for the fourth most populous state.[1] The Florida Legislature created the William G. "Bill" Bankhead, Jr. and David Coley Cancer Research Program in June 2006 as means of closing the gap between the health needs of Floridians and our cancer research infrastructure. The Program engages Florida researchers with competitively awarded grants addressing improved cancer prevention, diagnosis, treatment, and cure. Appendix A contains a copy of the Program's current enabling legislation, section (s.) 381.922, Florida Statutes *(F.S.)*.

Legislature Reaffirms Commitment to Program

The Legislature substantially increased its financial commitment to the Program, concurrent with passage of the cigarette and tobacco products surcharge in 2009. For fiscal year (FY) 2009-2010, Florida's lawmakers replaced the previous general revenue appropriation ($6 to $9 million) with a 2.5 percent share of the tobacco surcharge imposed by s. 210.02, *F.S.*, with an upper limit of $25 million. Actual surcharge revenues for 2009 yielded $23.4 million for the Program.

Principal Investigator Justin Summy, 2008 NIR, M.D. Anderson Cancer Center

In its sunset review of the Program in 2009, Senate staff examined the Program's performance, outcomes, and financial management, recommending re-enactment due to the Program's achievement of goals and tangible and intangible benefits to the state.[2] The Legislature took up the review during the 2010 Regular Session and renewed legislation authorizing the Program, reaffirming its commitment to the Program with an appropriation of $20 million from the state surcharge on tobacco.

Program Leadership and Partners Span Florida's Biomedical Research and Health Care Communities

The Program is managed by the Florida Department of Health (Department), and is supported by a contracting partner, Lytmos Group, Inc.

The Biomedical Research Advisory Council (Advisory Council) is an 11-member group of Floridians with expertise in biomedical, behavioral, social research, and commercialization who represent cancer programs, voluntary health organizations, professional medical organizations, and the general public. The Advisory Council guides the Department in managing the Program and builds appropriate bridges to the Program's external partners. See "The Biomedical Research Advisory Council" section for more detail.

Formal and informal linkages across the state create key strategic partnerships. These include the American Cancer Society, the Florida Center for Universal Research to Eradicate Disease (FL CURED), university directors of technology transfer, the Florida Office of Minority Health, and BioFlorida.

The Bankhead-Coley Program can put Florida research on the map. Since the Program has NCI-recognized funding, we can count our Bankhead-Coley grants when applying for NCI cancer center designation. Bankhead-Coley grants doubled the number of grants Miami could count for this application.

- Dr. Jennifer Hu
  University of Miami
  2010 RC1 Grant

Grant Types Strategically Chosen to Leverage Funds and Address Florida's Greatest Needs

On an annual basis, the Advisory Council recommends a collection of grant types designed to maximize the impact of Florida's investment. In doing so, they take into account Program goals, current federal funding priorities and trends, and a shared awareness of the needs of Florida's cancer research institutions (both large and small). A major objective of every grant is to aid the investigator in attracting additional funding. To date the Program has used 11 grant types to encourage collaboration, to foster development of new investigators, to bridge and accelerate research of experience investigators, to improve access to research equipment, and to increase commercial potential through early-stage funding. Appendix B contains brief descriptions of each of the grant types offered by the Program.

Competitive Awards Based on Scientific Merit

The underlying principles for awarding Program grants are to open the competition to all researchers regardless of institution affiliation and to fund the best science. Applications from researchers throughout Florida received in response to a call for applications compete for funding based upon merit. Each application is evaluated for scientific merit and cancer-relatedness in a peer review process involving experts from outside Florida. Lytmos Group then rank orders the merit scores and presents them to the Advisory Council for funding recommendations in a manner that blinds Advisory Council members to applicant identities, avoiding any conflicts of interest.

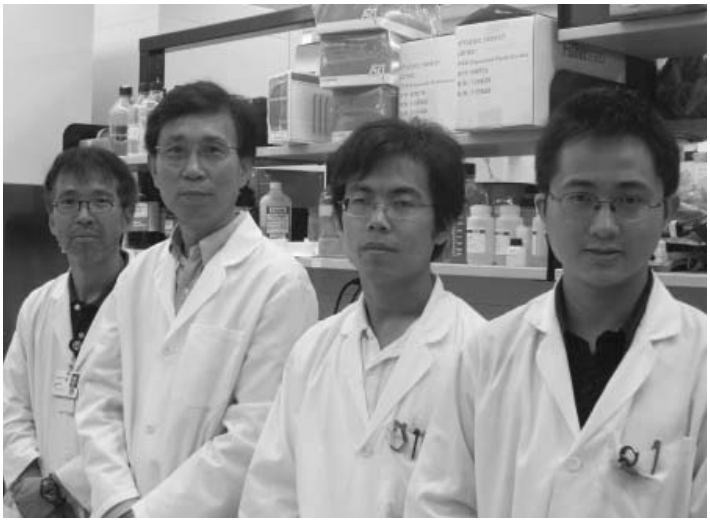
The Program's peer review and funding decision processes have earned special National Cancer Institute (NCI) recognition for Bankhead-Coley grants. Since 2007, Florida institutions have been able to count Program grants in the cancer research portfolio required to earn NCI Cancer Center designation.

Having this designation matters because it qualifies the institution for multi-year, multi-million dollar funding from the NCI, and it enhances the institution's ability to recruit leading researchers and offer state-of-the-art patient treatments. Moffitt Cancer Center & Research Institute and the Mayo Clinic are currently Florida's only NCI Cancer Centers; however, the Sylvester Comprehensive Cancer Center at the University of Miami and the University of Florida's Shands Cancer Center are working to achieve this designation.

More information about the Program's peer review process is provided in the "Program Operations" section of this report.

Strict Oversight Required to Ensure Accountability

During 2010, the Department managed a Program portfolio of 97 active grants, each comprising a contract for research services. Contract management is a statutory requirement for all state agencies. The Department uses business processes that comply with the Florida Department of Financial Services' requirements for grant/contract management and oversight, regularly reviewing and evaluating the performance of all Program grantees to ensure receipt of all deliverables over the life of a grant. See the section "Program Operations" for a detailed description of grant management practices that ensure research and financial accountability.



(From left to right): Laboratory member Donghwa Kim, Principal Investigator Jin Cheng, and Laboratory members Jianping Guo and Shaokun Shu, 2009 Bridge, Moffitt Cancer Center & Research Institute

2009 Special Competition for Grant Awards

Capitalizing on Opportunities with Additional 2009 Funding

The Program issues calls for applications in anticipation of next-year funding, typically projecting a level of funding comparable to the previous year. When FY 2009-2010 funding exceeded projections, the Program supplemented its regular annual competition with a second round of funding for different types of grants in a special call for applications. Because award information for the Special Call was unavailable at press time for the 2009 Annual Report, it is provided here along with the 2010 results.[3]

In the Special Call released on August 10, 2009, the Program solicited applications for the grant types shown in Table 1 below.

In response to an increase in funding, the Program conducted a second competition in 2009 and awarded 18 research grants totaling $9.7 million, bringing the total value of 2009 awards to $21.1 million.

Table 1 - Grant Types offered in 2009 Special Competition

Grant Types*	Purpose
Florida Research Challenge Grant (RC1)	This one-time opportunity is providing support for Florida's promising high-risk, high-reward cancer research proposals submitted to the National Institutes of Health (NIH) in response to the American Recovery and Reinvestment Act Fund requests for proposals.[4] The program determined the scientific merit of the RC1 applications by federal peer review scores along with Program peer review cancer-relatedness scores.
Shared Instrument Grant (SIG)	Last offered in 2006, this grant provides state-of-the-art research instruments that can only be justified on a shared-use basis for multiple cancer research projects.
Technology Transfer/ Commercialization Partnership Grant (TTCP)	This award is designed to encourage the collaboration of investigators and small businesses to stimulate technology transfer activities for promising cancer research discoveries. Applicants were allowed to submit TTCP proposals any time between August 10, 2009 and March 31, 2010.

* Refer to Appendix B for more information about these grant types.

Quick Facts: 2009 Special Competition

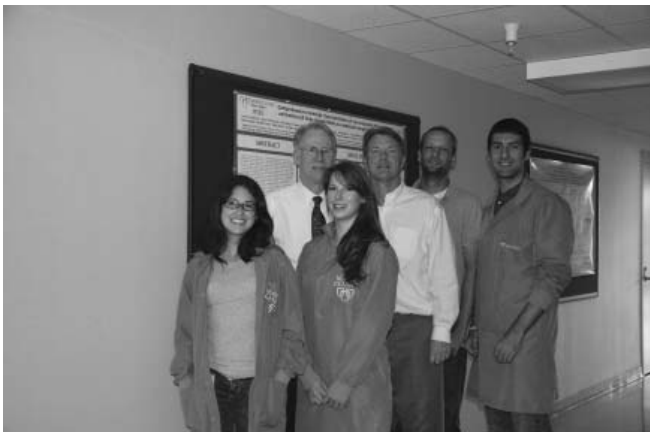
The 2009 Special Competition produced the following results:

Applications received: 46
Institutions participating: 11
Funds requested: $21.1M
Total awards made: 18
Total value of awards: $9.7M
Grant start date: January 1, 2010
Funds reserved for TTCP: $200,000

Completing the Picture of 2009 Awards

The outcome of the Special Call brought the total value of 2009 awards to $21.1 million. As illustrated in Figure 1, fourteen public and private research organizations throughout Florida benefited from these grants. Table 2 provides a breakdown of applications, success rates, and awards by grant type for the 2009 Calls.

Refer to Appendix C for more information about each awarded grant, including principal investigator, institution, award amount, project title, and abbreviated abstract.



(From left to right) Laboratory members Laura Marlow, Christina von Roemeling, Co-Investigator Robert Smallridge, Principal Investigator John A. Copland, Simon Cooper, and Stephen Rohl, 2007 Bridge, Mayo Clinic

Table 2 - Grant Applications Received/Awarded in 2009

Grant Types	Applications Received	Applications Awarded	Percent of Applications Awarded	Awarded Funding Amount
Bridge Grant	24	22	93%	$3,773,358
New Investigator Research Grant	37	15	41%	$5,606,114
Research Challenge Grant	19	12	63%	$8,050,247
Shared Instrument Grant	15	4	27%	$1,445,506
Specialized Program of Research Excellence	4	2	50%	$2,000,000
Technology Transfer/Commercialization Partnership Grant	12	2	17%	$200,000
2009 Total	111	57	51%	$21,075,225

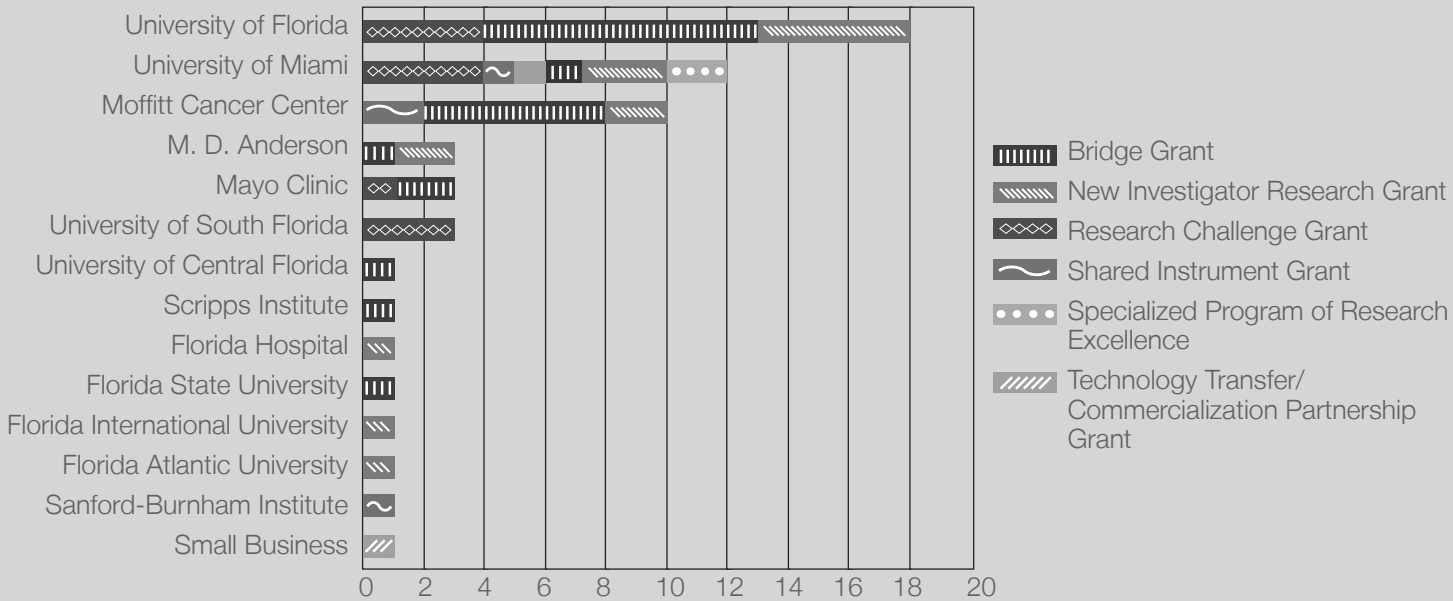


Figure 1 – 2009 Grants Awarded by Institution

Inviting Broader Participation for Florida Investigators in 2010

With more available funding, the Program was able to solicit applications for more grant types than offered in previous competitions, targeting diverse approaches to cancer research and a wide range of experience levels and priorities. The offerings attracted more experienced investigators than in previous years and encouraged translational and health disparities research. Table 3 describes grant types offered in 2010. The results were a record number of applications, reflecting the demand in Florida's cancer community for the opportunity to conduct research.

The Program awarded 36 grants totaling $17.2 million in 2010. Grant offerings included a broad range of types that appealed to both new and experienced investigators and a new award to facilitate technology commercialization.

Table 3 - Grant Types offered in 2010

Grant Types*	Purpose
New Investigator Research (NIR) Grant	Fosters development of new investigators so they can undertake independent research that will be competitive for national funding.
Postdoctoral Research Fellowship (PRF)	Attracts scientists into careers addressing cancer research questions and provides support to promising postdoctoral researchers.
Research Project (RPG) Grant	Supports investigators at all experience levels who are conducting research that brings discoveries closer to patient care and/or that seeks to reduce health disparities.
Team Science Program (TSP) Grant	Supports a collaborative, multidisciplinary research program with a well-defined theme that results in a national application.
Technology Transfer Feasibility (TTF) Grant	Offers early stage funding in order to develop intellectual property and improve a project's commercial potential and competitiveness for further development activities.
Technology Transfer/ Commercialization Partnership (TTCP) Grant	Encourages the collaboration of investigators and small businesses to stimulate technology transfer activities for promising cancer research discoveries.

* Refer to Appendix B for more information about these grant types.

Quick Facts: 2010 Competition

The 2010 Competition produced the following results:

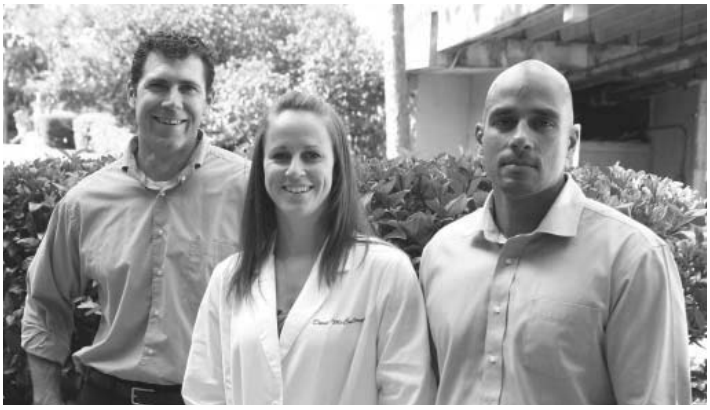
Applications received: 191
Institutions participating: 11
Funds requested: $166.5M
Total awards made: 36
Total value of awards: $17.2M
Grant start date: July 1, 2010
Funds reserved for TTCP: $700,000

2010 Competition and Results

During the 2010 competition, 191 applications were received and 36 awards were made. As Table 4 below illustrates only 19 percent of the applications received were funded. Figure 2 provides a breakdown of the number of grants awarded by institution.

TTCP and TTF applicants could submit proposals any time between June 15, 2010 and March 31, 2011, receiving award notifications within 60 days of application. The Program reserved $700,000 for these awards. As of October 15, 2010, no TTCP award had been made.

See Appendix C for information about each awarded grant, including principal investigator, institution, award amount, project title, and abstract. Information about all funded projects may also be accessed from the Program website, www.floridabiomed.com by selecting the menu option "Funded Projects."



(From left to right) Principal Investigator Brad Behnke, Laboratory members Danelle McCullough and Peter Adhihetty, 2010 NIR, University of Florida

Table 4 - Grant Applications Received/Awarded in 2010

Grant Types	Applications Received	Applications Awarded	Percent of Applications Awarded	Awarded Funding Amount
New Investigator Research Grant	53	8	15%	$3,182,143
Postdoctoral Research Fellowship	32	12	38%	$1,513,400
Research Project Grant	89	12	13%	$8,800,990
Team Science Program Grant	12	3	25%	$3,600,000
Technology Transfer Feasibility Grant	4	1	25%	$99,999
Technology Transfer/Commercialization Partnership Grant	1	0	0%	$0
2010 Total	191	36	19%	$17,196,532

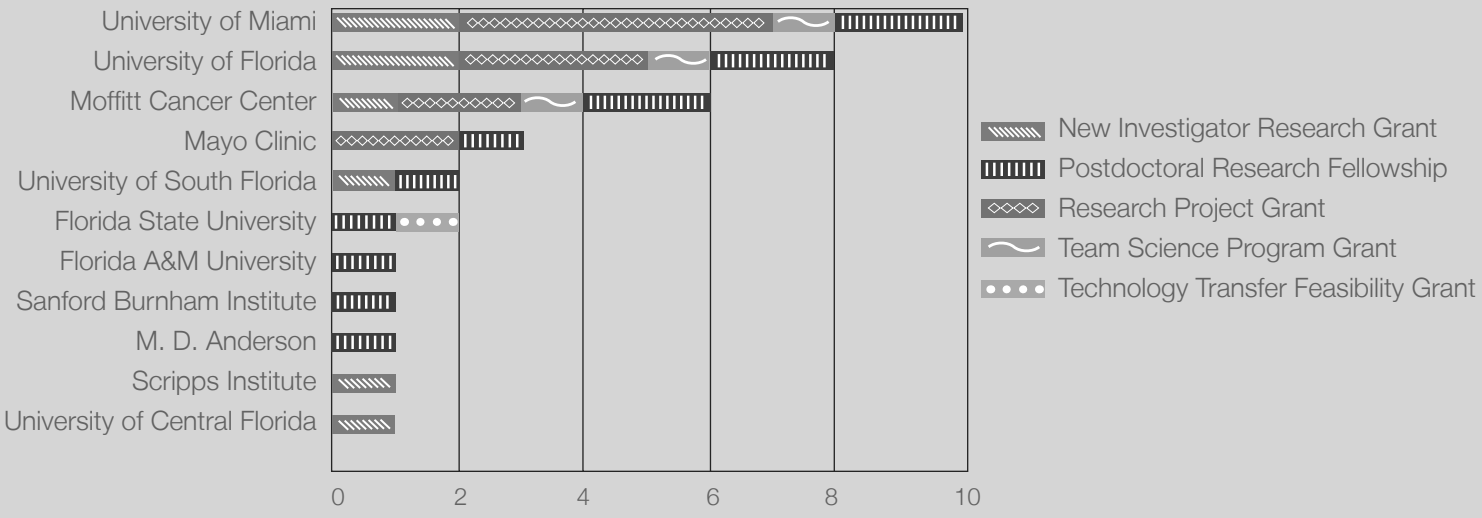


Figure 2 – 2010 Annual Grants Awarded by Institution

Bankhead-Coley Program Demonstrating Impact in Key Areas

Since January 2007, the Bankhead-Coley Program has invested $61.4 million in 177 cancer research projects in Florida. Four years after the first sponsored research projects got underway, the Program is already producing important research findings while making valuable contributions to Florida's cancer research capacity and helping build our technology-based economy.

Boosting Florida's Technology-Based Economy by Leveraging the State's Investment

To date, the Program has provided funds to 134 experienced Florida investigators to continue their pursuit of cancer knowledge and awarded grants to 43 new investigators embarking on independent cancer research careers in Florida. Grantees have leveraged these awards to attract more than $100 million in additional funding to Florida. Figure 3 compares the value of additional funding earned by Bankhead-Coley grantees to the amount of Florida's investment by year of Program award.

Increasing Florida's Skilled Workforce

The Program's contribution toward building and sustaining Florida's scientific workforce is significant. Each of these projects typically includes compensation for additional support staff, including graduate students, postdoctoral researchers, research associates, laboratory technicians, nurses, and biostatisticians. This additional funding has a multiplier effect on technology-based employment, bringing the estimated total number of jobs supported to 1,837.

Building Florida's Reputation for Excellence in Cancer Research

Bankhead-Coley cancer research findings are stimulating dialogue among Florida's own research community and helping to earn increasing national and international recognition for the quality of research being conducted in Florida. This is evidenced by the growth in the number of publications in peer-reviewed journals and presentations at scientific meetings (see Figures 5 and 6). Appendix E contains the list of the year's publications, as reported by Bankhead-Coley awardees.

Patents also signify unique and innovative research contributions. As of September 1, 2010, Bankhead-Coley grants have already produced five patent filings.

Sustained state funding for the Program since 2006 began paying dividends in 2008, when cumulative external funding exceeded Florida's total investment. Because there is typically a lag of up to two years before external funding can be expected – one year of research with Program funding and at least six months for a standard federal review cycle – a return of $109 million on Florida's investment after only four years is significant. This differential has continued to grow significantly throughout 2010. Appendix D contains a list of additional funding reported by Program grantees in 2010.

Indicators of Program Performance

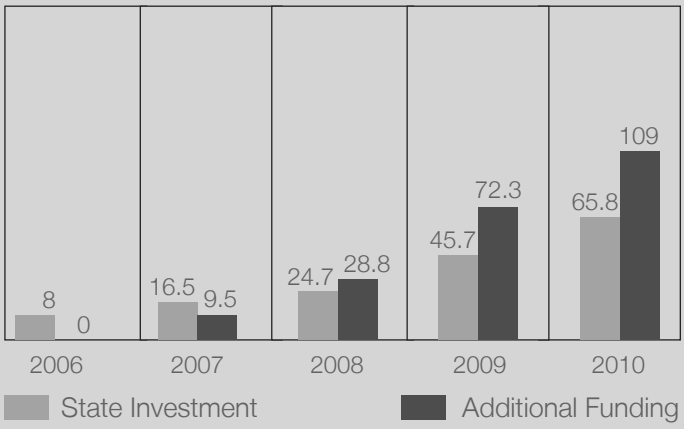


Figure 3 – Cumulative Additional Funding Based on Bankhead-Coley Grants ($ millions)

Pursuing Improved Cancer Prevention, Diagnosis, and Treatment

Bankhead-Coley grants have intensified the research effort in Florida to improve our understanding and ability to treat cancer in all its forms. The portfolio of funded projects represents a multi-faceted approach.

Roughly two-thirds of all awards have funded research targeting organ-specific cancers, as shown in Figure 4.

The remaining projects grouped into the general category of this figure are crosscutting, such as the basic science underlying the origin and development of tumors, improved diagnostic tools and treatment protocols, and state-of-the-art research instruments that benefit scientists conducting a variety of cancer research.

In the last two years, the Program has increased its emphasis on health disparities research and translational research. As a result, the number of projects addressing health disparities has increased from 10 by 2008 to 37 by 2010.

The percentage of funded projects classified as translating laboratory discoveries to patient treatments increased from 42 percent in 2009 to 62 percent in 2010.

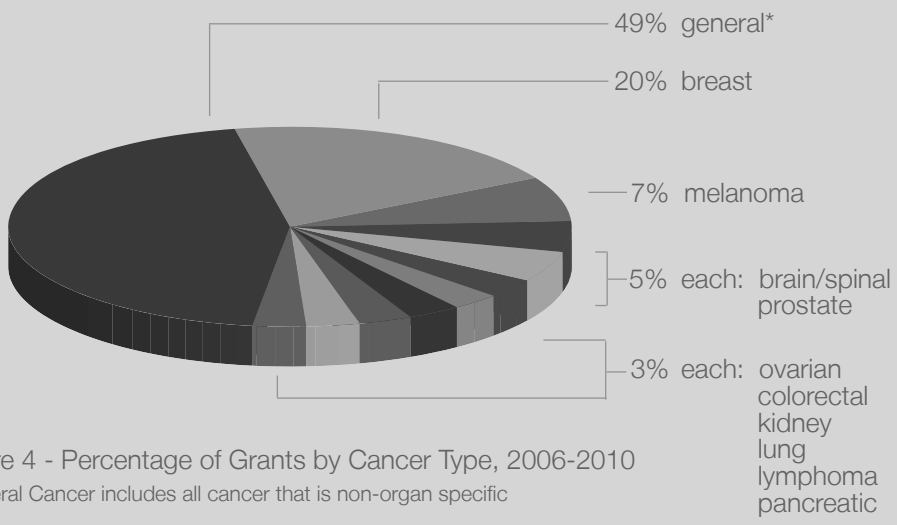


Figure 4 - Percentage of Grants by Cancer Type, 2006-2010
*General Cancer includes all cancer that is non-organ specific

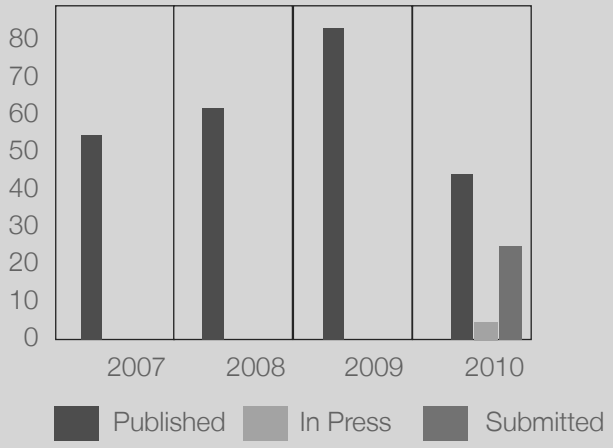


Figure 5 - Publications in Peer-reviewed Journals by Year

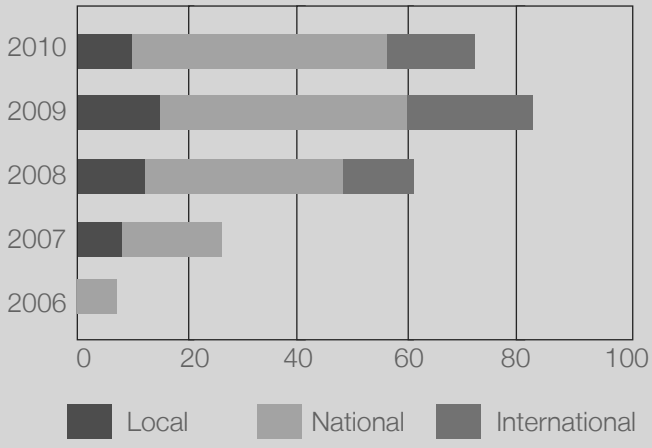


Figure 6 - Scientific Presentations by Year

Program Accomplishments
Goal: Expand Cancer Research Capacity in Florida

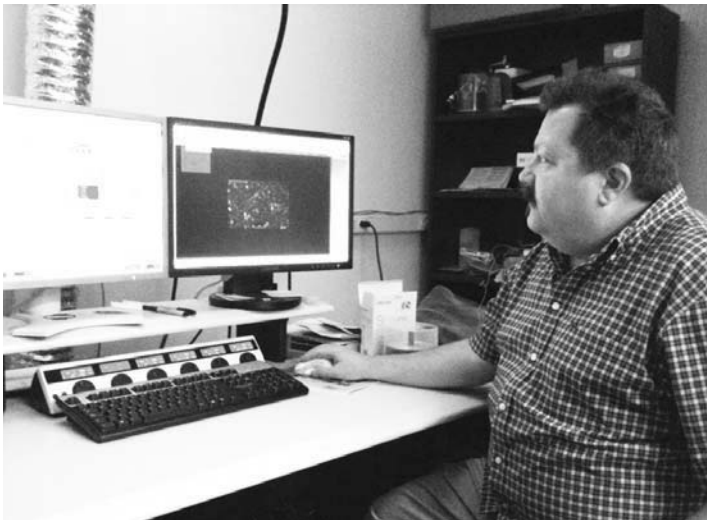
According to a report prepared by the State Science and Technology Institute (SSTI) for the Economic Development Administration of the U.S. Department of Commerce, seven elements are required to foster regional technology-based economies. The first four on the list are:

- Highly skilled technical workforce
- Mechanisms for transferring knowledge from one individual or company to another
- Intellectual infrastructure (universities and research laboratories that generate new knowledge and discoveries)
- Physical infrastructure (including high-quality computing)[5]

The Program helps attract and retain highly productive cancer researchers to Florida with grants that provide support geared to scientists at various experience levels as well as access to more state-of-the-art instruments.

These elements reinforce the importance of this statutory goal and underscore the value of the Program's accomplishments to date:

- Bankhead-Coley grants have helped 43 investigators launch independent research careers in Florida, helping the state's institutions compete globally for the best emerging talent. The awards help these scientists build their own data, publish and present their findings, and demonstrate the level of productivity required to earn long-term federal funding.



Steve McClellan, laboratory member on 2006 SIG led by Stephen Sugrue, University of Florida

- At least 60 of Florida's established researchers have provided mentoring to early-career scientists on Bankhead-Coley research projects, helping to cement long-term relationships within the Florida cancer research community. Mentoring is a required component for both the New Investigator Research Grant and the Postdoctoral Research Fellowship, and provides not only scientific training but also training in laboratory management, as well as opportunities for joint publications and grant applications, presentations, and new collaborations.

- Over 130 experienced scientists have maintained and grown their laboratories with Program awards. Amid increasing competition for federal funding, these grants help build momentum based on years of previous research findings, and are increasingly earning a strong reputation for Florida as a desirable home for cancer research.

- Eleven major instruments have been purchased for six different Florida institutions, enhancing the capabilities and future funding opportunities of the many researchers who share access to them. In return, institutions pay service agreements and provide dedicated personnel and instrument training.

Research Results: Expanding Cancer Research Capacity in Florida

The following pages illustrate how the statutory goals of the Program are being met through research funded by this Program.

Selectively Targeting Cancer-Promoting Enzymes

Dr. Yi Qiu, 2007 NIR grantee at University of Florida (UF), is developing a group of enzymes that influence many cancers. There is one drug on the market to inhibit the enzyme function, but it has no specificity in enzyme selection. She is developing a strategy to screen potential drugs that more selectively target cancer-promoting enzymes, without interfering healthy cell function.

When Dr. Qiu received her Bankhead-Coley grant, she was non-tenure track faculty, meaning she was limited in finding high-quality personnel and purchasing supplies for her lab.

"Universities only provide limited startup funding for non-tenured track faculty. The Bankhead-Coley grant gave me the opportunity to get research started in my lab. I now have an [NIH] R01 ($1 million over four years) and have recruited five to my lab from outside Florida."

The scientific community is recognizing her work by peer-reviewed decisions to publish her papers (eight already) and numerous invitations to present, including the prestigious Federation of American Societies for Experimental Biology (FASEB) Summer Research conference. With her Bankhead-Coley funding, a new cycle of research productivity has begun in Florida.

"We established our research, which benefits our university as well. I am now a tenure track assistant professor at University of Florida. The Program is very important for non-tenure track, new investigators because there are really not many opportunities for this group."

Developing Ways to Improve Chemotherapy's Effectiveness

Dr. Takeo Urakami of Sanford-Burnham Medical Research Institute has a 2010 PRF to conduct breast cancer research and to develop a more effective way for chemotherapy to reach cancer. "We want to improve chemo by making a highway to cancer by temporarily regulating the tumor vasculature. As a result we can reduce the amount of drug and harm to healthy tissue and improve the quality of patient life during chemo."

Mentoring is an important aspect of Dr. Urakami's career transition from industry to academia in Florida. "My mentor, Dr. Komatsu, has strong international collaborations, and I can develop relationships with those people. The Program is of great benefit for me to accomplish the research, develop independence, and to quickly move my research to the next step."

Principal Investigator Takeo Urakami, 2010 PRF, Sanford-Burnham Medical Research Institute

Studying the Effect of Environmental Pollutants on Breast Cancer

Dr. Quentin Felty, 2009 NIR grantee from Florida International University (FIU), is studying the effect of environmental pollutants on breast cancer. He explains the significance of his grant award: "We have very few breast cancer researchers here. This funding has given us an opportunity to train our graduate students in breast cancer research, which can help them in getting biomedical research jobs. When I arrived at FIU, the university mission began to change its focus to become more involved in research. This grant has helped to promote this mission. As we publish and present our findings, grants like this will help show that FIU is a place to do research.

"As a result of the grant's first year, I hired help, increased productivity, and published in Life Sciences. I also was awarded an NIH grant for $760,000 for a related project. I believe the Bankhead-Coley grant on my resume showed a track record and influenced my project's credibility. It's a great opportunity for me as a young investigator to get started and move to the next step."

Developing New Technologies for Improved Prostate Cancer Diagnosis

Dr. Qun Huo, University of Central Florida (UCF), is using 2009 Bridge funding to develop and test the feasibility of a new instrument and method for detecting unusual proteins present in prostate cancer. She described the method as "more accurate and convenient than current ones. The method gives scientists new capabilities to see reactions and biological processes, is lower cost than current tools, and should enable earlier, more accurate diagnosis." Dr. Huo has filed a patent application for the technology.

While developing a new research tool, Dr. Huo offers students the skills to establish their own scientific careers. "One of my graduate students did a substantial amount of work on this technology development and is a co-inventor. My students find jobs very quickly."

Dr. Huo started a new company, Nano Discovery, Inc. and is the business partner on a Bankhead-Coley TTCP Grant to commercialize the technology over the next two years. With collaborators at M.D. Anderson Cancer Center and UCF, Dr. Huo is currently selecting medical schools for test sites throughout Florida and the U.S.

Finding a New Target for Invasive Breast Cancer

Dr. Peter Storz, Mayo Clinic 2007 NIR grantee, studies how breast tumor cells migrate and invade surrounding tissue. "During the course of our project, we identified a potential new marker and target for invasive breast cancer. Long-term this will lead to new therapeutics."

Landing the first federally funded NIH R01 award is a career milestone for most biomedical researchers. Dr. Storz has already won two R01 grants totaling more than $4 million over five years, and he attributes his success to the Program. "The Bankhead-Coley grant allowed me to establish an independent research program, receive a career promotion, and serve as a reviewer for international journals and grant institutions. I am now mentoring other new investigators and have been able to attract outstanding students and postdoctoral fellows from U.S. and Europe."

Bankhead-Coley grants strengthen Florida's research institutions not only by establishing new individuals, but also by stimulating dynamic, synergistic partnerships. According to Dr. Storz, "Program grants have enhanced interactions between research, clinic, and education at Mayo and led to the formation of a translational research group focusing on breast cancer with outstanding clinicians and basic research working hand-in-hand to translate discoveries."

Principal Investigator Qun Huo, 2009 Bridge, University of Central Florida

Principal Investigator Suming Huang, 2007 NIR, University of Florida

Testing New Treatments for Multiple Myeloma

Dr. Dmitry Gabrilovich, Moffitt Cancer Center & Research Institute, received a 2006 Bridge grant to study multiple myeloma, a cancer of the plasma cells in bone marrow. Based on the data generated with this grant, the NCI awarded the team $1.3 million in 2008 to develop new therapies. One team member, Dr. Yulia Nefedova, a postdoctoral fellow during the Bankhead-Coley grant, served as a co-investigator on the project. In 2008, after her Bankhead-Coley work, Dr. Nefedova became Principal Investigator on the NCI grant, received a promotion to independent investigator at Moffitt, and won an additional $200,000 in 2010 from the Multiple Myeloma Research Foundation. In addition, this project has captured the attention of two pharmaceutical companies, Roche and Merck, who are interested in testing several compounds as lead candidates for drug development. According to Dr. Gabrilovich, all of this progress is a direct extension of the original Bankhead-Coley grant.

"The Bankhead-Coley grant gave us the opportunity to generate strong data and to publish in a high-visibility journal, *Blood*. Both of these convinced NIH to award more funding to this project. The grant gave us a chance to improve the scientific outcome terrifically and to move the work closer to improved health outcomes for people," said Dr. Gabrilovich.

Researching the Underlying Causes of Leukemia

Dr. Suming Huang, 2007 NIR grantee at University of Florida, studies the factors that control the development of leukemia and is working to alter disease progression. "Such basic research lays the foundation to reach our goal of improving human health," he explained.

Dr. Huang's Bankhead-Coley grant provided him the people and time to gather data, publish results (11 publications in 2 ½ years), and prepare competitive grant applications. As a result, he leveraged his Bankhead-Coley funding ($375,000 over three years) to win $4.3 million in five grants from the NIH and the National Heart, Lung, and Blood Institute. In three years' time, Dr. Huang has transitioned successfully from a new to established investigator at a Florida institution; ten people now receive training from this expert, and he has given presentations around the globe. With the reporting of results in esteemed journals, he has developed collaborations from Hong Kong to the UK to Florida's Moffitt Cancer Center & Research Institute, as well as among NIH and NCI faculty scientists. Such connections start a cycle of continuing research activity, and as Dr. Huang's research grows, Florida is strengthened as a place where high-quality biomedical research happens.

We use the Bankhead-Coley and James & Esther King Programs continually for recruitment of not only our basic scientific staff, but also our clinicians, because Mayo feels that it is very important that clinicians be involved in research. During interviews we let them know about the research opportunities the Program provides.

- Dr. Robert Smallridge
Mayo Clinic
2007 Bridge Grant Co-Principal Investigator

The Program has specifically encouraged research addressing health disparities in its Calls for Grant Applications and in the fundamental design of certain grant types. The number of grants classified as health disparities research increased from 10 to 37 between 2008 and 2010.

Program Goal: Reduce Impact of Cancer on Disparate Groups

Health disparities are differences in the incidence, prevalence, mortality, burden of diseases, and other adverse health conditions or outcomes that exist among specific population groups in the United States. Health inequality describes instances where the health outcomes among specific population groups differ despite comparative access to health care services.[6] Cancer remains the second leading cause of death in Florida[7], and the State's high cancer burden is impacted by its highly diverse populations.

Minority status: The African American population constitutes 16.1 percent of Florida's citizens. Hispanics are 21.5 percent of all Floridians, and Florida ranks third in the country in Hispanic population.[8] Overwhelming evidence shows that racial and ethnic minorities are prone to poorer quality health care than white Americans, even when factors such as insurance status are controlled.[9] As Figure 7 reveals, while cancer rates for all races are decreasing, a clear gap between white and non-white death rates remains.[10]

Socioeconomic status: The percent of Floridians living below poverty level in 2008 was 13.0 in urban areas and 17.8 in rural areas.[11] A large body of evidence indicates that socio-economic status is a strong predictor of health, and disease is more prevalent and life expectancy shorter the lower one is on the socio-economic status hierarchy.[12]

Rural status: Rural citizens comprise 7 percent of the State's population.[13] Geographic isolation, health risk behaviors, and limited job opportunities contribute to health disparities in rural communities.[14]

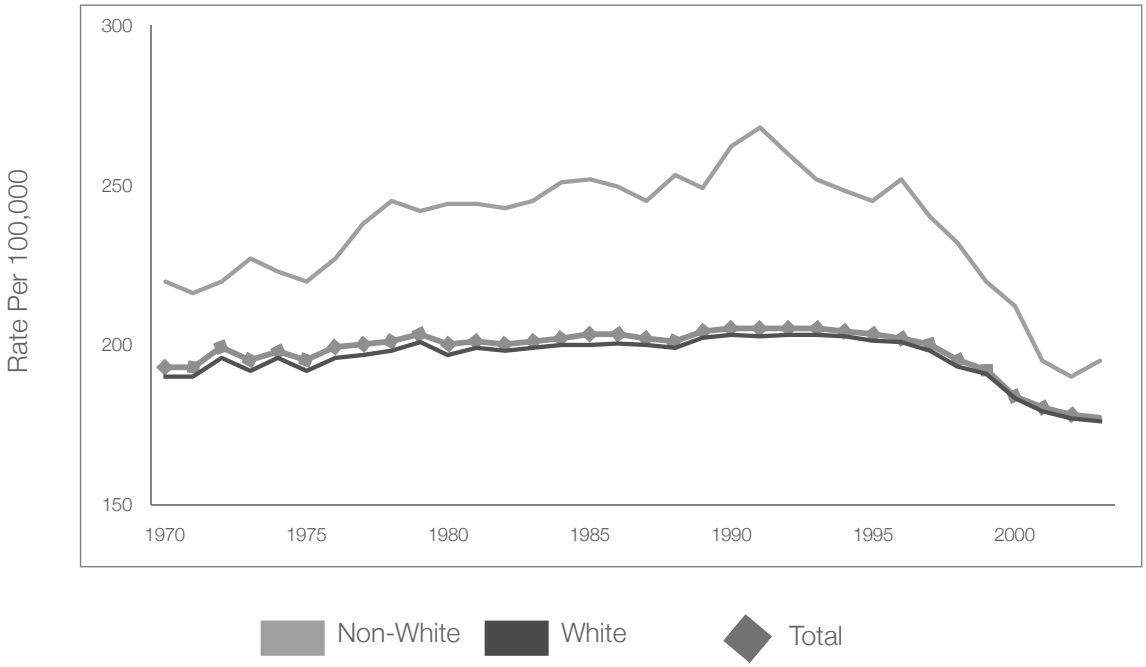


Figure 7 - Florida's Cancer Mortality Rates by Race

Research Results: Reduce Impact of Cancer on Disparate Groups

The following pages illustrate how the statutory goals of the Program are being met through research funded by this Program.

Evaluating DNA Repair and Breast Cancer in Minority Populations

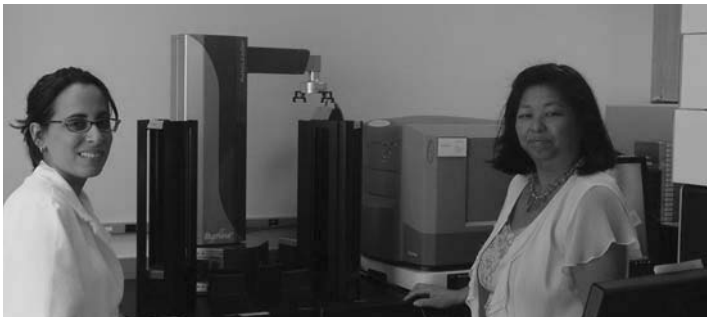
Miami-Dade County has 80 percent minority populations. Dr. Jennifer J. Hu, University of Miami 2010 RPG grantee, explained that "more of our population has late stage, advanced breast cancer-close to 30 percent at diagnosis-compared to ten percent at other medical centers. Minorities are at high-risk for more aggressive forms of the disease with worse outcomes."

Dr. Hu is investigating whether this group is genetically predisposed to serious forms of breast cancer by studying DNA repair. "No previous study has evaluated DNA repair in minority populations. In the long-term, we hope to improve the treatment and health of the underserved.

South Florida has a unique population which provides great opportunities for health disparities research," Dr. Hu explained. For her Bankhead-Coley project, she will use 1,200 samples (600 Hispanic and 600 African Americans) collected at Jackson Memorial Hospital and Sylvester Comprehensive Cancer Center.

As a member of an NIH study section, I have perspective on the Program from outside Florida. My colleagues are jealous of our state funding. The Program has a good reputation based on high-quality publications investigators produce.

- Dr. Jin Cheng
Moffitt Cancer Center & Research Institute
2007 Bridge Grant



(From left to right) Research Associate Yoslayma Cardentey and Principal Investigator Jennifer Hu with Illumina BeadStation, 2006 SIG, University of Miami

Studying Breast Cancer Gene Expression in Minority Populations

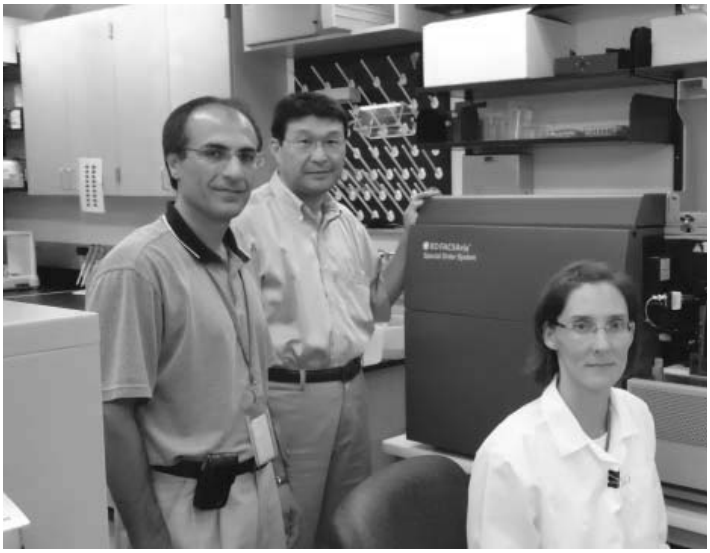
Dr. Lisa Baumbach, University of Miami 2009 RC1 grantee, explained that Bankhead-Coley funding has provided "a missing piece in our study of how breast cancer genes are expressed in different ethnicities. The Bankhead-Coley grant is a fantastic opportunity to allow us to move this work forward. This research is providing the groundwork for understanding disparities in African Americans (AA) and Caucasians. We will examine 25 normal breast tissue samples per group from African Americans and Caucasians to compare their gene expression patterns.

"It is well-known that AA women have a number of disparities in breast cancer," Dr. Baumbach explained. "The disease occurs more frequently, at younger ages, and in more aggressive forms with increased mortality."

"If we find there is a genetic tendency to higher incidence and worse outcomes in breast cancer, this sets the stage for treatments that can lead to a change in risk factors for this group."

The team is working with the Analytical Imaging Facility at University of Miami to employ a highly accurate state-of-the-art technology, laser capture microdissection, to study tissue samples.

The American Association for Cancer Research has asked Dr. Baumbach to chair and organize the breast cancer session at the National Cancer Disparities Meeting in Miami this year.



(From left to right) Fluorescence activated cell-sorter (FACS) Core Facility Director Mahyar Nouri-Shirazi, Principal Investigator Yoshimi Shibata, and FACS Core Facility Assistant Elisabeth Guinet with FACS, 2006 SIG, Florida Atlantic University

Bringing Benefits of Urban Radiation Oncology to Rural Areas

Dr. Jatinder Palta, University of Florida radiation oncology physicist and 2009 Bridge and RC1 grantee, is leading a collaborative effort to standardize computer protocols among radiation therapy equipment manufacturers to facilitate information sharing among systems. Vendors currently develop therapeutic devices without considering interconnectivity and interoperability.

This effort is likely to improve the quality of care for a broad spectrum of cancer patients, but patients in underserved or remote areas especially stand to benefit for several reasons. Physicians frequently desire an expert's second opinion for patient treatment plans. Interconnectivity would permit a peer review of imaging data by experts along with suggested treatment plans to minimize healthy tissue damage, which reduces patient toxicity and morbidity. In addition, interconnectivity would allow physicians to receive previous patient imaging and treatment information, preventing unnecessary testing.

"It's not easy for a cancer patient receiving daily treatment for 4-8 weeks to travel. With the information sharing described here, patients can get excellent treatment-no matter where they are. Our Center physicians get calls all the time from physicians and at times they are unable to help because they may not have the imaging and treatment plan data to formulate an opinion," explained Dr. Palta.

Ten major manufacturers of radiation therapy equipment (representing 97 percent of the equipment used nationwide) are allowing nearly 100 engineers from their companies to work on a voluntary basis on this project to implement consistent standards. According to Dr. Palta, "The state of Florida has given us the opportunity to leverage our grant. This contribution from manufacturers is worth millions to improve interoperability. The grant allows me to oversee that contribution." The work is supported by the American Society for Radiation Oncologists and grew out of a task force headed by Dr. Palta.

A prototype is expected by the end of next year followed by a pilot test. Once developed, a small company in Melbourne, Florida, called Sun Nuclear Corporation, is interested in developing the prototype into a commercial product. Clinical trial groups in Japan, Canada, and Australia have already expressed interest in the project.

Supporting Breast Cancer Screening in Underserved Areas

Dr. Mia Liza Lustria, 2007 NIR grantee, and her team at Florida State University (FSU) have developed a web-based reminder and patient management system called STEER to support breast cancer screening for underserved women and to understand their barriers to screening. "Women in rural and underserved areas face significant barriers; financial and transportation are the biggest issues. STEER helps document these barriers and matches women with resources they need. We have brought these issues to the attention of key stakeholders and interest groups such as faith-based ministries, DOH clinics, and the Northwest Florida Cancer Collaborative to coordinate outreach efforts."

Dr. Lustria pointed to the project as an important piece of health informatics at FSU. "STEER adopts a patient-centered approach to health informatics systems and has contributed to a better understanding of how to develop such systems for resource-limited communities. Key to the success of this approach is an interdisciplinary design including consultation with healthcare providers, patients, and experts in the areas of health informatics, rural and family medicine, and health promotion," explained Dr. Lustria.

Health Disparities Research Summit

This year, the Advisory Council and staff collaborated with FL CURED and the Department's Office of Minority Health in hosting an invitational summit on health disparities research. Held on October 26, the summit coincided with the BioFlorida Annual Conference, the state's premier gathering of biotechnology, biomedical, pharmaceutical, and medical device interests. A major goal of the summit was to begin defining a health disparities research agenda for Florida that could guide future Program grant offerings designed to address the problem of health disparities. Follow-on activities are underway as this report goes to press.

(From left to right) Principal Investigator Zhibin Chen, Laboratory Members Esperanza Bas Infante and Jason Miska, 2009 NIR, University of Miami

Turning a new idea into discovery requires intense focus on details rather than the big picture. "In the path from new idea, to discovery, to development, to practical application, multiple fields of expertise are required, and the same focus on detail that was required to make the discovery can prevent a scientist from seeing the potential uses of his or her discovery."[15]

Encouraging Research, Institutional, and Industry Partnerships

All Program grants encourage some degree of collaboration. As research progresses, projects frequently develop into efforts that become interdisciplinary and combine research and clinical expertise to apply findings to patient care. All of the grantees interviewed for this Annual Report have developed collaborations, and in some cases, were attracted to a Florida institution because of the potential for teamwork with experts.

In some projects, such as natural product development, research could not happen at all without a multidisciplinary team. In other cases, research is accelerated, leading to new findings and a cycle of growth that often extends to international levels and broad, collaborative, comprehensive cancer research efforts.

Florida researchers have formed collaborations in at least a dozen countries and at institutions across the state and nation. Of the grantees (30) interviewed for this report, every one responded that they had formed new collaborations through their grants, and the frequent result was more grant applications, publications, presentations, and additional funding.

People at the FASEB conference [Federation of American Societies for Experimental Biology] were very positive about Bankhead-Coley. It has a reputation for solid research and a high-quality peer review process.

- Dr. Silvia Tornaletti
University of Florida
2008 NIR Grant

Research Results: Give Preference to Projects Fostering Collaboration

The following pages illustrate how the statutory goals of the Program are being met through research funded by this Program.

Leading Team of 30 to Study Aggressive Forms of Breast Cancer

Dr. Joyce Slingerland, University of Miami 2009 SPORE grantee, is heading a team of more than 30 researchers who are concentrating their efforts on the most aggressive forms of breast cancer that do not respond to current therapies. They are uniting decades of experience to test new combinations of therapies and to develop innovative methods to grow breast tissue in the lab-all to find effective treatments with less toxicity for patients.

Each of the grant's four projects consists of a partnership between cancer researchers and clinicians, and discussions of progress among the entire team occur bi-weekly. In addition, another 70 researchers contribute to the team's thought processes during a monthly meeting of breast cancer researchers at Sylvester Cancer Center. Dr. Slingerland described the SPORE as a "wonderful mechanism to bring these groups together" and explained the benefits.

"Clinicians can help direct the questions of researchers based on what they see in patients—the work moves from the bench to the bedside in a very targeted way. During our meetings, people raise questions, provide feedback, and offer the creative input necessary to bring this work to fruition. We see an amplification of intellectual investment as we discuss the projects."

This effort will culminate in an application for the NCI Breast SPORE grant mechanism in May 2011. SPOREs are significant grants (up to $12.5 million over five years) designed to promote interdisciplinary research and to focus on a single specific human cancer.

Delivering a New Method for Looking at DNA

As a result of Dr. Silvia Tornaletti's grant, University of Florida 2008 NIR, scientists have a new method for assaying (determining the presence and amount of a substance) unusual DNA structures, which promote cancer. "Now we can isolate what we want to study and have high confidence in our results, because we have a way to confirm the structure."

The novelty and significance of this work has sparked partnerships at Stanford and with Italian researchers. In addition, she explained that, "The mentoring I received through the Bankhead-Coley grant allowed me to do things I am not equipped to do. Dr. Linda Bloom, my mentor, has the expertise and expensive machine to do a fluorescence method that I, as a junior investigator, do not have. My expertise is different than hers, and we've really found common ground and have developed a collaboration."

Since receiving her grant, she has developed a new method, is now a mentor herself, and has published, presented, and prepared a federal grant application based on her grant data.

This is an outstanding program that Florida has to retain its rich source of biomedical researchers.

- Respondent 61196304
DOH Grantee Satisfaction Survey Results
February 2010

Using a Team Approach to Develop Pancreatic Cancer Treatment

Dr. Esther Guzmán, Florida Atlantic University 2009 NIR, is looking inside the richness of Florida's marine life to find answers for one of the most aggressive cancers, pancreatic.

The journey from marine organism to clinical testing is a long-term, collaborative effort requiring many types of expertise and institutions. The process begins with a highly specialized retrieval system; technicians screen compounds, testing for anti-cancer activity; organic chemists analyze, synthesize, and purify the compounds (to preserve natural organisms). Cancer researchers conduct tests for effectiveness in animals and push the work to the clinic. A mentor at M.D. Anderson Cancer Center and collaborators at Torrey Pines Institute for Molecular Studies, Sanford-Burnham Medical Research Institute, and Florida Atlantic University are important partners in this research.

"It's fantastic to have a natural product chemist and microbiologist here to speed the research along. We have screened 1,200 compounds and identified five potential cancer inhibitors."

"This is a very collaborative effort, and whenever you have a big collaborative research endeavor, it attracts other people and leads to other work. Currently, we have a company interested in our compounds."

Utilizing an Instrument as a Centerpiece for Collaboration

Dr. John Koomen, Director of Proteomics at Moffitt Cancer Center & Research Institute, purchased a mass spectrometry system through a 2006 SIG. The instrument enables detection of specific targets in blood or tumor tissue to measure changes during cancer development. According to Dr. Koomen, "It is a centerpiece of collaboration between scientists and clinicians, translating findings from the lab to patient care: taking what we have learned about cancer and examining it in tumors."

The instrument also supports an interdisciplinary training program at Moffitt Cancer Center & Research Institute. Four undergraduates from under-represented backgrounds use the instrument for their research projects. In addition, they study minority health perspectives and interact with community groups that teach cancer awareness and prevention.

Perhaps the broadest collaboration generated by this instrument is an online database developed by Dr. Koomen. "We have developed tests for numerous biomarkers that are relevant to cancer treatment and are sharing them with the research community. This information can overcome research barriers and accelerate progress. Other researchers have expressed interest, and we expect more requests."

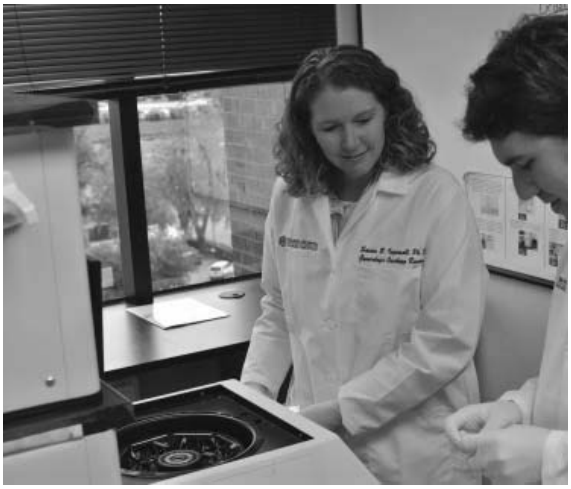
To date, $1.1 million has been awarded based on data generated using the instrument. At least 27 scientists and students use it to provide their teams with important pieces to the cancer puzzle.

Conducting a Clinical Trial with State, National, and International Collaborators

Dr. Jin Cheng, 2007 Bridge grantee at Moffitt Cancer Center & Research Institute, in collaboration with researchers at Moffitt, University of Florida, M.D. Anderson-Houston, John Hopkins, and Canadian and German groups, is conducting a clinical trial based on AKT1 work he completed during his Bankhead-Coley grant. AKT1 is a cancer-causing gene present in 57 percent of human tumors and associated with chemo resistance. The research applies to cancers of the lung, gastrointestinal tract, leukemia, and melanoma.

His team includes expertise in molecular oncology, chemistry, molecular biology, serum-based screening, drosophila models, and clinicians. The work has resulted in three patents, two licensing agreements with pharmaceutical companies (Rioquest and Samtheo), and work on Moffitt's lung cancer SPORE grant from the NCI. The collaboration with the German group has resulted in a new antibody, which is licensed with a biotech company, Millipore.

"We have shared data freely, and with good results," said Dr. Cheng.



Principal Investigator Susan Blaydes Ingersoll and laboratory member Gregory Stoltzfus, 2009 NIR, Florida Hospital Cancer Institute

Developing Partnerships to Study a Variety of Cancers

Dr. Yoshimi Shibata and The Cancer Research Program at Florida Atlantic University received a fluorescence-activated cell-sorter (FACS) through a 2006 SIG.

The FACS continues to play a major role in developing partnerships both without and within FAU. According to Dr. Shibata, "Cancer researchers here regularly discuss the highly sophisticated data generated by the FACS with collaborators at Virginia Tech, The University of Iowa, and Massachusetts General Hospital."

Dr. Shibata also described how the instrument will support new research partnerships at FAU. "This is the most important tool for cancer research. It is necessary for studying how cancer develops and how we can extend findings to human treatment. With the start of FAU's new medical college next year, we will have more clinical access, and the FACS will be an important tool for building those collaborations," Dr. Shibata explained.

Another collaboration this team is pursuing revolves around a compound they identified from crab/shrimp shells that has shown anti-cancer effects against breast and colon cancer in animal studies. The team has submitted a patent application and has begun exploring clinical and commercial partnerships for natural product development.

"These connections with other groups, as well as $2 million awarded in federal/state grants, would not have been possible without the FACS," Dr. Shibata pointed out.

Uniting Researchers and Clinicians in Thyroid Cancer Studies

Dr. John Copland, a cancer biologist, and Dr. Robert Smallridge, a clinician, launched a nine-member collaborative team at the Mayo Clinic with 2007 Bankhead-Coley Bridge funding, bringing together researchers and clinicians to find new treatments for thyroid cancer (anaplastic type, which has a four-month average survival rate). They have tested a new drug, CS-7017, in the laboratory and in a Phase 1 clinical trial.

"A team approach was essential because we needed patient samples before research could start. We built connections between research and the clinic because, ultimately, we want to help patients," Dr. Smallridge explained.

The team approach has paid off in the form of a grant from NCI worth $2.3 million and support (Phase 1 clinical trial) from a pharmaceutical company, Daiichi-Sankyo, to translate their findings into new therapies. They have now completed a Phase 1 clinical trial at nearly a dozen sites around the country from the University of Oregon Health & Science Center to Harvard. Dr. Smallridge's patient referrals have more than doubled in the last five years, a fact that he links to his research partnerships and involvement with clinical trials.

"The Bankhead-Coley has been astonishingly positive in terms of science being taken into patients today because of work supported by the Program. There is no question in my mind that providing the best patient care comes from a combination of education and research to take us to the highest level. We have to have support to do that, and there are simply not enough federal dollars. We owe it to the citizens of FL to continue Programs like this," said Dr. Smallridge.

The work has also spun off into a number of new collaborations:

- Dr. Smallridge was appointed Chair of a national collaborative effort coordinated by the American Thyroid Association to develop clinical guidelines for anaplastic cancer. "This appointment came as a direct result of the work we published from the Bankhead-Coley grant, which also led to a series of highly recognized review articles. The Bankhead work has been a critical component," he added.

- Dr. Smallridge has been invited to present at the 2010 International Thyroid Congress.

- Two of Dr. Copland's undergraduate students have chosen MD/research programs focused on cancer as a result of this work, and two clinician fellows have spent time in the lab learning basic research practices.

The Program has awarded 23 grants that focus on research related to increasing clinical trials in Florida; some of these projects are testing new treatments in patients while others are laying important foundations for stimulating more clinical trials in the future.

Clinical trials are strictly controlled studies involving living people that collect data regarding the safety of new drugs and treatments as well as their power to produce the desired effect.

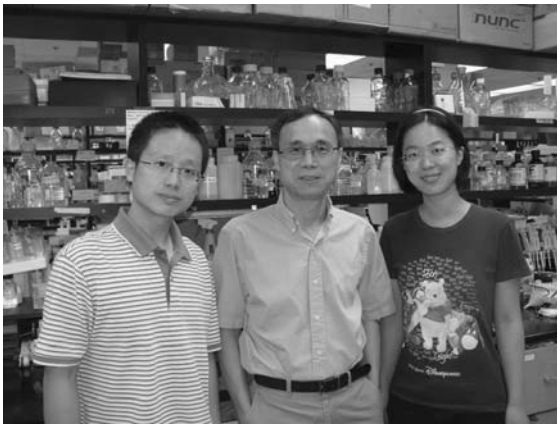
Clinical trials networks are partnerships between community healthcare providers and scientific researchers, often with support systems that facilitate the conduct of trials, such as providing patient education services, data registries, and tools for matching patients to existing trials. The objective is to offer patients a more active role in their health care, access to new medications or treatments before they are widely available, and the opportunity to help others by contributing to medical research. A challenge researchers face is recruiting enough patients to achieve statistically sound results. Without enough patients, it is difficult to conclude anything from results.

Striving to Increase Clinical Trial Participation

The Program has pursued several strategies for increasing participation in clinical trials in Florida. Of the 23 Bankhead-Coley awards to date related to clinical trials:

- Two Special Emphasis Project (SEP) grants have sought to identify barriers to the participation of Florida cancer patients in clinical trials and recommend interventions; one of these projects has enhanced the capabilities of the Florida Cancer Trials Network and both have gone on to earn additional funding to continue their work.
- One Florida Research Challenge (RC1) Grant is examining the ethics issues in the conduct of clinical trials.
- Six Specialized Programs of Research Emphasis (SPORE) Planning Grants have helped launch multi-disciplinary teams of basic and translational researchers studying organ-specific cancers and pursuing SPORE grants from the National Cancer Institute; the latter awards require a minimum of four translational research projects that will reach a living human endpoint within five years.
- Twenty grants of various types including some mentioned above have included the conduct of a clinical trial as part of the project.

In setting priorities for future Program funding, the Advisory Council has identified two new potential strategies for expanding support for clinical trials networks (see Strategic Planning section of this report).



(From left to right) Laboratory member Heng Yang, Principal Investigator Daiqing Liao, and Laboratory member Zhi Zheng, 2009 RC1, University of Florida

Research Results: Give Preference to Projects Fostering Collaboration

The following pages illustrate how the statutory goals of the Program are being met through research funded by this Program.

Testing New Vaccine Therapies for Brain Cancer

Dr. John Goldberg, pediatric oncologist and 2009 NIR grantee at University of Miami, is conducting a Phase 1 clinical trial through his Bankhead-Coley NIR grant to test a vaccine therapy for malignant glioma and glioblastoma multiforme (types of brain cancer) in adult and pediatric patients experiencing cancer recurrence. His initial trial includes 10 patients. (Phase 1 trials evaluate therapy safety in a small sample size, and are for patients with no other alternative treatments.)

"Our mission is to improve treatment and extend patient long-term survival, which is currently about 6 months after recurrence. The project is important for the people of Florida because we are building on cutting-edge laboratory science. My mentor, Dr. Eli Gilboa, is Director of the Dodson Interdisciplinary Immunotherapy Institute. He is well recognized and is the founding theoretician behind this work. My collaborator, Dr. Ian McNiece, Director of the Cellular Manufacturing Program, is a specialist in creating human cell therapies. Dr. McNiece is a world expert in manufacturing cellular treatments in a way that the FDA considers acceptable. These are two leading scientists who will be invaluable in developing the clinical trial."

Developing Guidelines for Clinical Trial Approval

Dr. Benjamin Djulbegovic, 2009 RC1 grantee at University of South Florida, is leading a study to show under which circumstances patients can benefit from clinical trials. "It is very important that the public understand what clinical trials are; they are indispensable to developing new treatments and a key for progress." He described two sometimes-conflicting views of the purpose of trials: clinicians tend to view trials as a way to provide the best treatment possible for the current patient; researchers tend to view the purpose as a means to help future patients.

The study's ultimate goals are to improve the Institutional Review Board (IRB) approval rates of studies that will benefit both current and future patients, increase patients' willingness to participate in clinical cancer research.

The team plans to survey members of IRBs across the country. (IRB members are responsible for approving and reviewing research involving humans in order to protect the welfare of the patients.) "Approvals all depend on their view of risks and benefits," he explained. "We want to clarify how people react to clinical trials and develop IRB guidelines so that trials can benefit both current and future patients."

Examining Biological and Quality of Life Factors in Colorectal Cancer Outcomes

Dr. Erin Siegel, Moffitt Cancer Center & Research Institute 2009 NIR grantee, is offering colorectal cancer patients an opportunity to participate in an observational clinical study. Her multi-disciplinary team of 12 includes surgeons, psychosocial scientists, biostatisticians, biomedical informatics, and epidemiologists. The team is following participants for a year after diagnosis to see how biological (insulin/glucose) and quality of life factors (e.g., diet, exercise) influence cancer outcomes. Her long-term goal is to offer patients scientifically proven ways to take control over lifestyle decisions that can improve their outcomes. She is also examining the link between obesity, diabetes, and cancer to identify new targets for treatment. The team has already received $100,000 from the Department of Defense for a related study.

Dr. Siegel has enlisted the help of a colorectal cancer surgeon and five additional clinicians. "We tried to make it very easy for clinicians to participate and made adjustments for their schedules. They are willing to participate because they believe in our research. We added one doctor at a time to introduce the study to their patients. Most patients are willing to participate, and to date we have accrued 65 patients."

Dr. Siegel has developed ongoing collaborations with a team that submitted a Program Project Grant (large, $30 million NIH NCI grant). "We used the Bankhead-Coley grant to generate data for our application, to show that patients will participate, and to demonstrate our ability to conduct these types of studies."

Conducting a Clinical Trial for New Vaccine/ Antibody Melanoma Treatment

Dr. Jeffrey Weber, a melanoma researcher and clinician at Moffitt Cancer Center, received a 2008 Bridge grant for preclinical melanoma experiments.

"The Bridge grant was critical; it gave me the time to gather data to support combining a vaccine with an antibody. I submitted the data to the FDA, and received approval and one NCI grant ($1.2 million) for Phase 1 trials."

"This is one of the first trials of its kind in the U.S., giving Florida patients access to an exciting new immunotherapy. Out of 15 patients we followed for 5-18 months, there has not been one single progression. Those kind of results are unheard of."

"The Bankhead-Coley Program benefits patients because it gives them treatment options they otherwise wouldn't have. Based on this work, we received another $1.9 million to offer more clinical trials. Through a collaboration with the Vaccine Gene Therapy Institute in St. Lucie, we will analyze patient blood samples to understand how the antibody/ vaccine combination is working."

"The Bankhead-Coley Program provides infrastructure and support for this kind of work, which shows pharmaceutical companies that Florida researchers can accrue patients quickly, get good blood samples, do a good job, and become very interested in doing clinical trials here. That's a big impact for Florida."

Identifying Barriers to Patient Participation in Clinical Trials

Dr. Margaret Byrne, 2007 Special Emphasis Project grantee from University of Miami, conducted a study to identify barriers to patient participation in clinical trials along with potential interventions. Through a collaboration with Florida International University's Institute for Public Opinion Research, she surveyed 1,100 patients to determine disparities and barriers to participation in clinical trials among Floridians. She found people feared they would be treated like guinea pigs or that insurance would not cover a trial. Findings from her study showed less African American participation in trials (although rates in Florida were higher than nationwide), and even less participation by Hispanics in Florida.

"The Bankhead-Coley work opened the door for me to receive $1.6 million from the NIH to develop decision aids for minorities to help them make more informed decisions about participation in clinical trials," Dr. Byrne explained. "There's such a need for better information."

This work is significant not only for Dr. Byrne's team and the scientific advantage of new knowledge, but also for the health benefit of helping minority patients make informed choices about cancer treatment.

Improving Patient Information about Florida's Cancer Clinical Trials

Dr. Karen Moffitt, 2007 Special Emphasis Project grantee at University of South Florida, has developed a clinical trials information infrastructure, the Florida Cancer Trials Navigation Service. In part, her Bankhead-Coley grant provided support for the project, which provides patients and medical professionals with accurate, accessible information about Florida clinical trials. "Our goal is to help people stay in Florida for treatment because they can maintain a normal life, enjoy the support of family, avoid the expense of travel, and have the potential of a life-saving or less toxic new treatment."

Dr. Moffitt has developed collaborations with 179 community hospitals in Florida, five major cancer centers, the American Cancer Society, and the Florida Association of Clinical Oncologists to provide accurate, current information. The organization matches an average of 228 patients per month to clinical trials in Florida, tracking trials at 197 different sites in 78 Florida cities. "It empowers patients and doctors to know what's available, and gives researchers a tremendous tool," she explained.

According to Dr. Moffitt, "Such a network (offered in Spanish and English) helps the state economically. Pharmaceutical companies are also extremely supportive of our work because it makes it easier for them to conduct trials here."

Dr. Moffitt and Dr. Philip Marty have received $1.2 million in federal grants since receiving the Bankhead-Coley grant to continue this work.

Clinical Trial Networks: Improving Patient Treatment Options

I was completely overwhelmed when I was diagnosed. You can't have too many weapons in your arsenal when you're fighting cancer, and clinical trials increased my options. The matching service provides the same contact person throughout treatment. I have them on speed dial so if I have a bad PET scan, I can talk to them immediately. Because of this service, I can walk into my doctor's office with options. He doesn't have time to find trials for me. . . . Today I met another patient in radiation, and passed the information about this service on to him. Because of a clinical vaccine trial I was in, I went three years without chemo and had a good quality of life. I could raise my son and go to his football games. From where I'm standing, it doesn't get much better than that.

- Kathy Howland
Florida Cancer Patient

Kathy Howland has used the services of the Florida Cancer Trial Navigation Services for several years and is currently enrolled in her second clinical trial in Tampa. The Florida Cancer Trial Navigation Services mentioned by this patient were developed in part by a Bankhead-Coley 2007 SEP grant to Dr. Karen Moffitt, University of South Florida.

With a small amount of funding to work with in the early years of the Program, the Biomedical Research Advisory Council prioritized Program goals and made tough choices in the face of high demand in Florida for cancer research grants. Each year, requests for funding greatly exceeded the available funds. In light of the increase in the Program's budget following the Regular Legislative Session of 2009, the Advisory Council began a strategic visioning process that took into account the possibility of stable funding in the $20–25 million per year range.

Defining Bold Priorities and Strategies with Increased Funding

In November 2009, the Advisory Council held a two-day strategic planning meeting with several specific objectives:

- Set a new course for a relatively stable increased funding base
- Thoughtfully reconsider Program statutory goals
- Analyze how the Program has performed to date
- Sharpen the Program's focus
- Define metrics that demonstrate the Program's commitment to the research enterprise, to State lawmakers, and to the people of Florida

The Advisory Council continued its deliberations on strategic planning at its January and March 2010 meetings, producing the following top priorities and strategies:

Priority 1. Target workforce recruitment, retention, and training

Strategy: Continue Bridge grant support for Florida cancer research projects with high potential for federal funding. A funding crisis looms in 2011-2012 after American Recovery and Reinvestment Act (ARRA) funds are depleted, and Florida researchers and their institutions may be hard pressed to maintain momentum. (See the section below "Implementing the Priorities in FY 2011-2012" for Program-planned initiatives.)

Strategy: Sponsor cluster hires to quickly build capacity in new areas of research and attract follow-on funding. One possible target, highly relevant to Florida's need, is health disparities research. The feasibility of this idea requires research to determine whether a grant type designed to support this could be offered without exceeding statutory authority. An institutional grant might be considered.

Strategy: Offer high-performing Program grantees additional awards as incentives to continue their work in Florida.

Advisory Council members emphasized the need to recruit and retain high quality researchers and a skilled research workforce in order to obtain the highest quality science, citing examples of recent talent losses due to recruitment by other states. Different strategies are required to recruit new talent versus retain Florida's best research personnel.

Priority 2. Build new research infrastructure

Strategy: Help establish core infrastructure resources to support research programs that require access to tools and collaboration with experts beyond the independent investigator's normal means through large Institutional grants in additions to smaller investigator-initiated grants.

Possible core resources include bioinformatics, high-throughput genome studies with broad sequencing, statistical sensors, innovative technologies for collecting outcome data, data management, a data safety monitoring board (DSMB), and a center to assist with clinical trial recruitment and retention of diverse populations. Such an approach builds research capacity. It also serves a dual purpose of supporting talent recruitment and retention, particularly of translational researchers, due to access to resources not available elsewhere.

Priority 3. Increase investment in clinical and translational research and health disparities research

Strategy: Provide funding for tools to increase patients' and community oncologists' awareness of existing clinical trials, to match patients to existing trials, and to help users navigate the enrollment process.

> *Bankhead-Coley is positioning Florida as the leader it needs to be in cancer research given our state's inordinately high cancer burden. Further enhancing our research capacity and infrastructure is the impressive drawdown of more federal dollars to institutions here, just as predicted when the Legislature wisely created this Program, with Florida's rank amongst the states in annual NCI support steadily rising.*
>
> - Paul Hull
> American Cancer Society - Florida
> VP for Advocacy and Public Policy

Strategy: Invest in a statewide framework to support collaboration between academic health centers and community oncologists to conduct new clinical trials.

Strategy: Convene a statewide work group to define a research agenda for Florida in health disparities as well as to identify infrastructure resources needed by Florida researchers for health disparities research. (See the section "Bankhead-Coley Goal: Reduce the Impact of Cancer on Disparate Groups" within Program Accomplishments for details.)

As is the case with Priorities 1 and 2, institutional grants may be the vehicle to accomplish this priority. While statutory goal two is to increase participation in clinical trials networks, the methods for achieving this are limited since the Program must only offer grants for research that are in turn awarded on the basis of scientific merit. A broader mission might be to offer grants for research and research support. In the case of the latter, such project grant proposals would not be required to pose a research question in order to qualify for an award. This would require thoughtful legislative change that includes parameters for the basis of awards since traditional peer review and the determination of scientific merit may not be appropriate.

Priority 4. Accelerate technology transfer

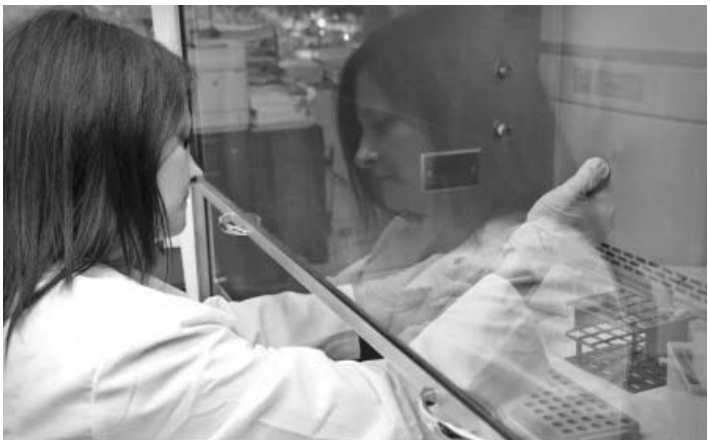
Strategy: Increase support for promising early stage projects through a new feasibility mechanism in addition to the existing commercialization partnership mechanism to help fill the pipeline of projects moving toward commercialization. (See "Pioneering Improvements in the Annual Funding Cycle" in the Program Operations section for details.)

Priority 5. Improve key processes

Strategy: Enhance the peer review process by introducing a means for resolving differences in reviewer opinions on the merits of individual proposals. (See the section below "Advisory Council Recommendations to Further the Program's Purpose.")

Strategy: Develop a standardized project classification system to characterize the portfolio of funded research more completely.

Strategy: Increase Program communication, public relations, and outreach efforts to solicit feedback from stakeholders in crafting mechanisms and refining business processes and to educate Florida's biomedical research community, its lawmakers, and the public regarding Program strengths, achievements, and vision for the future.



Ariel Fulton, laboratory member on 2009 NIR led by Erin Siegel, Moffitt Cancer Center & Research Institute

Implementing the Priorities in FY 2011-2012

In May and July 2010, the Advisory Council began using the strategic visioning document to determine grant types to offer for FY 2011-2012, and staff began implementing short-range initiatives recommended by the Advisory Council. In anticipation of next-year funding through the annual appropriation process of the Legislature, the Program released calls for applications for New Investigator Research Grants and Team Science Program Grants as this report was going to press for awards to begin on July 1, 2011. The Program will also offer Bridge Grants in three rounds (March, July, and November) in alignment with the anticipated award announcement schedule of the National Institutes of Health (NIH). By doing so, Florida applicants to the NIH who receive notices of non-funding due to budget shortfalls will be better able to submit applications to the Bankhead-Coley Program. If funded, they will conduct research to strengthen their federal application as they wait for the next opportunity to resubmit it to the NIH. Additionally, the Program will continue to offer Technology Transfer Feasibility and Technology Transfer/Commercialization Partnership grants in an open time frame.

In preparing for FY 2011-2012, the Advisory Council and staff were very concerned that the NIH will be able to fund significantly fewer applications as the ARRA funds are depleted, making federal funding more difficult to obtain, and therefore raising the importance of Program Bridge grants. With these and other factors considered, the Advisory Council recommended a conservative approach utilizing proven grant types in order to create a balance between researcher needs in Florida and Program goals.

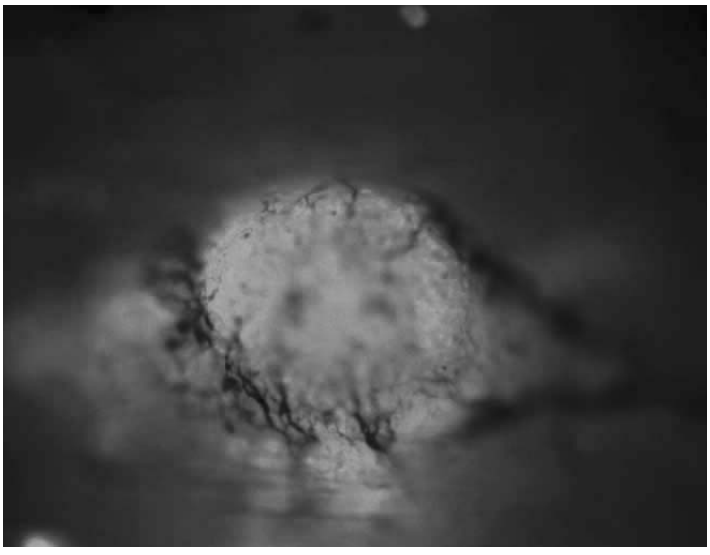
The Program intends to offer three rounds of Bridge Grants (March 2011, November 2011 and March 2012 starts) in alignment with the anticipated award announcement schedule of the National Institutes of Health, providing timely lifelines to Florida researchers who have missed federal funding by the narrowest of margins. Additionally, the Program will continue to offer Technology Transfer Feasibility and Technology Transfer/Commercialization Partnership grants in an open time frame.

Advisory Council Recommendations to Further the Program's Purpose

To further the Program's ability to pursue its goals, priorities, and strategies, the Biomedical Research Advisory Council has made the following set of recommendations to the Department:

1. **Advocate for stable State funding.** The demand for Program funding is very high, as evidenced by applicants' record-setting requests totaling $164.8 million in 2010; however, even this level of demand was constrained by the Program's limitations on research project emphases and applicant eligibility. Consistent investment is necessary to maintain the momentum built over the last five years.

2. **Recommend authority to carry forward funds for up to five years.** The Program is currently authorized to carry obligated funds forward for three years; however, certain types of grants would benefit from a longer period of support.



Tumor nodule from the research of Principal Investigator Dietmar Siemann, 2006 Bridge, University of Florida

Deepti Sharma and Ronald Hamelik on 2006 Bridge and 2009 TTCP led by Principal Investigator Awtar Ganju Krishan, University of Miami

3. **Remove the requirement that peer review panels be subject to Florida's open meeting law.** The industry norm for scientific peer review, as practiced by the National Institutes of Health, is that peer review panel communications are confidential. There is compelling evidence that allowing peer reviewers to interact in their determination of scientific merit improves inter-reviewer reliability. However, because the implementing statute requires a deviation from standard practice, the Program has modified its peer review procedures to limit review to independent peer evaluation.

4. **Maintain an adequate administrative expense allocation.** Administrative expenses are driven not only by the volume of grant applications processed and new grants awarded (a function of the annual appropriated budget), but also by the number of active grants being managed. The current portfolio of 97 active grants valued at $39.8 million requires contract oversight responsibilities independent of any new awards made.

Dr. Normann Recognized for Pioneering Efforts

In January 2010, Dr. Sigurd Normann announced his retirement from the Advisory Council after more than ten years of service. As a founding member of the Advisory Council, Dr. Normann represented the American Cancer Society. He was instrumental in crafting the original legislation creating Florida's first competitive, peer-reviewed biomedical research program following the historic 1997 tobacco settlement. At the January 2010 Advisory Council meeting, Dr. Richard Bookman, Advisory Council Chair, Mr. Paul Hull, Vice-President of Advocacy and Public Policy of the American Cancer Society, Florida Division, and Dr. Susan Phillips, Director of the Office of Public Health Research, Florida Department of Health, all spoke glowingly of the many contributions made by Dr. Normann over the years.

Dr. Normann reminded the Advisory Council of the five pillars on which the Program was built:

1. To be an annual and perpetual source of funding on which researchers could rely
2. To be a competitive program open to all qualified investigators regardless of institutional affiliation
3. To base awards on scientific merit, through a non-conflicted peer review process
4. To restrict administrative costs to a reasonable level (ten percent), thereby preserving the majority of funds for research
5. To provide professional, administrative, and scientific oversight by housing the Program at the Department of Health, while requiring an advisory council that is representative of the research community

(From left to right) Paul Hull, American Cancer Society (ACS) Vice President for Advocacy and Public Policy; Dr. Sig Normann, and Dr. Danny Armstrong, the new ACS designee to the Advisory Council.

Biomedical Research Advisory Council

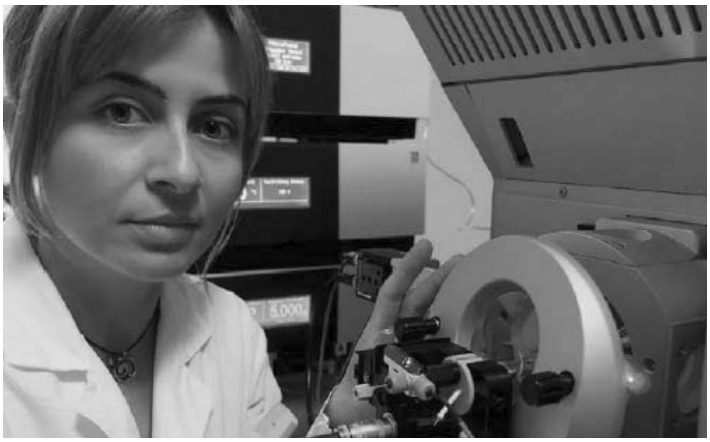
Section 381.922*, F.S.,* charges the Program with awarding grants for cancer research through the Bankhead-Coley Cancer Research Program (included in Appendix A). The Advisory Council meets this directive by advising the Office of Public Health Research at the Department of Health and the Florida State 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.

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 employs 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.

2010 Membership Changes

Two notable changes occurred in 2010 to the Advisory Council membership. The designated American Cancer Society representative switched from founding member Sigurd Normann, M.D., Ph.D. to Daniel Armstrong, Ph.D. The Biomedical Research appointment changed from Nikolaus Gravenstein, M.D., to Claes Wahlestedt, M.D., Ph.D.

(From left to right) Laboratory member Lillian Onwuha-Ekpete, Principal Investigator Vijaya Iragavarapu-Charyulu, and Laboratory members Stephania Libreros and Ramon Garcia-Areas, 2008 Bridge, Florida Atlantic University



Umut Oguz, staff scientist on 2006 SIG led by John Koomen, pictured with liquid chromatography coupled to mass spectrometry, Moffitt Cancer Center & Research Institute

The 11 appointees to the Biomedical Research Advisory Council include:

- 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, and 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

2010 Advisory Council Membership

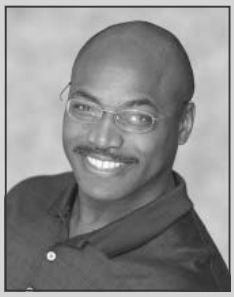
Veena Antony, M.D.
Professor of Medicine, Molecular Genetics and Microbiology
Division of Pulmonary Critical Care and Sleep Medicine
Vice Chair for Research, Department of Medicine
University of Florida
Seat: American Lung Association
Appointed: July 2007

Daniel Armstrong, Ph.D.
Professor and Associate Chair, Pediatrics
Director, Mailman Center for Child Development
University of Miami Miller School of Medicine
Seat: American Cancer Society
Appointed: January 2010

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

Randal Henderson, M.D., M.B.A.
Associate Medical Director, Proton Therapy Institute
Professor of Radiation Oncology
University of Florida, Jacksonville
Seat: House - Cancer Program (ACoS)
Appointed: April 2007

Myra Hurt, Ph.D.
Senior Dean, Research, Graduate, and Undergraduate Programs
Florida State University College of Medicine
Seat: Research University
Appointed: February 2006



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

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

Penny Ralston, Ph.D.
Professor, Dean Emeritus and Director
Center on Better Health & Life for Underserved Populations
Institute of Science & Public Affairs
Florida State University
Seat: Senate - Behavioral/Social Research
Appointed: July 2006

Mary Lou Sole, R.N., Ph.D., CCNS, FAAN
College of Nursing Professor
College of Health & Public Affairs
University of Central Florida
Seat: House - Professional Medical Organization
Appointed: April 2007

Claes Wahlestedt, M.D., Ph.D.
Professor
Neuroscience and Molecular Therapeutics
The Scripps Research Institute
Seat: Biomedical Research
Appointed: April 2010

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

As of October 11, 2010, the Program was providing oversight to 97 active grants. In a 2010 survey, 94 percent of the Program grantee respondents selected "very satisfied" or "satisfied" to rate their overall satisfaction with their Bankhead-Coley grant experience.

Continued administrative funding at ten percent is necessary for several reasons. First, Florida's CFO requires that state agencies perform contract monitoring. Each grant awarded through the Program has both standard and unique terms and conditions that the Program must monitor for compliance.

Second, Florida has invested nearly $43 million in the last two years in the Bankhead-Coley Program and now has a portfolio of 97 active grants as of October 11, 2010.[16] Figure 8 below illustrates the growing number of grants requiring management. This investment in active projects requires continued administrative oversight of financial and scientific progress through grant completion as detailed in the next section.

Maintaining Administrative Costs and Program Quality

The Program by statute can use up to ten percent of the appropriated funds for administrative expenses. As shown in Table 5 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.

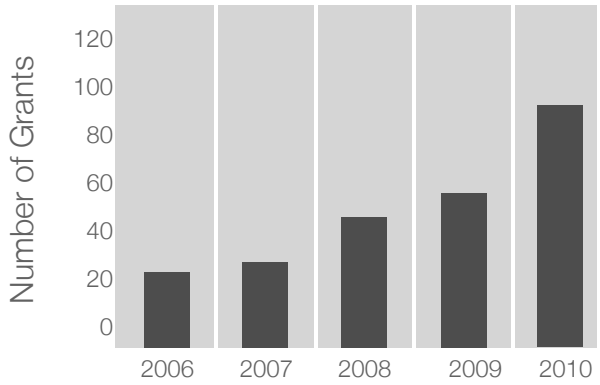


Figure 8 - Grants Requiring Administrative Oversight

Table 5 - Program Expenditures (Millions)

Fiscal Year	Appropriation	Grant Awards	Percent	Administrative Expenses	Percent
FY 10-11	20.00	18.20	91%	1.80[a]	9%
FY 09-10	23.36	21.25	91%	1.38	6%
FY 08-09[b]	9.00	8.10	90%	0.81	9%
FY 08-09[c]	6.75	6.08	90%	0.66	10%
FY 07-08	9.00	8.15	91%	0.73	8%
FY 06-07	9.00	8.10	90%	0.82	9%
Totals (excluding FY 10-11)	48.11	43.58	91%	3.59	8%

[a] Projected expenses (includes $250,000 for the Center for Universal Research to Eradicate Disease.)
[b] Original grant awards and projected expenses prior to mid-year budget reduction.
[c] Mid-year revision due to budget reduction.

Incorporating Best Practices in Grant and Program Management

Grant management involves active monitoring and includes review of a number of grantee deliverables including quarterly financial reports, yearly progress reports, mechanism-specific deliverables, continuation and no-cost extension requests, and a site visit during the life of multi-year grants to evaluate the scientific and financial health of the project.

The Program uses industry best practices to ensure financial and research accountability, to support grantees, and to maintain compliance with grant terms and conditions, as illustrated in Table 6. Reporting requirements are intended to ensure progress rather than add administrative burden. Annual continuation of multi-year grants is dependent on satisfactory performance as well as the availability of funds.

Table 6 - 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

Delivering Program Support

At a Program level, a number of planning, development, and analysis and evaluation activities are required to inform the decision-making and strategic planning activities of the Advisory Council.

The processes in Table 7 support the smooth implementation of Program planning efforts and coincide with the yearly grant funding cycle.

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)

Pioneering Improvements in the Annual Funding Cycle

In anticipation of next-year funding through the annual appropriation process of the Legislature, the Program traditionally follows an annual cycle for soliciting applications and making awards, as illustrated in Figure 9 below.

An open competition for grants typically begins in November with the release of calls for applications and the announcement of a deadline, typically in late-January to mid-February.

In 2010, the Program pioneered an open-ended application deadline for Technology Transfer/Commercialization Partnership grants and Technology Transfer Feasibility grants that will continue into 2011.

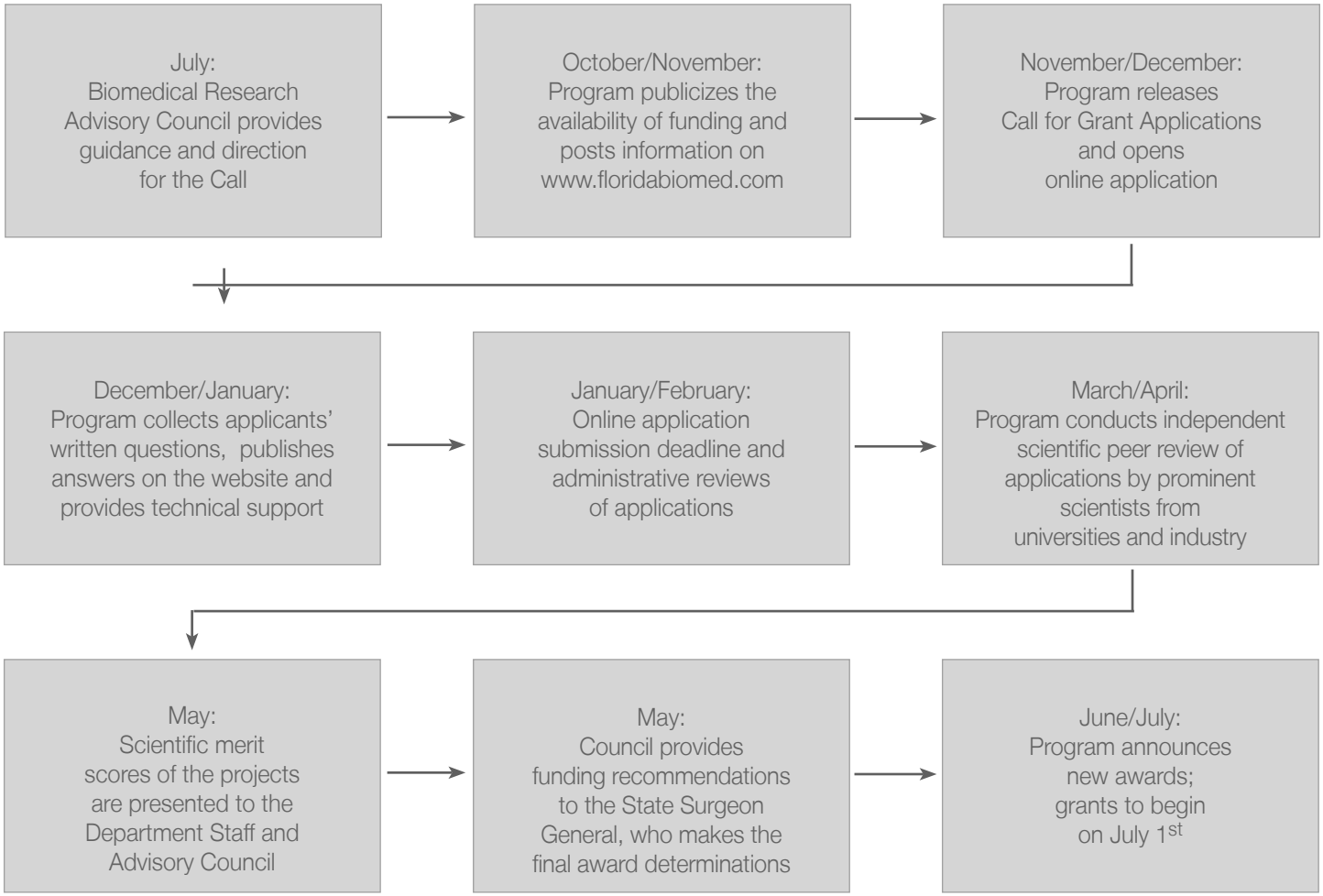


Figure 9 - The Annual Funding Cycle

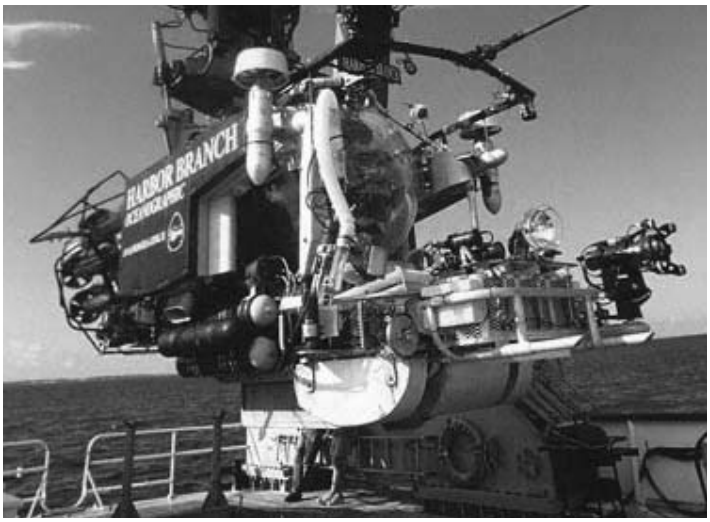
This Program has been instrumental in helping me to further develop my program of research. I received very helpful feedback from the site visit team and progress report reviewers.

- Respondent 60662583
DOH Grantee Satisfaction Survey Results
February 2010

Employing Innovative Peer Review to Ensure Merit-Based Awards

In evaluating proposals, the Program draws on the expertise of a pool of more than 700 independent subject matter experts from outside Florida. These peer reviewers evaluate grant applications that match their specific expertise, rating scientific and technical merit and project fit with Program goals. Unlike other peer review processes in which reviewers consult with each other, these reviews are performed independently and scores are averaged. 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 and cancer relatedness 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.



Principal Investigator, Esther Guzman, 2009 NIR, Florida Atlantic University, uses this submersible to study the anti-cancer properties of marine specimens.

I found many of the reviewers' comments very helpful, and it was even more satisfying and unique to receive comments for the progress report.

- Respondent 61658548
DOH Grantee Satisfaction Survey Results
February 2010

Using a Partnership to Support Applicants, Grantees, and Advisory Council

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

From 2006 through 2010, Lytmos Group, Inc. has filled the contracting role. In preparation for the expiration of the original contract at the end of 2010, the Department conducted a competitive procurement for these services. After negotiating with the top two vendors submitting proposals, the Department awarded a new contract to Lytmos Group, Inc.

Jointly, the Office of Public Health Research and the Lytmos Group, Inc. fulfill a number of behind-the-scenes responsibilities, providing a seamless interface to support applicants, grantees, and the Advisory Council.

Excellent review system, outstanding grant management system, extremely competent grant manager/personnel, and timely report/feedback.

- Respondent 60145391
  DOH Grantee Satisfaction Survey Results
  February 2010

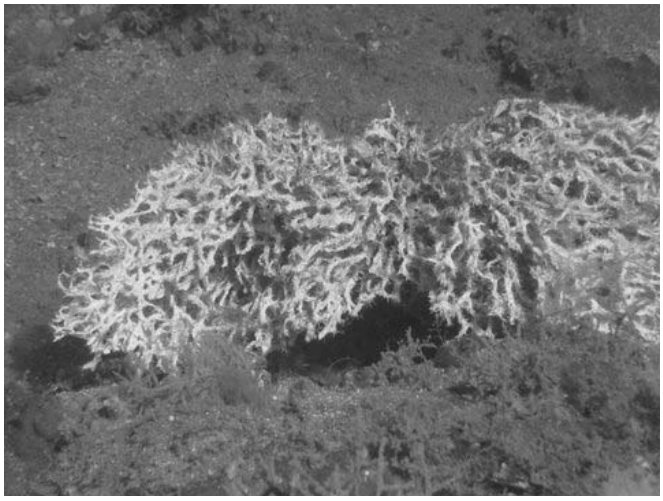
Grantee Satisfaction Survey

In order to remain responsive to the needs of Florida's research community, feedback is solicited in surveys of applicants and grantees. Survey topics have encompassed grant management and design as well as application and procedural questions to gather comprehensive feedback. As a result, Bankhead-Coley Program staff have incorporated improvements to processes and procedures. Surveys are planned on a regular basis and viewed as a valuable part of process evaluation and improvement. When asked to rate responsiveness of their grant manager, 96 percent of respondents were very satisfied or satisfied (3 percent selected N/A).

Demonstrating Program Accountability

The Program employs a number of strategies to communicate clearly and openly regarding all aspects of its operations and to proactively seek feedback from stakeholders in order to continuously improve the effectiveness of its strategies and tactics.

- Comprehensive and timely information is maintained on the Program's website, www.floridabiomed.com, including funding opportunities and outcomes, detailed minutes for all Advisory Council meetings, and Program policies and procedures as documented in the Grant Administration Manual.
- Progress is measured and reported against metrics developed from the Program's statutory goals.
- Feedback is solicited in surveys of potential applicants, principal investigators, sponsored research office officials, and technology transfer offices, among many others.



Example of coral that may provide a compound for synthesis to treat pancreatic cancer used by Principal Investigator Esther Guzmán, 2009 NIR, Florida Atlantic University

The Program has significantly helped in funding of the project and served as a good starting point for my academic career.

- Respondent 61656754
  DOH Grantee Satisfaction Survey Results
  February 2010

Appendix A. Section 381.922 *Florida Statutes* - William G. "Bill" Bankhead, Jr., and David Coley Cancer Research Program

(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 following goals, as those goals support the advancement of such cures:
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.
(b) Preference may be given to grant proposals that foster collaborations among institutions, researchers, 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 State 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 State 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) The William G. "Bill" Bankhead, Jr., and David Coley Cancer Research Program is funded pursuant to s. 215.5602(12). Funds appropriated for the William G. "Bill" Bankhead, Jr., and David Coley Cancer Research Program shall be distributed pursuant to this section to provide grants to researchers seeking cures for cancer and cancer-related illnesses, with emphasis given to the goals enumerated in this section. From the total funds appropriated, an amount of up to 10 percent may be used for administrative expenses. From funds appropriated to accomplish the goals of this section, up to $250,000 shall be available for the operating costs of the Florida Center for Universal Research to Eradicate Disease.

History.
—
s. 11, ch. 2004-2; ss. 7, 8, ch. 2006-182; s. 32, ch. 2008-6; s. 2, ch. 2009-5; s. 4, ch. 2009-58; s. 6, ch. 2010-34; s. 14, ch. 2010-161.
Note.
—
Subparagraphs (2)(a)1.-3. former s. 381.921.

Appendix B. Grant Types Designed to Achieve Program Goals

Table B-1 below provides details for all of the grant types offered throughout the Program's History.

Table B-1 - Grant Types Offered Throughout the Program's History

Grant Type	Purpose	Maximum Amount & Duration
Bridge Grant	To provide interim support for promising cancer research projects that received high ratings in federal peer-reviewed competitions but were not funded due to budgetary constraints. (Offered 2006 – 2009, 2011)	Up to $200,000 for one year
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 American Recovery and Reinvestment Act Funds. (Offered 2009)	Up to $1,000,000 over two years
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. (Offered 2007 – 2011)	Up to $425,000 over three years
Postdoctoral Research Fellowship (PRF)	To attract scientists into careers addressing important cancer research questions and to provide support to promising postdoctoral researchers who have the potential to become productive and independent cancer researchers. (Offered 2010)	Up to $58,350 per year for one to three years
Research Project Grant (RPG)	To support experienced investigators who are conducting cancer research in translational and/or health disparities and who will submit a national application to continue the research. (Offered 2010)	Up to $1.5 million over five years (including contract renewal)
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 multiple meritorious cancer research projects. (Offered 2006, 2009)	Up to $500,000 for a single instrument
Special Emphasis Project (SEP)	To identify specific factors contributing to Florida's very low cancer patient participation in clinical trials and to investigate policies, interventions, and incentives that may increase enrollment. (Offered 2007)	Up to $500,000 over two years
Specialized Program of Research Excellence (SPORE) Planning Grant	To assemble, prepare, and equip strong interdisciplinary teams of Florida researchers to plan and compete successfully for NCI SPORE grants. (Offered 2007 – 2009)	Up to $1,000,000 over two or three years
Team Science Program (TSP) Grant	To support a broadly based, collaborative, multidisciplinary research program with a well-defined theme that results in a national application to continue the research. (Offered 2010 – 2010)	Up to $1,500,000 over three years
Technology Transfer/ Commercialization Partnership (TTCP) Grant	To encourage the collaboration of investigators and small businesses; to stimulate technology transfer activities for promising research discoveries that could lead to innovations; and to strengthen a project's economic feasibility and commercialization prospects. (Offered 2009 – 2011)	Up to $100,000 for one year
Technology Transfer Feasibility (TTF) Grant	To offer early stage funding in order to develop intellectual property and improve a project's commercial potential and competitiveness for further development activities. (Offered 2010)	Up to $100,000 for one year

Appendix C. Abbreviated Abstracts of Grant Awards

The following is a list of grants awarded by the Program in the special round of 2009 and the annual funding round of 2010.

Defining Ethnic-Specific Transcriptional Differences in Breast Tissue

Baumbach, Lisa
2009 RC1
University of Miami
$544,463

Breast cancer (BC) is the second leading cause of cancer death among African-American (AA) women, and mortality is approximately 20 percent greater than that of Caucasian women. Ethnic-specific differences in BC stage of presentation and survival rates are well recognized. These differences are undoubtedly a result of extrinsic influences and inherent factors, i.e., genetic composition. A remaining challenge is to better understand and delineate these factors and their interactions, which confer differential risks for morbidity and mortality across racial/ethnic populations. Our long-term research goal is improved understanding of the genetic basis of BC in women of African ancestry and the translation of this knowledge into clinical practice. Recent observations by our group suggest distinct ethnic-specific gene expression patterns in both matched cancerous and normal breast tissue samples. We are exploring the question: Are there ethnic-specific differences in the transcriptome (expressed genes) of normal breast tissue? In this study, archived normal breast tissue samples from 25 AA and 25 Caucasian women with no BC history will be analyzed and compared for genome-wide gene expression differences. These observations may imply that AA women have an underlying pre-disposition to more aggressive BC due to gene-expression differences in normal breast tissue.

Development of a New Bioanalytical Instrument for Biomolecular Research and Diagnostics

Buffa, Mike
2009 TTCP
Nano Discovery, Inc.
$100,000

Cancer is among one of the most malignant diseases that our society has been battling for a long time. Approximately 7.6 million people die from cancer each year according to a survey conducted by the American Cancer Society. Early detection of cancer is critical for selection of the most effective treatment, increasing survival rate, and reducing the economic burden to society. Nano Discovery is developing a highly innovative bioanalytical technology and product that will greatly enhance our understanding of cancer and lead to the development of new diagnostic tests for early cancer detection. The market potential for Nano Discovery's new technology and product is estimated to be very high. The success of Nano Discovery's development has the potential to bring immediate economic benefit to the society, as well as improve the well-being of humankind.

New Thyroid Cancer Cell Lines - Comprehensive Molecular Characterization

Copland, John
2009 RC1
Mayo Clinic
$651,180

The scientific community needs a set of well-defined human thyroid cancer cell lines developed from patient thyroid cancer tissues removed at the time of surgery. These cell lines are key to identifying new drugs effective against the four major types of thyroid cancer. Because cancer cell lines are immortal and can continually grow forever, they are replicated and used around the scientific world to study thyroid cancer in efforts to better understand the disease and develop new treatments. Thyroid cancer cell lines do exist but a recent publication, in which we are co-authors, showed that 17 thyroid cancer cell lines (42.5 percent) were identified incorrectly, and the origin of others are poorly characterized. Thus, the data derived from studies using these cell lines and hundreds of publications may be incorrect related to thyroid cancer. This is cause for alarm. In this grant, we will develop new thyroid cancer cell lines from surgical tissues and characterize each new thyroid cancer cell line. The novelty will include molecular and genomic characterization of the parent tumor tissue and its cell line. Thus at any time, years from now, a cell line can be matched to its original tumor tissue. Completion of this project will lead to new, well-characterized cell lines for thyroid cancer. The broad impact will improve the diagnosis, treatment, and prognosis of thyroid cancer from new research using these lines.

When Are Clinical Trials Ethical for Both Future and Study Patients?

Djulbegovic, Benjamin
2009 RC1
University of South Florida
$595,409

Clinical trials are widely considered the most important vehicle for generating evidence about successful treatments that can improve outcomes of patients with cancer. Unfortunately, design and conduct of clinical trials are often ripe with ethical dilemmas, the chief of which is related to so-called therapeutic misconception [TM], a state that "exists when individuals do not understand that the defining purpose of clinical research is to produce generalizable knowledge regardless of whether the subjects enrolled in the trial may potentially benefit from the intervention under study." The scientific and ethical problems related to TM are further exacerbated by the existing disagreements between ethicists (who maintain that the purpose of clinical trials is to benefit future patients) and doctors/researchers (who believe that well-designed studies benefit current patients more than treating them outside of the research protocols). Our goal is to find the common ground between these two diametrically opposite positions by identifying those clinical situations when enrollment into clinical trials serves equally well both trial and future patients. We hypothesize that this in turn will improve IRB approval rate of such studies, increase patients' willingness to participate in clinical cancer research, and thus help speed discovery of new therapeutic interventions against cancer.

The overall goal of the studies is to develop a novel therapy for estrogen receptor (ER)-negative breast cancer based on the re-expression of ER and restoration of anti-estrogen responses. Approximately 30-35 percent of breast cancer lacks expression of the estrogen receptor (ER). ER-negative breast cancer carries a worse prognosis, but more importantly, does not respond to hormonal therapies, must be treated with toxic chemotherapies, and frequently is resistant to these chemotherapies. The project has three specific aims. First, to perform a pilot clinical trial to determine if treatment with AZD6244 (a substance being studied in the treatment of several cancer types) increases ER protein expression in ER-breast cancer in humans. Second, to determine the frequency of ER re-expression and restoration of anti-estrogen sensitivity achieved and gene expression/phospho-protein expression patterns associated with this in in vitro models with AZD6244. Third, to perform correlative analyses on specimens from both non-responding and responding clinical trial participants that will determine potential mechanisms underlying lack of re-expression of ER in non-responders and whether re-expression of ER in responders restores functional ER signaling and response to anti-estrogen therapy. If we determine this to be feasible, this could have a major impact on the treatment of ER-breast cancer.

Restoring ER Expression and Anti-Estrogen Response in ER-Negative Breast Cancer

El-Ashry, Dorraya
2009 RC1
University of Miami
$607,586

Stem cells serve as a renewable source of differentiated cells, which perform essential functions in the human body. Recent studies have revealed that besides normal stem cells, tumors of breast, prostate, and nervous system also have tumor stem cells that are a perpetual source for tumor growth. To identify and study normal and tumor stem cells, antibodies to a stem cell marker are labeled with a fluorescent dye and laser flow cytometry is used to detect the presence of cells with a particular stem cell marker expression. Flow cytometers are expensive to purchase and maintain and are often located in a central core laboratory in most academic institutions. In this project, we seek to develop a dedicated, low-cost flow cytometer, using specific UV/Violet and blue solid-state lasers needed for analysis of normal and tumor stem cells. As the cost of solid-state lasers and other electronics hardware has significantly come down, we believe we can build a dedicated flow cytometer for stem cell work for less than $30,000. This unit will have automatic features for alignment, calibration, sample preparation and loading, data acquisition and analysis, and will reduce the cost of tumor stem cell research. The prototype flow cytometer will be tested at the University of Miami Medical School, and data collected will be compared with a commercial flow cytometer for its validity and reliability.

A Dedicated Flow Cytometer for Monitoring of Stem Cells

Ganju-Krishan, Awtar
2009 TTCP
University of Miami
$100,000

This project is for the purchase of an instrument system for quantitative proteomics, which yields quantitative information about all proteins in a sample. The system includes the Waters NanoAcquity ultra high-pressure liquid chromatograph coupled to a Thermo TSQ Vantage triple quadrupole mass spectrometer. This system will be placed in the Proteomics Facility at the Moffitt Cancer Center and used for liquid chromatography-multiple reaction monitoring (LC-MRM) of peptides obtained from complex biological mixtures. Specifically, the instrument will be used to quantify biologically and clinically relevant targets in complex samples including cell lysates, tumor tissue homogenates, and biological fluids. In addition, this instrument will play a major role in biomarker validation experiments and the development of assays that can be directly applied to patient samples to derive a molecular basis for personalized medicine and provide additional tools for patient assessment. The molecularly driven research at the H. Lee Moffitt Cancer Center & Research Institute will greatly benefit from the addition of this instrument to our Proteomics facility. This LC-MRM system will complement the existing analytical tools and significantly strengthen the infrastructure available to the cancer center's researchers for conducting basic scientific, translational, and clinical research.

Quantitative Mass Spectrometer for Preclinical Modeling and Cancer Patient Assessment

Koomen, John
2009 SIG
Moffitt Cancer Center
$498,684

Histone acetyltransferases (HATs) and histone deacetylases (HDACs) play important roles in shaping epigenetic landscapes in the cell. They are enzymes whose activities are fundamentally altered in cancer cells, resulting in abnormal epigenetic modifications. Such epigenetic alterations are implicated in causing human cancer. Fortunately, unlike genetic mutations, epigenetic modifications are reversible by chemical agents that modulate the activities of HATs, HDACs, and other enzymes. Consequently, such agents have important therapeutic potentials for treating cancer. Indeed, one agent that inhibits HDACs was approved for clinical therapies against cancer by the FDA, and multiple clinical trials are ongoing for treating diverse human cancers. However, currently available inhibitors of HATs and HDACs suffer noted limitations such as toxicity and low efficacy. We have engineered cell lines that show promise for identifying novel and more effective agents for inhibiting HATs and HDACs. As a joint effort between University of Florida and Scripps Florida as well as access to one of the best screening facilities in the world, we propose to use engineered cell lines to screen one of the largest drug-discovery chemical libraries. The outcomes of this grant include the discovery of important lead compounds as potential anticancer agents that may benefit cancer patients.

Identification of Chemical Modulators of Histone Modifications through High-Throughput Screening

Liao, Daiqing
2009 RC1
University of Florida
$605,441

Appendix C. Abbreviated Abstracts of Grant Awards

The Role of PKR in Chronic Inflammation and Leukemogenesis

May, W. Stratford
2009 RC1
University of Florida
$721,785

Inflammation is the process by which chemicals and cells from the body's immune system are released into the blood and circulate to affected tissue in response to infectious or other foreign agents. Prolonged inflammation, or chronic inflammation, arises when the immune response is not completely shut off due to persistent stress like cigarette smoke or certain infections. By affecting the interaction between cells and their surrounding environment, chronic inflammation plays an important role in driving tumor formation. To better understand the mechanism by which chronic inflammation can promote cancer, we are developing two novel mouse models. These mice will express specifically in blood and immune system cells either increased amounts of the gene PKR or a mutant nonfunctional form of PKR. Since, the PKR protein is a critical activator of inflammatory systems and cell death, we expect that mice with increased PKR will be prone to bone marrow failure disorders and preleukemias including Myelodysplastic Syndrome or aplastic anemia. In contrast, mice expressing mutant, nonfunctional PKR are expected to have bone marrow cells resistant to death and the development of leukemia. Importantly, these studies are expected to provide valuable new insights into how chronic inflammation can cause cancer and may in the future lead to the development of novel anti-cancer agents targeting PKR-driven inflammation.

Targeted Gene Therapy by SNAP Delivery Method for Treatment of Lung Cancer

Mohapatra, Shyam
2009 RC1
University of South Florida
$710,791

This grant aims to develop a novel treatment for lung cancer that utilizes lung-targeting Sertoli cells (SCs) to deliver nanogene particles (SNAPs). Such particles are designed to express peptide(s) that inhibit atrial natriuretic peptide receptor A (NPRA), a novel anti-cancer target that was designated a 'lead discovery' in Oncology in 2008. Previously, chitosan nanocomplexes of gene(s) encoding NPRA inhibitor showed significant reduction of lung cancers in mice. The recent discovery of the SNAP method, which increases delivery of drug/gene therapeutics to tumors in deep lung, has led to the hypothesis that SNAP-delivered NPRA inhibitors may provide a novel means of treatment for metastatic lung cancer. The first aim of the project is to optimize and develop a robust, lung-targeted gene delivery and expression system by combining SNAP-mediated lung delivery using reporter genes. The second and third aims are to evaluate the efficacy of the SNAP delivery system using cancer cell-targeted, multi-functional nanoparticles (MCNs) carrying NPRA inhibitor in a model of lung metastasis and then in a model of lung cancer. Together, the studies are expected to lead to an effective, cell-based nanogene delivery system for metastatic lung cancers.

Nanohole Sensor-based Detection Technology for Cutaneous Metastatic Melanoma

Mohapatra, Subhra
2009 RC1
University of South Florida
$621,968

Based on the unique feature of nanohole array sensor-based detection technology (NST), it is hypothesized that NST can be exploited to develop a novel diagnostic and prognostic device for early detection of cutaneous metastatic melanoma, which is the most aggressive and has the worst prognosis of all skin cancers. The NST platform permits extraordinary optical transmission through metallic, sub-wavelength holes (nanoholes) that can be measured as surface plasmon (charge oscillations from reflected light) resonances (SPRs) by their angular distribution, reflected spectra, and intensity. To test this hypothesis, we plan to develop surface chemistry using SPR and nanohole array chip technology; to optimize assays and determine the limit of detection sensitivity plots for individual metastatic melanoma blood biomarkers, and to develop multiplexed NSTs for simultaneous detection of multiple melanoma antigens for early detection of metastatic melanoma.

Securing the Power of Interoperability in Radiation Oncology

Palta, Jatinder
2009 RC1
University of Florida
$639,667

Radiation therapy devices are continuously being developed by vendors without much consideration to interconnectivity and interoperability, thus presenting greater technical challenges with regard to efficient sharing, transfer, and storage of electronic radiotherapy data. Furthermore, non-uniform data archive and communication standards hinder the development of universally accessible electronic health record systems for cancer patients treated with radiation therapy. The recognition of these issues within the healthcare system has led to the Integration of the Healthcare Enterprise in Radiation Oncology (IHE-RO) initiative, which seeks to promote the coordinated use of established standards. It is anticipated that the IHE-RO compliant software developed by industry will eliminate ambiguities, reduce configuration and interface costs, and ensure a higher level of practical interoperability. The elements of a common platform will fulfill the expectations and requirements of an individual-user electronic health record for all cancer patients. The aims of this project are to establish a consensus view of interconnectivity and interoperability problems; develop a technical framework for the implementation of a seamless workflow in radiation oncology; and to test the interconnectivity and interoperability of this framework among radiotherapy system vendors. The outcomes are expected to improve efficiency and safety in radiation oncology facilities while reducing costs.

The implementation of novel radiation treatment modalities, such as Intensity Modulated Radiotherapy (IMRT) contributed significantly to reducing toxicity of prostate cancer treatment. However, rectal and urinary side effects, sexual dysfunction, and diminution in quality of life are still quite substantial. We hypothesize that these effects are predominantly a consequence of genetic predisposition and amount of radiation received by the normal tissues. The integration of genomic and dosimetric information in this study will facilitate the development of models that better predict complication risk and consequently quality of life. We plan to analyze Single nucleotide polymorphisms (SNPs) in the DNA-extracted from blood lymphocytes in a unique group of prostate cancer patients treated in a Phase III trial (n=303). The distribution of the received radiation dose and the SNP data will be related to the side effects measured in terms of rectal and bladder toxicity, erectile dysfunction, and quality of life. Building an effective clinical risk model would help physicians identify patients who are either relatively sensitive to radiation (making a case for dose de-escalation or modality modifications) or are resistant to radiation damage (allowing for safe dose escalation). The minimization of the side effects and the maximization of treatment efficacy will bring us much closer to the paradigm of optimizing individualized care.

Genomic and Dosimetric Determinants of Radiotherapy Outcome in Prostate Cancer

Pollack, Alan
2009 RC1
University of Miami
$884,621

E2F1 and MDM2 are two proteins that have dependent and independent functions in regulating cell death. Prostate cancer (PC) cell killing is pronounced when E2F1 is upregulated and MDM2 is downregulated, and is even greater when these agents are combined with radiation (RT) ±hormone therapy (also referred to as androgen deprivation therapy or ADT). Since E2F1 overexpression is capable of promoting cell growth and the transformation of normal cells to tumor cells, this portion of the molecule was removed. Truncated E2F1[108] continues to promote cell killing to the same degree with and without MDM2 knockdown using antisense (AS-MDM2), RT, ADT and combinations. A major objective of this study is to determine the effects of an adenoviral vector containing E2F1[108] with AS-MDM2 on PC growth in cell culture and in mice, and to analyze the underlying molecular mechanisms. To reduce the complexity of using multiple agents in clinic, we developed a nanosphere vector that has the potential to deliver E2F1[108] protein with siRNA to MDM2 concurrently along with an antibody that specifically targets prostate cancer cells. E2F1[108] overexpression and MDM2 knockdown combined therapy has never been tested before and shows considerable promise, especially when combined with ADT±RT. Directed nanosphere delivery of both agents together could be used to enhance responses in the prostate, as well as metastatic tumor cells in distant locations.

Prostate Cancer Imaging and Gene Therapy Delivery Using a Nanosphere Vector

Pollack, Alan
2009 RC1
University of Miami
$764,455

The use of flow cytometry in cancer research is a vital tool employed to facilitate the understanding of the complex processes that can lead to the initiation and subsequent development of malignant tumors, thus advancing progress towards potential cures. This grant is for an LSR-Fortessa-HTS flow cytometer. This instrument, the first in Florida, uses five lasers and nineteen fluorescence detectors, to measure, at high speed and sensitivity, light at multiple wavelengths from specifically targeted fluorescent reagents. Researchers can use this state-of-the-art instrument to perform many novel experiments, enabling them to employ the latest technologies to expand and to enhance the repertoire of assays that they can perform, many of which have been unavailable before now. Such novel experiments would include the use of fluorescent assays to dissect the processes and mechanisms involved in oncogenesis and malignancy by measuring, at high throughput and high speed, the presence of wide combinations of targets, with high statistical precision. Flow cytometry thus enables the rapid screening of cells for the molecular markers and cellular processes that may be associated with tumor growth, leading to the identification of potential targets for future therapeutic drugs and treatments.

L.S.R. Fortessa + H.T.S. Flow Cytometry Analysis System

Riley, Richard
2009 SIG
University of Miami
$492,334

The process of cancer drug discovery starts with the identification of a cellular protein that is believed to play a key role in cell growth or death. In order to study the function of the protein and to determine its precise role in cancer, scientists must find a molecule that can specifically interact with that protein. This search is known as high throughput screening, and a million or more compounds are often tested against a protein in an automated manner. This intersection of basic chemistry and biology, resulting in the discovery of a biologically active compound, initiates the process where further studies occur with the active compounds and where they are developed into a new medicine. Overall, the discovery of a new medicine can take up to 10-12 years of research with costs near $1 billion. Technologies that speed the drug discovery process are welcomed. Mass spectrometry has emerged as a powerful high throughput screening technology for drug discovery and can allow for the screening of large mixtures of compounds in an efficient manner. Protein assays are developed very rapidly on this platform and allow a cancer researcher to find chemical probes that interact with the proteins of interest. This grant allows the purchase of a 'high-definition' liquid chromatography-mass spectrometry system and the establishment of an open access laboratory for Florida's cancer researchers.

HTS Using Affinity Selection Mass Spectrometry

Roth, Gregory
2009 SIG
Sanford-Burnham Medical Research Institute
$331,035

Appendix C. Abbreviated Abstracts of Grant Awards

Acquisition of the Illumina BeadXpress System for Bead Array-Based Genotyping & Gene Expression Analysis

Sellers, Thomas
2009 SIG
Moffitt Cancer Center
$123,452

Research on cancer has shifted from the study of individual molecules to the large-scale survey of the tumor and the individual affected by the disease. High throughput technologies now provide thousands of pieces of information about the factors that predispose the development of cancer, the specific mutations that gave rise to an individual tumor, the physiology of a tumor, and the physiology of the patient. The volume of data produced from the analysis of each tumor/patient allows for a more comprehensive molecular evaluation of individual tumors and will be essential, in the future, for establishing the correct form of treatment for individual patients. The Illumina BeadXpress system is a medium-to-high throughput system for the analysis of genotypes, gene expression, and protein expression that will allow researchers to perform several different types of large-scale surveys of tumors and native DNA. This instrument can be used for targeted genome analysis in epidemiological studies of the causes of cancer and for the validation of gene expression and protein expression markers of cancer types identified by other technologies. The coordinated evaluation of the data generated with the Illumina BeadXpress system will greatly enhance our understanding of how individuals vary in their predisposition to cancer, contribute to the development of molecular profiles indicative of specific treatment regimens, and define risks for specific side effects of therapy.

Generation of Pancreatic Islet Beta-cells from Patient-Specific, Viral-free, iPS Cells

Yang, Li-Jun
2009 RC1
University of Florida
$702,876

Diabetes and its complications are a major healthcare burden affecting 200 million people worldwide. Since a common feature is diminished numbers of insulin-producing cells (IPCs), islet cell replacement has been studied as a potential curative therapy. However, pancreatic islet cells are not readily available, and immunosuppressive therapy increases susceptibility to infections and cancer. These two obstacles hinder the clinical use of islet cell transplantation. Recent progress in human-induced pluripotent stem cells (iPSCs) provides the promise of generating patient-specific IPCs for cell therapy. Generation of iPSCs involves reprogramming somatic cells to become embryonic stem cells. The common method employs viral vectors to introduce transcription factors. However, this strategy introduces viral genes into the iPSCs, which could increase cancer risk. In this project, we use a novel strategy to induce iPSCs from blood cells of diabetics by delivering reprogramming factors with protein transduction technology. This new technology enables one to add a "signal" to an engineered protein, allowing it to freely enter cells without the help of viral vectors. Our objectives are to produce iPSCs from diabetics using non-viral reprogramming methods based on four engineered reprogramming factor proteins, and to develop highly effective methods to differentiate iPSCs towards IPCs, and to test their insulin-secreting ability following a glucose challenge.

Combination Immunotherapy for Soft Tissue Sarcomas

Antonia, Scott
2010 TSP
Moffitt Cancer Center
$1,200,000

Soft tissue sarcomas are relatively rare tumors that affect all age groups (15 percent < 15 years old, 40 percent > 55 years old). In 2009, 10,660 new cases will be diagnosed, and 3,800 deaths are expected in the United States. With few exceptions, traditional treatments (surgery, radiotherapy, and chemotherapy), have little impact on the disease. Cancer cells produce new, unfamiliar, tumor-associated antigens (TAAs). When recognized as foreign, the immune system mounts a full-fledged attack that directly targets them to eradicate the cancer cells. Thus, immunizing patients against their tumors (immunotherapy) has obvious appeal and represents a dramatic shift in anticancer therapy that does not replace traditional treatments but rather, complements them. Our focus is on dendritic cell (DC)-based immunotherapy because DCs represent the most potent antigen-presenting cells, are involved in mechanisms of immune escape and tolerance, and are easy to manufacture. Our research includes two clinical projects. In the first project, DC-based vaccines are used in localized and advanced disease to induce an antitumor immune response capable of systemic effects to achieve the primary, long-term objective of improving disease treatment and prognosis. In the second project, which is pre-clinical research, we plan to modify the DCs genetically to express additional TAAs and enhance the known antitumor immune response induced by our vaccines.

Inhibition of the Transport of Glutamine, Essential Amino Acids, & Lactate as a Multi-targeted Strategy for Cancer Chemotherapy

Bannister, Thomas
2010 NIR
Scripps Research Institute
$400,000

Cancer drugs often target unique properties of tumor cells. For example, cancers tend to grow rapidly, demand a large blood supply, and spread quickly. Tumor cells need high levels of nutrients to fuel their growth. Cancer researchers have long studied the ways by which tumors meet their high-energy demands, but only recently have they described techniques to find drugs that work by disrupting energy input. Many nutrients enter cells using proteins called transporters. Glutamine, an important amino acid, enters cells by a transporter. Glutamine is also a fuel for other transporters, including one that delivers essential amino acids. Tumors also use transporters to rid themselves of wastes, including lactate, which they must pump out or else they become acidic. We have recently found that a substance that blocks lactate transport halts growth and even kills human lymphoma cells. A wide range of cancer types have very high levels of the transporters for glutamine, essential amino acids, and lactate. We wish to find the first drug that blocks them. We have made experimental substances that disrupt two transporters at once and found that they kill lymphoma cells. Such drugs may be broadly effective, having two modes of action that both target properties shared by tumor cells. Importantly, they may prove useful against tumors resistant to all available drugs, such as lymphomas and breast, brain, colon, skin, lung, and prostate cancers.

Matrix metalloproteinases (MMPs) are a family of enzymes in the body important for prenatal development and wound healing, but in cancer, MMPs are overproduced and contribute to cancer growth and spread. Drugs that block MMP function might slow cancer growth and limit cancer spread, but synthetically produced MMP-blocking drugs performed poorly in a series of cancer clinical trials due in part to strong negative side effects. Tissue inhibitors of metalloproteinases (TIMPs) are a family of natural inhibitors of MMPs that are produced by the body. Among these, TIMP-1 is the best inhibitor of MMP-9, an MMP that has been specifically implicated in cancer growth and metastasis. Thus, TIMP-1 represents a possible anticancer therapeutic. However, use of TIMP-1 at potentially therapeutic levels has been shown to interfere with important cellular processes by binding to CD63, a protein found on the surface of all cells. Our purpose is to create a modified TIMP-1 that does not interact with CD63 but that retains the ability to block the cancer-promoting effects of MMP-9, using sophisticated molecular structural analysis and protein engineering tools. We hypothesize that the modified TIMP-1 that we will generate will be an important starting point for a novel therapeutic strategy that will be both well tolerated and much more effective than existing anti-MMP compounds.

Defining Binding Determinants of Tissue Inhibitor of Metalloproteinases-1 (TIMP-1) Responsible for Paradoxical Roles in Cancer

Batra, Jyotica
2010 PRF
Mayo Clinic
$159,750

With any increase in energetic demand (e.g., walking up stairs, gardening, exercise) blood flow and oxygen delivery are directed toward compliant tissues, analogous to electricity following the path of least resistance. Exercise is commonly prescribed to cancer patients to combat muscle weakness and fatigue; however, little is known regarding the effect of exercise on tumor blood flow and oxidative capacity. This project is testing the global hypothesis that exercise augments tumor blood flow and oxidative capacity, and thus induces structural and functional alterations within the tumor. Specific Aims will investigate mechanisms of prostate tumor blood flow at rest, during acute and chronic exercise, as well as how exercise alters tumor oxygenation and mitochondrial function. These studies utilize an integrative approach, examining effects from the cell to the whole organism. Knowledge about the relationship of tumor growth and exercise is extremely important because: 1) It is likely that exercise may enhance the blood flow and density of blood vessels in tumors. 2) Exercise in combination with various tumor-targeting agents may represent a powerful therapeutic paradigm to combat tumor growth and metastasis. Therefore, the long-term goal is to utilize the research findings from this project to translational and, ultimately, therapeutic investigations within cancer patients.

Is Exercise Bad for the Tumor Microenvironment?

Behnke, Bradley
2010 NIR
University of Florida
$382,200

Colorectal cancer accounts for 10.2 percent of all new cancers in Florida. While early detection and appropriate treatment can improve survival, colorectal cancer is still the third deadliest cancer in the U.S. Unfortunately, colorectal cancer is surrounded by some significant health disparities. Not only are Blacks more likely than Whites to be diagnosed at a more advanced stage of disease, but it also appears that race, age, gender, and income interact to influence whether patients receive all the treatment they need to survive. The reasons for these disparities are unclear, but we suspect that one factor is the decision that patients make to have or not have adjuvant chemotherapy after initial treatment. The purpose of this study is to explore what influences some patients not to have adjuvant chemotherapy, even if it may have survival benefit for them. We will study a group of patients from before they have a colonoscopy to detect cancer all the way through their decision making to have adjuvant chemotherapy. We are particularly interested in their early interactions in the disease process with primary care physicians and gastroenterologists. Are there any "cues" in their communications that lead patients to think adjuvant chemotherapy is a good or bad thing for them? Also, we are interested in the advice they receive from other members of their care team (nurses, surgeon) and their caregivers.

Health Disparities in Colorectal Cancer Treatment Decision Making

Curbow, Barbara
2010 RPG
University of Florida
$1,185,984

Over the last 25 years, nearly 75 percent of anticancer therapeutics approved by the FDA have been derived from natural products or are considered natural product mimics. Although the pharmaceutical industry largely abandoned natural product screening with the advent of combinatorial chemistry (the synthesis of large numbers of distinct molecules), a new pipeline of marine-derived anticancer agents has renewed interest in natural, product-based drug discovery. Synthetic organic chemistry acts as a bridge between the discovery of new chemical entities and their development into useful therapeutics. The invention of efficient methods to access scarce compounds is vital for the optimization of potency, selectivity, and pharmacological properties of anticancer leads. The aims of this project are to synthesize and investigate the biological profiles of bisebromoamide and lucentamycin A, two marine-derived peptides (short chains of amino acids) that exhibit potent anticancer activity and feature structural subunits unprecedented in the natural product literature. We will complete the first chemical synthesis of each compound to provide material for further biological studies. Our long-term objective is to develop analogues (synthetic compounds that have high chemical similarity to natural compounds) of promising peptide natural products for use as novel anticancer agents.

Chemical and Biological Studies of Marine-Derived Non-Ribosomal Peptides

Del Valle, Juan
2010 NIR
Moffitt Cancer Center
$399,999

Appendix C. Abbreviated Abstracts of Grant Awards

Early Detection Markers for Smoking-Induced HNSCC

Franzmann, Elizabeth
2010 RPG
University of Miami
$1,200,000

Head and neck squamous cell carcinoma (HNSCC) is a debilitating and deadly disease that strikes 50,000 people in the U.S. yearly with a cure rate of only 50 percent due to late-stage diagnosis. African American patients and those of low socioeconomic status suffer disproportionately from this disease for reasons that are poorly understood but may have to do with exposure to risk factors such as tobacco. Prior work has identified a higher HNSCC incidence and smoking prevalence in Liberty City, a minority-rich and economically disadvantaged neighborhood within Miami-Dade County. Our laboratory is developing a simple and inexpensive early detection test designed to alleviate the burden of HNSCC in high-risk populations like Liberty City. In Aim 1, we will determine the levels of salivary soluble CD44 (solCD44), which is an early detection tool for HNSCC, and protein in oral rinses from subjects enrolled in a Liberty City head and neck screening clinic and examine a) how they vary with demographic and risk factors and b) how they change over time. In Aim 2, we will determine changes in oral rinse solCD44 and protein marker status with smoking cessation. The purpose of Aim 3 is to evaluate perceived acceptability of the test and its likelihood to influence smoking cessation in the population. This work will help determine whether this simple and inexpensive oral rinse test is likely to relieve the burden of HNSCC in high-risk communities.

A Novel, Low Cost, Ultra-Sensitive Nanosensor for Early Detection of Ovarian Cancer

Guldiken, Rasim
2010 NIR
University of South Florida
$399,946

There is a tremendous need to develop a safe, simple, cost-effective, reliable method to detect early stage ovarian cancer. The lack of clear symptoms and the absence of a reliable screening test for ovarian cancer results in over 70 percent of women being diagnosed after the disease has spread beyond the ovary so that the prognosis is poor. Median survival time after diagnosis is short, and the five-year survival rate is less than 40 percent. Our goal in this project is to develop a prototype of a disposable, tiny nanosensor chip enabling early ovarian cancer detection by measuring urinary protein, Bcl-2. Advantages of our nanosensor are: 1) low cost (<$1) and battery operation; 2) simple operation (reminiscent of a pregnancy test) not necessitating trained personnel; 3) cost-feasible, easy urinary test, allowing testing to be done at home, in a physicians' office, or at a patient's bedside. The research findings may significantly impact women worldwide including medically underserved locations and disparate groups.

Design, Synthesis, and Evaluation of Novel Selective Inhibitors of FAK and IGF-1R Function in Pancreatic Cancer

Hochwald, Steven
2010 RPG
University of Florida
$1,200,000

Pancreatic cancer (PC) is a leading cause of cancer death in the U.S., and there is no effective therapy. Human cancer cells grow and survive due to the overabundance of focal adhesion kinase (FAK) and insulin-like growth factor receptor-1 (IGF-1R). FAK interacts with IGF-1R, which contributes to the malignant behavior of PC. Our data shows that inhibition of both FAK and IGF-1R increases PC death compared to inhibition of either protein alone. While scientists are evaluating drugs that inhibit the enzyme function of FAK or IGF-1R, these drugs are not very specific or effective and result in increased side effects. Recently, the approach of inhibiting direct protein interactions rather than enzyme function has been shown to be effective. Our hypothesis is that the protein interaction of FAK with IGF-1R promotes PC growth and survival. Our studies will identify novel compounds that will prevent the protein interaction of FAK and IGF-1R. These compounds will have widespread effects by inhibiting the cellular processes that FAK and IGF-1R control including cell growth and survival. In addition, this effect will be specific for FAK and IGF-1R with minimal inhibition of other molecules, therefore, decreasing potential side effects of these compounds. Targeting FAK and IGF-1R protein interactions in PC will allow for the development of more specific and effective treatments for patients with this deadly disease.

Impact of Molecular Genetics on Disparities of Breast Cancer Risk and Prevention

Hu, Jennifer
2010 RPG
University of Miami
$1,200,000

Breast cancer is a serious public health challenge. Minorities, low income, and medically underserved women remain at a higher risk of dying from breast cancer. Therefore, the elimination of the unequal burden of breast cancer is one of our overarching long-term research goals. To achieve our long-term goal of reducing breast cancer disparities, the research will evaluate breast cancer risk prediction models and identify targets for intervention. We hypothesize that breast cancer with worse diagnoses occur more frequently in underserved minorities due to: (1) genetic defects in DNA repair, (2) elevated DNA damage, and (3) gene-environment interactions. We will test a new paradigm that genetic and non-genetic regulation of DNA damage/repair contributes to breast cancer disparities. Investigating this new paradigm will identify women at high risk of more aggressive cancer who will benefit from targeted interventions. With a large underserved minority patient cohort (n=3,200; 40 percent minorities), this will be the largest and most comprehensive evaluation of molecular genomics of DNA damage/repair of minority breast cancer patients to date. The results will impact breast cancer risk assessment, treatment, intervention, and ultimately improve survival of underserved and understudied minority breast cancer patients with more aggressive tumor phenotype and worse clinical outcome.

Smoking is implicated in many diseases other than lung cancer. For example, smokers are at a higher risk for developing and dying from colon cancer, and are more likely to develop Crohn's disease (CD), a chronic inflammatory condition of the colon. CD alone is a risk factor for colon cancer. Therefore, smoking triggers inflammation, and this inflammation is conducive to the development of CD and cancer. However, the underlying mechanisms for these events are unclear. Mutation of the gene ATG16 is a risk factor for CD. ATG16 is essential to autophagy, a process that kills bacteria. When ATG16 is mutated, our cells kill bacteria less well, and resulting bacterial persistence promotes inflammation. Persons with mutant ATG16 are ~8 times more likely to have CD if they smoke, but whether their disease is more severe is unknown. We propose that smokers with mutant ATG16 will have more severe CD, and we will study this by reviewing their medical and smoking histories. Next, we propose that white blood cells (WBC) are negatively affected by smoking and ATG16. We will study this by measuring bacterial killing and inflammatory chemicals from WBC in these patients. This work is important because it will aid our understanding of how behavior and genes interact to alter our risk for CD and cancer, and will allow for improved risk-stratification and patient care.

The Role of Smoking in Promotion of Crohn's Disease, a Predisposing Condition to Colon Cancer

Iovine, Nicole
2010 NIR
University of Florida
$400,000

Allogeneic stem cell transplantation (SCT) is the primary curative therapeutic modality for many patients with relapsed and/or high-risk hematologic malignancies. Unfortunately, many patients who might otherwise be cured by SCT are unable to be transplanted due to the lack of a suitable family or registry donor. For these patients, historically discarded placental and umbilical cord blood (CB) represents a potentially life-saving source of hematopoietic cells. Unfortunately, cord blood transplantation (CBT) is limited by delayed recovery of donor-derived cells, including those that fight infection. This is particularly true in adults, because the numbers of cells in CB products are often too few to promote rapid recovery of recipient white blood cells and immune function. Poor immune recovery often leads to infection, which is the major cause of death after CBT. In this project, we plan to conduct two trials where CB products are manipulated outside of the body to significantly expand cell numbers. The first will use a novel expansion strategy to try and improve white blood cell recovery and function in recipients. The second trial will additionally expand a special white blood cell population capable of preventing graft-versus-host disease, an important complication of CBT. In both studies, we will carefully assess recipient clinical outcomes and the impact of our interventions on recipient immune recovery.

Improving Cord Blood Transplantation via Expansion of Myeloid and Regulatory T Cells

Komanduri, Krishna
2010 RPG
University of Miami
$1,200,000

Since 1986, over 1.8 million adults have participated in nationally representative health surveys of the National Center for Health Statistics (NCHS), including the National Health Interview Survey (NHIS). Collectively, these surveys contain substantial information on demographics, medical expenditures, health status, and health behaviors, including cancer specific and risk factors. In addition, there are periodic cancer supplements (e.g., screening behaviors), as well as mortality linkage. Our long-term objective is to seek R01 funding to create a Consortium to perform a data linkage with the 1.8 million records from these studies with all State cancer registries (including SEER). Using Florida Cancer Data System (FCDS) records, representing ~6 percent of total U.S. annual cancer incidence, we will establish the feasibility of developing such a Consortium by: 1) Comparing cancer-related Florida NHIS data with data from the other 49 states to explore health disparities; 2) Performing a FCDS cancer registry linkage with NHIS data and depositing a de-identified file at the NCHS Research Data Center for merging with linked NHIS files; 3) Analyzing linked FCDS-NHIS data to demonstrate its utility to perform hypothesis-driven research in health disparities, cancer control, and prevention; and 4) beginning recruitment of all U.S. cancer registries into the Consortium in the preparation of a National Cancer Institute R01 application.

Florida Cancer Health Disparities: the FCDS/ NCHS Cancer Linkage

Lee, David
2010 RPG
University of Miami
$719,998

Natural products show outstanding potential as starting points in drug discovery, especially in the quest for anticancer drugs. Over half of the currently approved anticancer drugs are derived from natural products but are directed against a small number of targets in the cancer cell. The objectives of the proposed research are the validation of a new mechanism of drug action for anticancer therapy and the assessment of the therapeutic potential of a class of marine natural products termed apratoxins, which act via this unexplored mechanism. Our preliminary data indicate that apratoxins deplete cancer cells of several receptors and other proteins that are overexpressed or overactive in cancers. Apratoxins interfere with the synthesis of these cancer-associated molecules, and we are testing the possibility that inhibition of their synthesis may be exploited for anticancer drug development. This research will characterize the mode of action, structure-activity relationship, and anticancer drug potential of the apratoxins and, more generally, this mechanism, and identify targets for rational combination therapy.

Chemistry and Biology of Apratoxins

Luesch, Hendrik
2010 RPG
University of Florida
$1,150,000

Appendix C. Abbreviated Abstracts of Grant Awards

A High Throughput Cell-based Metabolic Analysis of Anticancer Drugs Using Nano-structure-enhanced Mass Spectrometry

Ma, Liyuan
2010 NIR
University of Central Florida
$400,000

For the majority of cancer patients, chemotherapy is mostly used as a systemic treatment where drugs travel throughout the whole body to reach and kill fast-growing cancer cells. Ideally, a drug should reach the site of action intact, kill cancer cells, and leave the body after it completes its mission. However, a potential drug can be metabolized or excreted from the body too fast, so that the drug cannot reach its therapeutic effects, which causes drug resistance. On the other hand, it may also be metabolized too slowly so that it stays inside the body for a long time, causing side effects. Thus, the ability to detect and quantify the metabolic products of anticancer drugs is very important for anticancer drug design, preclinical and clinical pharmacology, and toxicology. However, the analysis of small drug metabolic products is challenging for most existing techniques because of the wide variety of metabolites (substances produced by metabolism) in varying amounts. This project will develop a novel high-throughput technique (high-throughput is a method that allows researchers to quickly conduct millions of tests), to analyze the cellular level metabolic products of anticancer drugs by combining nanostructure-enhanced laser desorption/ionization mass spectrometry, and aptamer based on-chip separation and enrichment. This proposed new method has the potential to be more efficient than existing techniques for anticancer drug screening.

Exploiting Oncolytic Virotherapy to Selectively Target Human Hematopoietic Cancer Stem Cells

McFadden, Grant
2010 TSP
University of Florida
$1,200,000

The purpose of this project is to develop an oncolytic ("cancer-killing") virus called myxoma virus for a new clinical procedure to eliminate cancer cells from preparations of bone marrow-derived stem cells that are needed to restore the patient immune system following high-dose chemotherapy. This is a new strategy to make autologous blood and marrow transplantation (ABMT) available for many more cancer patients, such as those with advanced leukemias and lymphomas, who are currently ineligible for ABMT because their stem cell preparations are contaminated with their own cancer cells. The project exploits the natural ability of this virus to selectively infect and eliminate a variety of human cancer cells, including leukemic stem cells, prior to transplant but spare the normal human blood stem cells needed for immune reconstitution. The selective cancer-killing potential of this particular virus for human cancer cells has now been validated in a variety of animal models of brain cancer and metastatic melanoma. This new project offers the near-term potential to establish clinical trials that will allow many more leukemia and lymphoma patients to become eligible for ABMT therapy in the future.

Epigenomic Mapping of Mammary Epithelial Stem Cells and Tumor-Initiating Cells

Nabilsi, Nancy
2010 PRF
University of Florida
$159,750

Despite a promising initial response to modern breast cancer therapies, many patients relapse and develop recurrent tumors. One explanation for this recurrence is the existence of small populations of tumor cells that resemble stem cells. These cells are unique in their ability to continually grow, initiate tumors, and evade conventional therapies. Our broad objective is to identify the unique biological properties of tumor-initiating cells, which could help us design therapies to target these cells, thereby eradicating primary tumors and preventing recurrent disease. Improper genetic and epigenetic information contribute to tumor formation and disease progression. While genetic mistakes are permanent, epigenetic mistakes can be reversed, making them attractive targets for cancer therapy. Our specific aims are to isolate and characterize tumor-initiating cells from patient breast tumors and to examine their epigenetic marks at thousands of regions across the genome. By comparing their features to those from non-tumorigenic cells, we expect to identify the epigenetic abnormalities that make tumor-initiating cells unique. These findings will help us: 1) understand the origin and disease-forming capabilities of tumor-initiating cells, 2) uncover new targets for epigenetic-based drug therapies, and 3) uncover epigenetic patterns that will provide important information to cancer clinicians for diagnostic or prognostic purposes.

Regulation of miR-155 by Oncogenic IRFs in EBV Latency and Associated Tumors

Ning, Shunbin
2010 NIR
University of Miami
$399,998

Virus infection accounts for up to 20 percent of cancers. Epstein - Barr virus (EBV) was the first identified human cancer virus and is associated with a large range of malignancies of lymphocytic and epithelial origin. Interferon Regulatory Factors (IRFs) are a small family of transcription factors (proteins that bind to specific DNA sequences and regulate gene expression), some of which possess oncogenic properties. Interestingly, these oncogenic IRFs are associated with EBV latency, and may account for the regulation of cellular growth regulatory genes and even microRNAs (miRNAs). miR-155 is a miRNA that has been implicated in many human B cell lymphomas including EBV-associated lymphomas, and like oncogenic IRFs, is associated with EBV latency. However, little is known about how miR-155 expression is regulated in cancers, and the relation between oncogenic IRFs and miR-155 in EBV latency and associated tumors has not been studied to our knowledge. The project will focus on transcriptional regulation of miR-155 by oncogenic IRFs, the correlation between oncogenic IRFs and miR-155 in EBV latency and associated tumors, and the potential contribution of the IRFs/miR-155 interaction to EBV transformation. This research may lead to better understanding of IRFs-mediated tumorigenesis and may benefit the treatment of viral infection and prevention of cancers caused by viral infection.

Liver cancer is the third leading cause of cancer-related deaths in the world, and frequently occurs in patients with liver cirrhosis from viral hepatitis. Liver transplantation is one of the best treatment options for patients with liver cirrhosis and liver cancer, and is frequently performed in the United States. However, liver tumors return in about 10-20 percent of these patients even though chemotherapy is performed, highlighting the need for additional therapies. More than 30 years ago, blood cells were found which could kill cancer cells. These cells were named natural killer (NK) cells. The mechanism of killing and the character of NK cells are now better known. Recent advancement of research has made it possible to purify, educate, and activate NK cells. Our laboratory has been able to take out cells from the donor and activate them to kill cancer cells without harming the patient. We plan to use this method in liver transplant patients with liver cancer. We intend to study NK cells and clarify their mechanism of killing the cancer cells. Although NK immunotherapy has been tried, this method has never been applied to liver transplantation with liver cancer. The goal of our program is to improve the quality of life of the patient through advancement of scientific research.

A Novel Immunotherapy for Liver Transplant Patients with Hepatocellular Carcinoma

Nishida, Seigo
2010 RPG
University of Miami
$719,927

The discovery of the BRCA genes almost 15 years ago allows us to identify people who have changes in these genes. A woman with a gene change has a high chance to develop breast and ovarian cancer. Yet, it is still difficult to spot people with these changes due to the small number of medical experts familiar with the BRCA genes. As such, many practitioners and patients in the community are not aware of these genes. Roughly, 5 percent of all people with BRCA gene change know that they carry this change. Florida has the second highest number of new cancer cases and very few experts in the topic of Clinical Cancer Genetics. Because of this, many practitioners and patients are less aware of BRCA mutations, which could lead to misinformed healthcare decisions. We propose to boost information access about BRCA gene changes to healthcare providers and patients through an existing network of community practitioners called the Moffitt Affiliate Network (MAN). This would allow MAN practitioners to contact Moffitt-based experts for information on the identification and management of those with BRCA changes. Patients with BRCA changes from MAN sites would also be able to join our Inherited Cancer Registry (ICARE). This registry would carry out research on those with BRCA gene changes to develop better care options for them. The eventual goal of our efforts is to improve the care given to those with BRCA gene changes in Florida.

Inherited Cancer Registry (I CARE) Initiative

Pal, Tuya
2010 RPG
Moffitt Cancer Center
$1,069,292

Young Black women get breast cancer less often than White women do, but are more likely to die from it. This may be caused by a type of aggressive breast cancer called triple negative (TN) disease, which is more common in Black women. We plan to study why young Black women get the more serious type of TN breast cancers. We will recruit 600 Black women diagnosed with breast cancer at or below age 50 through the Florida State Cancer Registry. Based on our earlier study in similar women, we believe we can accomplish our goals. We will collect information about each participant through a detailed questionnaire, medical records review, and genetic testing. The participants will be followed every two years for the duration of the study to track how they do. Our study provides no-cost genetic counseling and testing for the participants. The test results could allow participants and their families to make important decisions about their healthcare. Our research team includes Black community members, who help us make sure our research is relevant; recruitment and study procedures are conducted in a sensitive manner; and help us share important findings with the Black community. Through our study, we hope to better understand why young Black women get TN breast cancers and why they die from the disease more often. Ultimately, we need this information to lower the number of TN breast cancers in these women.

Black Women: Etiology and Survival of Triple-negative Breast Cancers (BEST) Study

Pal, Tuya
2010 RPG
Moffitt Cancer Center
$1,199,864

Men who are diagnosed with prostate cancer face difficult decisions regarding when and how to be treated. Current methods for determining a patient's need for treatment and the aggressiveness of the treatment needed remain problematic. Our goal is to better define key decision points in men who have different stages of the disease by investigating biomarkers from tissue and blood. The study's clinical trials have been designed to address key questions and gain insight into the potential applications of biomarkers when considered across patient groups. To our knowledge, this approach has not been used previously, and the technologies we use to obtain and analyze prostate tissue and blood cancer cells are unique. The clinical trials involve men with distinct options who 1) have early prostate cancer and are candidates for no treatment (active surveillance), 2) have intermediate to high-risk localized prostate cancer and are candidates for radiotherapy, 3) have experienced a rising PSA after surgical removal of the prostate and are candidates to receive salvage radiotherapy to the surgical area, and 4) have had spread of the cancer and have become resistant to hormone and chemotherapy. The projects are highly integrated and novel because of the application of new imaging technology to better direct prostate biopsies and analyze blood products, and the plan to investigate this in patients with different stages of prostate cancer.

Integrated Biomarker Profiling for Individualized Prostate Cancer Therapy

Pollack, Alan
2010 TSP
University of Miami
$1,200,000

Appendix C. Abbreviated Abstracts of Grant Awards

Role of Histone Deacetylases in DNA Mismatch Repair

Radhakrishnan, Rangasudhagar
2010 PRF
Moffitt Cancer Center
$111,300

Colon cancer is one of the leading causes of death among the elderly population. Various risk factors have been identified to be associated with increased colon cancer incidence among the elderly population. Among the risk factors, two genetic elements have been identified as potential causes for colon cancer genesis. They are the germ line mutations in genes that are involved in either Adenomatous Polyposis Coli (APC) or DNA Mismatch repair pathways (MMR). This project focuses on the gene that is involved in the DNA mismatch repair pathway. A functional MMR is not only required for the cells to maintain the genomic integrity in the event of DNA replication errors, but also for initiating cellular response to certain chemotherapeutic drugs that give rise to mismatches. The net results are either correction of the mismatch and promotion of cell survival in case of DNA replication errors, or mounting an apoptotic response to kill the cancer cells in case of chemotherapy. Failure of this system because of mutations in the genes that are involved in DNA mismatch repair leads to accumulation of errors in DNA and cells' loss of sensitivity to chemotherapeutic agents. This research attempts to identify the role of acetylation of MSH2, a critical gene that is involved in colon cancer etiology, in DNA mismatch repair, and colon cancers (Since acetylation of proteins has been shown to alter its function, the present study is highly significant).

TNFRSF25 Agonists as Multifunctional Cancer Vaccine Adjuvants

Schreiber, Taylor
2010 PRF
University of Miami
$51,850

Cancer is a genetic disease that arises when our cells acquire DNA mutations, which enable them to escape normal restrictions on their growth and death. Fortunately, humans have evolved many defenses against cancer, one of which is our immune system. Over the past decade, the secrets to how the immune system identifies and destroys tumor cells have begun to be uncovered. These important discoveries have enabled the design of a new class of cancer drugs, called immunotherapies that are quickly becoming an important addition to traditional surgical, chemo-, and radiotherapies. Because cancer cells are so similar to our own cells, precautions must be taken when using immunotherapies to guard against the induction of autoimmune disease. The Podack laboratory has previously developed a cancer immunotherapy based on a heat shock protein that is being tested in Phase I clinical trials and that can cure some cancers in animals. Our laboratory has also developed a second immunotherapy that both increases the activity of the heat shock protein therapy and induces a type of immune cell, called a regulatory T cell, which can prevent autoimmune disease. This project will test whether combining both of these therapies enhances the rejection of experimental tumors in mice, while simultaneously inducing regulatory T cells that may prevent the potential for autoimmune disease during cancer immunotherapy.

Structural Dynamics of Human MDM2 and MDMX Interactions with p53 and Antagonistic Ligands by Multidimensional NMR Spectroscopy

Shan, Bing
2010 PRF
Florida State University
$159,750

The protein p53 plays a key role in many cellular processes, including tumor suppression, DNA repair, and aging. p53's function can be disabled by specific interactions with other proteins, in particular MDM2 and MDMX. Therefore, disruption of these interactions by peptides and small molecules (drugs) is of considerable pharmaceutical interest. However, only a few peptides and small molecules developed so far have been found to have in vivo activity. MDM2 and p53 interact, and the complex formation involves a significant conformational change to MDM2 and global conformational change in p53. Thus, a series of complex structural dynamic events play a key role in the function of MDM2/MDMX, whose characterization evades traditional structural biology approaches. The goal of this project is to understand these processes at an atomic level and to determine how they can be disrupted by small molecules using state-of-the-art Nuclear Magnetic Resonance Spectroscopy available through the Department of Chemistry and Biochemistry at Florida State University and the National High Magnetic Field Laboratory. The knowledge gained in this research is crucial for the development of new chemotherapeutic agents for the treatment of p53-related diseases.

Identification of Oncogenic CDK-independent Functions of p27 in Regulating Acquisition/ Proliferation of Cancer Stem-cell Populations

Sharma, Savitha
2010 PRF
Moffitt Cancer Center
$107,900

Uncontrolled cell division, evasion of cell death, and tumor invasion and metastasis are among the hallmarks of cancer. p27Kip1, this study's focus, is a protein that controls cell cycle by inhibiting the activity of cyclin-dependent kinases (CDK), a group of protein kinases (type of enzyme) involved in the regulation of the cell cycle. p27Kip1 protein levels and activity are decreased in numerous cancers, leading to uncontrolled cell division. Thus, p27Kip1 was thought to be a tumor-suppressor. Numerous recent studies, however, have shown an oncogenic, CDK-independent role for p27Kip1. Expression of a p27Kip1 mutant that is deficient for cyclin/CDK binding in mice resulted in increased, spontaneous multi-organ tumorigenesis and proliferation of the stem cell populations in these organs. These observations suggest a novel role for p27Kip1 in regulating stem cell biology. We hypothesize that p27Kip1 contributes to development and/or expansion of cancer stem cell (CSC) population. CSCs are a very rare group of cancer cells found within tumors that are capable of self-renewal. They are proposed to persist in tumors after chemotherapy and are capable of initiating new tumors. Therefore, understanding pathways that give rise to new CSCs and mechanisms that regulate CSC proliferation, which are currently poorly understood, are crucial to developing new therapies that will effectively target the cancer at its roots.

The role of ERBB2/HER2, a protein giving higher aggressiveness in some cancers, has been extensively studied. Several targeted treatments have shown significant success for patients; however, resistance is a major challenge, and its mechanisms are complex and poorly understood. Several lines of evidence show that the way in which cells' surface receptors interact with their immediate membrane environment, and how this environment is restructured can dictate the complex system of communication that governs basic cellular activities and possibly drug resistance. Our purpose is to investigate the role of gangliosides, which are carbohydrate-containing lipids on the cell surface known to be altered in cancers yet with less understood consequences. Gangliosides can act as mediators between the lipid environment and embedded proteins and structure the immediate environment of cell receptors. We will evaluate whether gangliosides alter the accessibility or outcome of Herceptin (a cancer treatment) binding to ERBB2 and whether they influence ERBB2's cleavage to a more aggressive species. The identification of specific gangliosides and ganglioside-protein interactions can lead to both novel targeted therapies that are distinct enough to benefit combination treatments, as well as biomarkers that could facilitate the selection of the best treatment regimen.

Gangliosides as Organizing Elements of ERBB2 (HER2) Signaling Platforms and Therapeutic Targets in Cancer

Sicard, Renaud
2010 PRF
University of Miami
$56,550

A difficulty in breast cancer therapy is that clinically used compounds that mainly target proliferating cells are not very effective in targeting invading cells to prevent recurrence. There is a need to identify key-proteins affecting tumor cell invasion that can serve as new drug targets. Another issue is the lack of molecular markers that allow prediction of metastatic breast cancer or recurrence. In this project, we are investigating if a protein named PKD1 is a molecular switch that acts as a suppressor of breast tumor cell invasion. We will test if this can be utilized to predict the potential for metastasis or recurrence of tumors and to develop new avenues for therapeutic intervention. Our goals are to understand how PKD1 is inactivated in highly-invasive breast cancer cells and if this inactivation can serve as a predictive marker for the potential of tumors to metastasize; to understand the mechanism this protein utilizes to mediate its anti-invasive functions; and to test a reactivation strategy for PKD1 as a therapeutic approach. Successful completion of this project will identify new prognostic markers for metastatic breast cancer and tumor recurrence. A second outcome is that we will re-activate a silenced tumor suppressor, which is a novel and innovative strategy, and once tested in our orthotopic animal model will allow a relatively quick adaption for a clinical application in Phase I trials.

Protein Kinase D – A Marker and Target for Invasive Breast Cancer

Storz, Peter
2010 RPG
Mayo Clinic
$1,199,996

Triple negative breast cancer affects some 30,000 women yearly in the U.S., with a predominant effect on young women and those of African descent, and is the most challenging type of breast cancer from a clinical standpoint. The disease is heterogeneous, some women do well while others do poorly; and there are no targeted therapies available for this type of breast cancer. Thus, there are two pressing clinical needs. We need new biomarkers to assess the risk of relapse in women with triple negative cancer, and we need to identify new therapeutic targets for treatment. These are our objectives. We will use massively parallel DNA sequencing protocols to identify a novel sort of mutation that arises due to gene fusion in primary tumors from triple negative patients. These mutations are absolutely tumor specific, not found in normal cells, and are therefore ideal biomarkers for risk prediction and stratification of this class of breast cancer. Since these mutations are tumor specific, they are also ideal therapeutic targets; and our objectives include identification of fusion gene mutations (which occur when two different genes are accidentally broken and stitched back together to form a new gene) that are required for tumor survival, growth, and/or spread. Our long-term goal is to apply this technology to individual patients, identify every mutation in each tumor, and tailor therapy to the specific types of mutations that drive the tumor.

Translational Genomic of Triple Negative Breast Cancer

Thompson, Aubrey
2010 RPG
Mayo Clinic
$1,199,996

Unlike conventional radiation beams that damage healthy cells along their path to the tumor, proton beams can be tailored to deposit most of the dose in a well-defined volume and at a specific depth inside the body. However, proton beams are very sensitive to patient-specific variables, such as motion during delivery or the presence of heterogeneities (bone and lung tissue) in the beam path. This is why it is critical to ensure that radiation dose distributions are being accurately delivered to cancer patients. The most direct approach to dose verification is PET/CT imaging of patients after each treatment. This technique is based on measuring the spatial distribution of proton-beam activated positron emission and superimposing it onto a CT data set, which provides information about the spatial distribution of dose in relation to relevant anatomical sites and allows making treatment plan adjustments. However, the relationship between dose and PET activity is complex and has not been thoroughly studied. This project will investigate the characteristic features of PET activity distributions under different clinically relevant circumstances. Unlike earlier studies that compared measured PET signal to calculated dose, this project will use a unique, proton-sensitive 3D polymer gel dosimetric phantom that allows us to directly correlate delivered dose to activity in the same device.

Proton Beam Dose Verification Using PET/CT Imaging in Conjunction with 3D Polymer Gel Dosimetry

Tirpak, Olena
2010 PRF
M. D. Anderson Cancer Center
$111,300

Appendix C. Abbreviated Abstracts of Grant Awards

Novel Approach for Enhancing the Efficacy of Breast Cancer Chemotherapy by Vascular Normalization Effect of R-Ras

Urakami, Takeo
2010 PRF
Sandford-Burnham Medical Research Institute
$164,450

Chemotherapy is the most common treatment for breast cancer. However, the immature and abnormal nature of tumor blood vessels significantly impairs delivery of chemotherapeutic agents to the target tumor cells. Normalization of the tumor vasculature could enhance drug delivery and therefore improve the efficacy of chemotherapy treatments. A breast cancer drug called Avastin prevents the growth of tumor vessels that supply the tumor with nutrients that facilitate tumor growth. Clinical studies have shown an improved benefit for breast cancer patients when Avastin was used in combination with standard chemotherapy. This project's goal is to determine how important tumor vascular normalization is for the efficacy of chemotherapy. The cellular signaling protein called R-Ras promotes vessel normalization. Therefore, the first goal is to examine the role of R-Ras in breast cancer chemotherapy using R-Ras-deficient mice bearing human breast cancer. The second goal is to use a new genetic mouse model to up-regulate R-Ras expression in tumor vascular endothelial cells. This model will determine the vascular normalization effect of R-Ras and its synergistic effects with conventional chemotherapy. The results may open a possibility for a new treatment regimen to improve the efficacy of breast cancer chemotherapies.

Molecular Genetics of Radiation-Induced Skin Toxicities in a Tri-Racial/Ethnic Post-Mastectomy Breast Cancer Cohort

Wright, Jean
2010 NIR
University of Miami
$400,000

Studies show that radiation therapy after mastectomy for breast cancer, or post-mastectomy radiation (PMRT), improves survival in high-risk patients. PMRT carries the risk of side effects, including damage to the skin, or early adverse skin reactions (EASR), including skin reddening/darkening, peeling, and pain. In patients receiving PMRT, such reactions are common and result in a treatment break in up to 1/3 of patients, which can cause increased risk of breast cancer recurrence. The severity of EASR is variable; studies suggest that genetic factors as well as racial and ethnic differences play a critical role, with minority populations often developing more severe side effects and requiring treatment breaks. These factors may contribute to the finding that minority populations have a higher risk of dying from breast cancer. We are examining relationships between genetic factors and EASR in patients receiving PMRT. We will collect blood samples before and after radiation for genetic analysis, assess radiation-induced EASR, and perform statistical analyses to determine associations between genetic factors and EASR. Ultimately, the proposed work could lead to identification of genes that increase the risk of EASR due to radiation. Identifying these genes could lead to changes in radiation therapy to decrease toxicity and resultant treatment breaks, ultimately increasing survival in breast cancer patients.

Role of MicroRNA in Mediating Oncogenetic Effect of Notch Signaling in Melanoma

Yin, Ling
2010 PRF
University of Miami
$159,750

Melanoma is the most dangerous skin cancer. The tumorigenic signals driving melanoma progression remain largely unknown. Notch signaling (a cell signaling system) has been demonstrated to be one of such driving forces. The Notch signaling pathway is active in human melanomas, and the activation of Notch signaling can promote melanoma progression to metastasis. However, the molecular mechanism underlying the tumorigenic effects of Notch signaling on promoting melanoma progression needs to be explored. We have recently found that seven microRNAs, (microRNAs regulate gene expression), were mis-expressed in response to Notch pathway activation in melanoma. We therefore propose that Notch signaling aberration causes the epigenetic alteration (changes caused by the activation and deactivation of genes without any change in DNA sequence) in microRNAs, which in turn mediate the Notch signaling-induced melanoma progression. The knowledge from this proposed study will greatly help us to identify innovative targets for melanoma diagnosis, prognosis, and therapy.

Appendix D. Related Awards Reported by Grantees in 2010

The following list represents $39.1 million in additional single and multi-year awards reported since October 2009 by current and past grantees that are based directly on research findings from projects funded by the Program. Grants are presented in alphabetical order by last name of the principal investigator.

Abaffy, T. (2008 Bridge), "Detection of melanoma by canine olfactory receptors." National Cancer Institute, $516,375.

Bai, W. (2006 Bridge), "Vitamin D and Ovarian Cancer Prevention and Treatment." National Cancer Institute, $1,221,910.

Blaydes Ingersoll, S. (2009 NIR), "MicroRNA expression profile of ovarian cancer: correlation to cellular therapy." Florida Hospital Gala Endowed Program for Oncologic Research, $20,000.

Bloom, L. (2008 Bridge), "Dynamics of protein-DNA interactions in DNA replication." National Institute of General Medical Sciences, $397,966.

Bloom, L. (2008 Bridge), "Dynamic eukaryotic replication machines." National Institute of General Medical Sciences, $1,147,792.

Briegel, K. (2008 Bridge), "Regulation and function of transcription factor Lbh in breast cancer." Department of Defense, $291,000.

Brown, K. (2006 Bridge), "ATM in breast tumor suppression." National Cancer Institute, $439,500.

Byrne, M. (2007 SEP), "A targeted decision aid to improve minority participation in clinical trials." National Center on Minority Health and Health Disparities, $1,652,599.

Byrne, M. (2007 SEP), "Resource and QOL consequences of lung cancer screening." National Cancer Institute, $132,432.

Cheng, J. (2007 Bridge), "AKT2 oncogene and human oncogenesis." National Cancer Institute, $228,571.

Cheng, J. (2008 Bridge), "MicroRNAs in human ovarian cancer." National Cancer Institute, $2,087,500.

Copland, J. (2007 Bridge), "RhoB in cancer pathogenesis and as a target in combinatorial therapy." National Cancer Institute, $1,679,090.

Copland, J. (2007 Bridge), "TGF beta receptor biology in human renal cell carcinoma." National Cancer Institute, $686,814.

Cress, W. (2008 Bridge), "E2F's impact on therapeutic efficacy." National Cancer Institute, $950,199.

Felty, Q. (2009 NIR), "Estrogen-induced Pyk2 signaling in the abnormal growth of vascular cells." National Cancer Institute, $325,125.

Heller, R. (2006 Bridge), "Therapeutic potential of IL-15 plasmid delivery to tumors using electroporation." National Cancer Institute, $1,875,000.

Huang, S. (2007 NIR), "Regulation of insulator function and globin gene expression by USF and associated co-factor." National Institutes of Health, $1,250,000.

Hughes, J. (2006 Bridge), "Gene delivery based on microbes." National Institute of Neurological Disorders and Stroke, $468,462.

Kato, Y. (2006 Bridge), "The mechanism of notch signaling pathway in radial glial development." Eunice Kennedy Institute of Child Health & Human Development, $294,000.

Kato, Y. (2006 Bridge), "Novel regulator of notch signaling in determination of left-right asymmetry during embryogenesis." National Institute of General Medical Sciences, $426,120.

Kerr, W. (2007 Bridge), "The kinomes of non-hodgkin lymphoma." National Cancer Institute, $95,680.

Kerr, W. (2008 Bridge), "SHIP and immunoregulatory cell function." National Heart, Lung and Blood Institute, $1,423,000.

Konduri, S. (2009 NIR), "Inhibition of MGMT impacts triple negative breast cancer growth." Susan G. Komen Breast Cancer Research Foundation, $475,000.

Lokeshwar, V. (2008 Bridge), "19th annual SBUR meeting: molecular targets for diagnostic and therapeutics." National Institute of Diabetes and Digestive and Kidney Diseases, $10,000.

McFadden, G. (2010 TSP), "Myxoma virus (mv) oncolysis for treating human cancer." National Cancer Institute, $1,215,952.

Moffitt, K. (2007 SEP), "Florida cancer trials navigation service – reducing barriers." Health & Human Services, $495,000.

Muir, D. (2009 Bridge), "Anti-angiogenic therapeutic approaches to NF1 tumors." Children's Tumor Foundation, $50,000.

Muir, D. (2009 Bridge), "Photodynamic therapy for neurofibroma." STOP! Children's Cancer, Inc., $75,000.

Qiu, Y. (2007 NIR), "The role of HDAC1 acetylation on corepressor complex activity and hematopoiesis." National Heart, Lung and Blood Institute, $1,465,000.

Radisky, E. (2007 NIR), "Lana and cellular gene expression in Kaposi's sarcoma." National Cancer Institute, $680,082.

Appendix D. Related Awards Reported by Grantees in 2010

Radisky, E. (2007 NIR), "Studying the role of KSHV-encoded microRNAs." National Cancer Institute, $2,065,170.

Radisky, E. (2007 NIR), "Targeting mesotrypsin-induced prostate cancer progression." Department of Defense, $688,500.

Sarosi, G. (2006 Bridge), "Bile salt reflux and growth signaling in Barrett's esophagus." Veteran's Health Administration, $390,000.

Shibata, D. (2006 Bridge), "STAT1 activation and HPP1 tumor suppression." National Cancer Institute, $1,732,625.

Siegel, E. (2009 NIR), "A platform for examining the molecular basis for targeting therapy selection in colon cancer." Department of Defense, $100,000.

Smalley, K. (2009 NIR), "Melanoma pilot research." Comprehensive Melanoma Research Center, $75,000.

Sondak, V. (2007 SPORE), "Designing lymph nodes for cancer therapy." National Cancer Institute, $1,250,000.

Sorg, B. (2009 NIR), "Immunodelivery of nanoparticles to tumors for photothermal therapy." University of Florida Shands Cancer Center, $30,000.

Sorg, B. (2009 NIR), "Differential laser-induced perturbation spectroscopy – a novel approach to biosensing." University of Florida, $86,834.

Sotomayor, E. (2009 Bridge), "Targeting negative regulatory pathways for immunotherapy of B-cell lymphomas." National Cancer Institute, $2,441,080.

Storz, P. (2007 NIR), "Protein kinase D in oncogenic oxidative stress signaling." National Cancer Institute, $1,269,900.

Storz, P. (2007 NIR), "Role of protein kinase D in actin remodeling and cell motility." National Institute of General Medical Sciences, $1,071,000.

Storz, P. (2007 NIR), "Role of protein kinase D in actin remodeling and cell motility." American Cancer Society, $720,000.

Terada, N. (2006 Bridge), "Developing male contraceptives by targeting ANT4." National Institute of Child Health and Human Development, $1,186,650.

Vieweg, J. (2008 SPORE), "Elimination of immature myeloid cells." National Cancer Institute, $463,500.

Weber, J. (2008 Bridge), "Dendritic cell vaccination during lymphoid reconstitution." National Cancer Institute, $1,207,490.

Weber, J. (2008 Bridge), "CD40 and TLR agonists in melanoma." National Cancer Institute, $663,164.

Wright, A. (2008 Bridge), "Creation of a marine natural products library to enhance life science research." National Center for Complementary & Alternative Medicine, $1,599,934.

Since October 2009, current and past grantees reported $9.7 million in awards that are based indirectly on research findings from projects funded by this Program. Grants are presented in alphabetical order by last name of the principal investigator.

Briegel, K. (2008 Bridge), "Role of transcription factor TBX2 in breast cancer." Flight Attendant Medical Research Institute, $325,000.

Gabrilovich, D. (2006 Bridge), "P53 based vaccine for small cell lung cancer." National Cancer Institute, $486,846.

Gabrilovich, D. (2006 Bridge), "Mechanism of dendritic cell differentiation in cancer." National Cancer Institute, $2,055,032.

Goldberg, J. (2009 NIR), "Retinal Scaffolds: Synaptic and Stem Cell Integration." National Eye Institute, $764,972.

Jakymiw, A. (2008 NIR), "RNA silencing in the oral cavity." National Institutes of Health, $941,400.

McFadden, G. (2010 TSP), "Studies in poxvirus host range genes and tropism." National Institutes of Allergy and Infectious Disease, $1,793,425.

McFadden, G. (2010 TSP), "NAPPA Core." Southeast Regional Center of Excellence for Emerging Infections, $500,000.

Tan, W. (2007 Bridge), "Real-time and quantitative determination of biomolecules in living specimen." National Institute of General Medical Sciences, $805,704.

Tan, W. (2007 Bridge), "Development of molecular probes for biomedical applications." National Institute of General Medical Sciences, $723,858.

Tan, W. (2007 Bridge), "Enrichment and detection of exfoliated cancer cells." National Cancer Institute, $307,650.

Terada, N. (2006 Bridge), "iPSC generation using protein injection and site-selective HDAC inhibition." National Institute of General Medical Sciences, $965,446.

Since October 2009, Florida investigators have reported a total of $24.6 million in additional funding made possible by access to equipment purchased with the Program's Shared Instrument Grants. These awards are presented in alphabetic order by last name of the principal investigator on the Shared Instrument Grant.

Hu, J. (2006), "The role of SATB1 in metastatic breast cancer." Suffolk County Community College, $60,000.

Hu, J. (2006), "Genetic and dosimetric determinants of toxicity in men treated with radiotherapy for prostate cancer." Suffolk County Community College, $60,000.

Hu, J. (2006), "Environmental factors and epigenetic alterations in head and neck cancer disparities." Suffolk County Community College, $50,000.

Hu, J. (2006), "Molecular genetics of treatment response in lung cancer disparities." Suffolk County Community College, $50,000.

Hu, J. (2006), "Manipulation of STAT3 signaling for muscle preservation in cancer cachexia." National Cancer Institute, $1,901,650.

Hu, J. (2006), "Regulation of innate immune response." National Cancer Institute, $1,637,038.

Hu, J. (2006), "Impact of genomics on disparities in breast cancer radiosensitivity." National Cancer Institute, $2,440,308.

Koomen, J. (2006), "Quantitative Mass Spectrometry Assays to Detect Multiple Myeloma and Assess Relapse after Therapy." National Cancer Institute, $404,000.

Koomen, J. (2006), **Perez, L.** "Clonogenic Characterization of Myeloma Progenitor Cells." National Cancer Institute, $404,000.

Koomen, J. (2006), **Dalton, WS.** "ET-CURE: Leaders in New Knowledge-Emerging Technologies." National Institutes of Health, $332,943.

Koomen, J. (2006), "Phosphoproteomic strategies to evaluate tyrosine kinase signaling pathways in lung cancer." Department of Defense, $415,000.

Koomen, J. (2006), "Modeling efficacy of chemotherapy in multiple myeloma using quantitative detection of drug targets and apoptosis-related proteins." Department of Defense, $160,884.

Koomen, J. (2006), **Gabrilovich, D.** "Correction of dendritic cells defects in cancer." National Cancer Institute, $1,400,000.

Meeks, S. (2006), **Santhanam, A.** "Incorporating 3D lung dynamics for real-time radiotherapy." Florida High Tech Corridor Matching Research Program, $331,179.

Meeks, S. (2006), "Image-guided focal dose intensification and conformal dose de-escalation of radiotherapy for localized prostate cancers." National Institutes of Health, $567,090.

Meeks, S. (2006), **Langen, K.** "Effect of target motion on IMRT plans using solid compensators and MLCs." .decimal Inc., $120,000.

Shibata, Y. (2006), **Lu, M.** "AR in advanced prostate cancer." FAU Research Corporation, $400,000.

Shibata, Y. (2006), **Wei, J.** "Regulation of BimEL phosphorylation in the pathogenesis of Huntington's disease." National Institutes of Health, $211,200.

Shibata, Y. (2006), **Nouri-Shirazi, M.** "The impact of nicotine on dendritic cells and host immunity." Phillip Morris, $148,192.

Srivastava, A. (2006), **May, WS.** "The role of PKR in a novel IL-3 signal transduction pathway." National Institutes of Health, $1,465,000.

Srivastava, A. (2006), "UF/Moffitt Collaborative Research Grant." University of Florida/H. Lee Moffitt Cancer Center, $100,000.

Srivastava, A. (2006), **Yamamoto, J.** "Protective CMI mechanisms of a dual-subtype FIV vaccine." National Institutes of Health, $1,480,080.

Srivastava, A. (2006), **Cohn, M.** "Targets of endocrine disruptors in external genitalia." National Institutes of Health, $2,087,605.

Srivastava, A. (2006), "Next generation of recombinant AAV serotype vectors for gene therapy." National Cancer Institute, $2,533,104.

Srivastava, A. (2006), "Targeting leukemia hemangioblat activity." Leukemia and Lymphoma Society, $1,800,000.

Srivastava, A. (2006), **Ishov, A.** "Function of Daxx in mitosis that determines paclitaxel sensitivity in breast cancer." National Institutes of Health, $1,391,750.

Srivastava, A. (2006), **Gibbs, P.** "Intra-tumoral heterogeneity in osteosarcoma: Implications for tumorigenicity and malignant reversion." National Cancer Institute, $1,250,000.

Srivastava, A. (2006), **Kladde, M.** "Single-molecule epigenomic profiling of mammary stem cells and progenitor cells." Department of Defense, $111,375.

Srivastava, A. (2006), **Kladde, M.** "Single-molecule MAPit analysis of the epigenome of mammary epithelial stem and tumor-initiating cells." Department of Defense, $111,375.

Srivastava, A. (2006), **Gutierrez, M.** "Nucleosome interactions in the binary transcriptional response of the GAL1 promoter in single molecules." CONACYT Postdoctoral Fellowship Award, $16,000.

Srivastava, A. (2006), "Recombinant AAV tyrosine mutant and protein phosphatase 5 vectors for potential gene therapy of hemophilia A." Bayer Hemophila Special Project Award, $400,000.

Sugrue, S. (2006), **Brown, S.** "Irradiated autologous tumor cell-mediated nanotherapy for breast cancer." Department of Defense, $109,875.

Sugrue, S. (2006), **Denslow, N.** "Nanoparticle transport to oocytes and toxicological consequences in fathead minnows." National Science Foundation, $339,999.

Sugrue, S. (2006), **Grobmyer, S.** "Exploiting Altered Glucose Metabolic Pathways for Targeting Ultrasmall Therapeutic Nanoparticles to Breast Cancer." Department of Defense, $109,875.

Appendix E. Grantees Publications Reported in 2010

These publications are presented in alphabetical order by last name of the principal investigator.

Abdelrahim M, Konduri S, Basha R, Philip PA, Baker CH. Angiogenesis: an update and potential drug approach. *Int J Oncol*, 2010;36(1):5-18.

Hirsch-Kuchma M, Komanski C, Colon J, Teblum A, Masunov A, Alvarado B, Babu S, Seal S, Summy J, **Baker C**. Phosphate ester hydrolysis of biologically relevant molecules by cerium oxide nanoparticles. *Nanomedicine*, 2010;(6):738-44.

Saloura V, Wang LC, Fridlender ZG, Sun J, Cheng G, Kapoor V, Sterman DH, Harty RN, Okumura A, **Barber GN**, Vile RG, Federsiel MJ, Russell S, Litzky L, Albelda SM. Evaluation of an attenuated vesicular stomatitis virus (vsv) vector expressing interferon-beta for use in malignant pleural mesothelioma: heterogeneity in interferon-responsiveness defines potential efficacy. *Hum Gene Ther*, 2010;21(1):51-64.

Niesen M, Osborne A, Lagor W, Zhang H, Kazemfar K, Ness G, **Blanck G**. Technological advances in the study of the HLA-DRA promoter regulation: extending the functions of CIITA, Oct-1, Rb,and RFX. *Acta Biochem Biophys Sin (Shanghai)*, 2009;41(3):198-205.

Suzuki J, Ricordi C, **Chen Z**. Immune tolerance induction by integrating innate and adaptive immune regulators. *Cell Transplantation*, 2010;19(3):253-68.

Kim D, Sun M, He L, Zhou QH, Chen J, Sun XM, Bepler G, Sebti SM, **Cheng JQ**. A small molecule inhibits Akt through direct binding to Akt and preventing Akt membrane translocation. *J Biol Chem*, 2010;285:8383-94.

Guo J, Shu S, Esposito NN, Coppola D, Koomen JM, **Cheng JQ**. Ikkepsilon phosphorylation of eralpha-ser 167 and contribution to tamoxifen resistance in breast cancer. *J Biol Chem*, 2010;285:3676-84.

Zhao JJ, Lin J, Lwin T, Yang H, Guo J, Kong W, Dessureault S, Moscinski LC, Rezania D, Dalton WS, Sotomayor E, Tao J, **Cheng JQ**. MicroRNA expression profile and identification of mir-29 as a prognostic marker and pathogenetic factor by targeting cdk6 in mantle cell lymphoma. *Blood*, 2010;115:2630-39.

Yuan Z, Kim D, Shu S, Wu J, Guo J, Xiao L, Kaneko S, Coppola D, **Cheng JQ**. Phosphoinositide 3-kinase/akt inhibits mst1-mediated proapoptotic signaling through phosphorylation of threonine-120. *J Biol Chem*, 2010;285:3815-24.

Kim D, Shu SK, Coppola MD, Kaneko S, Yuan ZQ, **Cheng JQ**. Regulation of proapoptotic mammalian ste20-like kinase mst2 by the igf1-Akt pathway. *PLoS ONE*, 2010;5:e9616.

Ma Y, Kurtyka C, Cubit C, **Cress WD**. A novel e2f inhibitor, hlm006474, blocks expression of mitotic genes and synergizes with other chemotherapeutic compounds. *PLoS ONE*, 2009;4(10):e7524.

Cosino P, Horenstein N, Ostrov D, Rowe T, Law M, Barret A, Aslanidi G, **Cress WD**, **Law B**. A Novel Class of Cyclin-dependent Kinase Inhibitors Identified by Molecular Docking Act through A Unique Mechanism. *J Biol Chem*, 2009;284(43):29945-55.

Kokura K, **Fang J**. In vitro histone demethylase assays. *Methods Mol Biol*, 2009;523:249-261.

Ganju-Krishan A. Flow immunocytochemistry of tumor associated marker expression in cells from body cavity fluids. *J Can Cytopath*, 2010;77(2):132-43.

Erickson SJ, Ge J, Sanchez A, **Godavarty A**. Fast surface imaging using a hand-held optical device: in-vitro and in-vivo fluorescence studies. *Trans Oncology*, 2010;3(1)16-22.

Gutwein L, Sharma P, Brown SC, Fernando S, Fletcher B, Moudgil B, **Grobmyer SR**. Antibody targeting of nanoparticles to cancer cells for theranostic applications. *Nanomedicine*, 2010;62(2):150-65.

Singh RK, **Gunjan A**. Epigenetic therapy: targeting histones and their modifications in human disease. *Fut Med Chem*, 2010;2:543-48.

Smyth F, Stack A, Wang H, **Gunjan A**, Kabbaj M. The effects of social defeat on behavior and histone modifications in the hippocampus, amygdale, and prefrontal cortex. *Neuropsychopharma*, 2010;211(1):69-77.

Zhou Z, Li X, **Huang S**, Bungert J. Usf and nf-e2 cooperate to regulate the recruitment and activity of RNA polymerase II in the B-globin gene locus. *Nuc Acids*, 2010;285(21):15894-5905.

Lou Y, Jian W, Stravreva D, Fu X, Hager G, Bungert J, **Huang S**, **Qiu Y**. Trans-regulation of histone deacetylase activities through acetylation. *J Biol Chem*, 2009;284(50):34901-10.

Luo Y, Stavreva D, **Huang S**, Hager G, **Qiu Y**. Regulation of histone deacetylase 2 activity by histone deacetylase. *Mol Cell*, 2009;284:34901-10.

Jakymiw A, Patel RS, Deming N, Bhattacharyya I, Shah P, Lamont RJ, Stewart CM, Cohen DM, Chan EK. Overexpression of dicer as a result of reduced let-7 microRNA levels contributes to increased cell proliferation of oral cancer cells. *Genes Chromo Can*, 2010;49(6):549-59.

Konduri SD, Medisetty R, Kaipparettu BA, Srivastava P, Brauch H, Fritz P, Swetzig WM, Gardner A, Khan SA, Das GM. Mechanism of estrogen receptor antagonism towards p53: implications in breast cancer therapeutic response and stem cell regulation. *Proc Natl Acad Sci USA*, 2010;107(34):15081-6.

Bobustuc GC, Baker CH, Limaye A, Jenkins WD, Pearl G, Avgeropoulos NG, **Konduri SD**. Levetiracetam enhances p53-mediated MGMT inhibition and sensitizes glioblastoma cells to temozolomide. *Neuro Oncol*, 2010;12(9):917-27.

Daurkin I, Eruslanov E, Vieweg J, **Kusmartsev S**. Generation of antigen-presenting cells from tumor-infiltrated CDIIB myeloid cells with DNA demethylating agent 5-AZA-2'-depxycytidine. *Can Immuno*, 2010;59(5):697-706.

Appendix E. Grantees Publications Reported in 2010

Kusmartsev S, Vieweg J. Enhancing efficacy of cancer vaccines in urologic oncology: new directions. *Nat Rev Urology*, 2009;6(10):540-49.

Lin T, Ponn A, Hu X, **Law BK**, Lu J. Requirement of the histone demethylase LSD1 in Snai1-mediated transcriptional repression during epithelialmesenchymal transition. *Oncogene*, 2010;29(35):4896-904.

Law M, Corsino P, Parker N, **Law B**. Identification of a small molecule inhibitor of serine 276 phosphorylation of the p65 subunit of nf-kb using in silico docking. *Cancer Lett*, 2009;291(2):217-24.

Corsino P, Rowe T, Horenstein N, Ostrov D, Davis B, Law M, **Law B**. ldentification and characterization of a novel class of cyclin-dependent kinase inhibitors. *J Biol Chem*, 2009;284:29945-55.

Liao D. Emerging roles of the ebf family of transcription factors in tumor suppression. *Mol Can Res*, 2009;7(12):1893-901.

Bohen SP, Lossos C, Martinez-Climent JA, Ramos JC, Cubedo-Gill E, Alizadeh AA, Harrington WJ Jr, **Lossos IS**. Expression profiles of adult t-cell leukemia lymphoma and associations with clinical response to interferon and zidovudine. *Luek Lymphoma*, 2010;51(7):1200-16.

Li X, Hu X, Zhou Z, Qiu Y, Felsenfeld G, Bungert J, **Huang S**. Regulation of histone acetylation and chromatin looping by PRMT1 mediated H4R3 methylation. *Genes & Dev*, 2010;115(10):2028-37.

Li X, Hu X, Patel B, Zhou Z, Liang S, Ybarra R, Qiu Y, Felsenfeld G, Bungert J, **Huang S**. H4r3 methylation facilitates B-globin transcription by regulating histone acetyltransferase binding and h3 acetylation. *Blood*, 2010;115(10)2028-37.

Hockla A, Radisky DC, **Radisky ES**. Mesotrypsin promotes malignant growth of breast cancer cells through shedding of cd109. *Breast Cancer Res Treat*, 2010;124(1):27-38.

Radisky ES, Radisky DC. Targeting matrix metalloproteinase-induced epithelial-mesenchymal transition in breast cancer. *J Mammary Gland Biol Neoplasia*, 2010;15(2):201-1256.

Salameh MA, Robinson JL, Navaneetham D, Sinha D, Madden BJ, Walsh PN, **Radisky ES**. The amyloid precursor protein/protease nexin 2 Kunitz inhibitor domain is a highly specific substrate of mesotrypsin. *J Biol Chem*, 2010;285(3):1939-49.

Radisky E. Cathepsin D: regulation in mammary gland remodeling, misregulation in breast cancer. *Can Biol Ther*, 2010;10(5).

Siegel EM, Ulrich CM, Poole EM, Holmes RS, Jacobsen PB, Shibata D. The effects of obesity and obesity-related conditions on colorectal cancer prognosis. *Cancer Control*, 2010;17(1):52-7.

Melis M, Hernandez JM, Ly Q, Nair R, **Siegel EM**, McLoughlin J, Lewis J, Jensen E, Alvarado M, Eschrich S. Gene expression profiling of colorectal mucinous adenocarcinomas. *Dis Colon Rectum*, 2010;53(6):36-43.

Hnatyszyn HJ, Liu M, Hilger A, Herbert L, Gomez-Fernandez CR, Jorda M, Thomas D, Rae JM, El-Ashry D, Lippman ME. (**Slingerland, J**) Correlation of greb1 mRNA with protein expression in breast cancer: validation of a novel greb1 monoclonal antibody. *Breast Cancer Res*, 2009;122(2):371-80.

Haass NK, **Smalley KS**. Melanoma biomarkers: current status and utility in diagnosis, prognosis, and response to therapy. *Mol Diag Ther*, 2009;13(5):283-96.

Smalley KS. Introduction to the biochemical pharmacology special issue on targeted cancer therapy. *Biochem Pharmacol*, 2010;80(5):549.

Fang B, Haura EB, **Smalley KS**, Eschrich SA, Koomen JM. Methods for investigation of targeted kinase inhibitor therapy using chemical proteomics and phosphorylation profiling. *Biochem Pharmacol*, 2010;80(5):739-47.

Smalley KS. PLX-4032, a small-molecule B-Raf inhibitor for the potential treatment of malignant melanoma. *Curr Opin Investig Drugs*, 2010;11(6):699-706.

Smalley KS. Understanding melanoma signaling networks as the basis for molecular targeted therapy. *J Invest Derm*, 2010;130(1):28-37.

Messina JL, **Sondak VK**. Refining the criteria for sentinel node biopsy in patients with thinner melanoma: a road map for the future. *Cancer*, 2010;116:1403-05.

Sondak VK. Nonsentinel node metastases in melanoma: do they reflect the biology of the tumor, the lymph node or the surgeon? *Annals of Surgical Oncology*, 2009;16(11):2978-84.

Brayer J, Cheng F, Wang HW, Horna P, Suarez I, **Sotomayor EM**. Enhanced CD8 T Cell Cross-Presentation by Macrophages with Targeted Disruption of Stat3. *Immuno Lett*, 2010;131:126-130.

Zhao J, Lin J, Tint, L, Guo, J, Kong, W, Dessureault, S, Moscinski, L, Rezania D, Dalton W, **Sotomayor EM**, Tao J, Cheng J. Micro RNA Expression Profile and Identification of MiR-29 as Prognostic Marker and Pathogenetic Factor by Targeting CDK6 in Mantle Cell Lymphoma. *Blood*, 2010;115(13):2630-2639.

Lio G-Y, **Storz P**. Reactive Oxygen Species in Cancer. *Free Radical*, 2010;44(5):479-96.

Gopalakrishnan S, Van Emburgh B, Shan J, Su Z, Fields CR, Vieweg J, Hamazaki T, Schwartz PH, **Terada N**, Robertson KD. A novel DNMT3B splice variant expressed in tumor and pluripotent cells modulates genomic DNA methylation patterns and displays altered DNA binding. *Mol Cancer Res*, 2009;7:1622-34.

Weigel-Van Aken K. Pharmacological activation of guanine nucleotide exchange factors for the small gtpase rap1 recruits high-affinity b1 integrins as coreceptors for parvovirus b19: improved ex vivo gene transfer to human erythroid progenitor. *Hum Gene Therapy*, 2009;20:1-14.

Yin L, Velazquez OC, Liu ZJ. Notch signaling: emerging molecular targets for cancer therapy. *Biochem Pharma*, 2010;80(5):690-701.

Locovei AM, **Yin L**, D'Urso G. A genetic screen for replication initiation defective (rid) mutants in schizosaccharomyces pombe. *Cell Division*, 2010;5(1):20.

Shirk K, Jin H, **Yu H-G**. Condensins promote co-orientation of sister chromatids during meiosis I in budding yeast. Genetics, 2010;185(1):55-64.
Zeidan O. Gel Dosimetry for Proton QA. *Med Phys*, Epub Jun 2010.

Tirpak O, Hsi W, Meeks S, Maryanski M, Kupelian P, **Zeidan O**. Dosimetric Validation of the Proton-Sensitive BANG3-Pro2 Polymer Gel Dosimeter Irradiated Buy Single Field Therapeutic Proton Beams. *Med Phys*, 2009;36:2733.

Zeidan O, Hsi W, Tirpak O, Maryanski M, Meeks S, Kupelian P, Palta J. Assessment of Proton Beam in-vivo Dose Verification by directly Comparing Doses Measured in Tissue-Equivalent Polymer Gels Post Irradiation. *Med Phys*, 2009;36:2810.

Zeidan OA, Hsi WC, Sriprisan I, Maryanski MJ, Lopatiuk-Tirpak O, Kupelian PA, Meeks SL, Li Z, and Palta JR. Dosimetric evaluation of a novel protonsensitive polymer gel dosimeter for proton therapy. *Med Phys*, 2010;37(5):2145-52.

Sriprisan SI, Maryanski MJ, **Zeidan OA**. Imaging Properties of the OCTOPUS-IO Scanner in combination with a new Polymer Gel Dosimeter. *Med Phys*, 2010;37:3247.

Yuan F, Song L, Qian L, Hu JJ, **Zhang Y**. Assembling an orchestra: fanconi anemia pathway of DNA repair. *Front Biosci*, 2010;15:1131-49.

Song L, Yuan F, **Zhang Y**. Does a helicase activity help mismatch repair in eukaryotes? *IUBMB Life*, 2010;62(7):548-53.

Zhou Y, Wang J, **Zhang Y**, Wang Z. The catalytic function of the rev1 dcmp transferase is required in a lesion-specific manner for translesion synthesis and base damage-induced mutagenesis. *Nuc Acids*, 2010;38(15):5036-46.

Li X, **Zhu F**. Identification of the nuclear export and adjacent nuclear localization signals for orf45 of Kaposi's sarcoma-associated herpesvirus. *J Virol*, 2009;83:2531-2539.

Florida investigators have reported the following publications that were made possible by access to equipment purchased with the Program's Shared Instrument Grants. These publications are presented in alphabetic order by last name of the principal investigator on the Shared Instrument Grant.

Iorns E, Hnatyszyn HJ, Seo P, Clarke J, Ward T, Lippman M. (**Hu, J**) The role of SATB1 in breast cancer pathogenesis. *J Natl Cancer Inst*, 2010;102(16):1284-96.

Clarke J, Seo P, Clarke B. (**Hu, J**) Statistical expression deconvolution from mixed tissue samples. *Bioinformatics*, 2010;26(8):1043-9.

Chen Y, Gruidl M, Remily-Wood E, Liu RZ, Eschrich S, Lloyd M, Nasir A, Bui MM, Huang E, Shibata D, Yeatman T, **Koomen JM**. Quantification of betacatenin signaling components in colon cancer cell lines, tissue sections, and microdissected tumor cells using reaction monitoring mass spectrometry. *J Proteome Res*, 2010;9(8):4215-27.

Thomas CE, Sexton W, Benson K, Sutphen R, **Koomen JM**. Urine collection and processing for protein biomarker discovery and quantification. *Can Epidemiol Biomarkers Prev*, 2010;19(4):953-9.

Waghorn BJ, Shah AP, Ngwa W, **Meeks SL**, Moore JA, Siebers JV, Langen KM. A computational method for estimating the dosimetric effect of intra-fraction motion on step-and-shoot IMRT and compensator plans. *Phys Med Biol*, 2010;55(14):4187-202.

Min Y, Santhanam A, Neelakkantan H, Willoughby TR, **Meeks SL**, Kupelian PA. A GPU-based framework for modeling real-time 3D lung tumor conformal dosimetry with subject-specific lung tumor motion. *Phys Med Biol*, 2010;55(17):5137-50.

Santhanam A, Willoughby TR, **Meeks SL**, Kupelian PA. Modeling simulation and visualization of conformal 3d lung tumor dosimetry. *Phys Med and Biol*, 2009;54(20):6165-80.

Ngwa W, **Meeks SL**, Kupelian PA, Schnarr E, Langen KM. Validation of a computational method for assessing the impact of intra-fraction motion on helical tomotherapy plans. *Phys Med and Biol*, 2009;54(21):6611-21.

Leon R, Bhagavatula N, Ulukpo O, McCollum M, Wei J. (**Shibata, Y**) BimEL as a possible molecular link between proteasome dysfunction and cell death induced by mutant huntingtin. *Eur J Neurosci*, 2010;31:1915-20.

McCollum M, Ma Z, Cohen E, Leon R, Tao R, Wu J-Y, Maharaj D, Wel J. (**Shibata, Y**) Post-MPTP treatment with granulocyte colony-stimulating factor improves nigrostriatal function in the mouse model of Parkinson's disease. *Mol Neurobiol*, 2010;41(2-3):410-9.

Zeng M, Guinet E, Nouri-Shirazi M. (**Shibata, Y**) Comparative analysis of dendritic cells and anti-CD3/CD28 expanded regulatory T Cells for application in transplantation. *Transplant Immuno*, 2009;22:82-92.

Rahman MM, Madlambayan GJ, Cogle CR, McFadden G. (**Srivastava, A**) Oncolytic viral purging of leukemic hematopoietic stem and progenitor cells with myxoma virus. *Cytokine Growth Factor Reviews*, 2010;21(2-3):169-75.

Madlambayan GJ, Meacham A, Hosaka K, Mir S, Jorgensen M, Scott EW, Siemann D, Cogle CR. (**Srivastava, A**) Leukemia regression by vascular disruption and antiangiogenic therapy. *Blood*, 2010;116(9);1389-90.

Petrs-Silva H, Dinculescu A, Li Q, Min SH, Chiodo V, Pang J, Zhong L, Zolotukhin S, **Srivastava A**, Lewin AS, Hauswirth WW. High-efficiency transduction of the mouse retina by tyrosine-mutant aav serotype vectors. *Mol Therapy*, 2009;17:463-71.

Glushakova L, Lisankie M, Eruslanov E, Ojano-Dirain C, Zolotukhin I, Zhong L, Liu C, **Srivastava A**, Stacpoole PW. AAV3-mediated transfer and expression of the pyruvate dehydrogenase E1 alpha subunit gene causes metabolic remodeling and apoptosis of human liver cancer cells. *Mol Genet Metabl*, 2009;98(3):289-99.

Jayandharan GR, Zhong L, Sack BK, Rivers AE, Li M, Li B, Herzog RW, **Srivastava A**. Optimized AAV-protein phosphatase 5 helper-viruses for efficient transduction by single-stranded AAV vectors: therapeutic expression of factor IX at reduced vector doses. *Hum Gene Therapy*, 2010;21(3):271-83.

Kauss MA, Smith LJ, Zhong L, **Srivastava A**, Wong Jr KK, Chatterjee S. Enhanced long-term transduction and multilineage engraftment of human hematopoietic stem cells transduced with tyrosine-modified recombinant adeno-associated virus serotype 2. *Hum Gene Therapy*, 2010;21(9):1129-36.

Dismuke WM, Ellis DZ. (**Sugrue, S**) Activation of the bk(ca) channel increases outflow facility and decreases trabecular meshwork cell volume. J Ocul *Pharma Ther*, 2009;25(4):309-14.

Endnotes

[1]Estimated Number of New cancer cases and Deaths by State-2009. American Cancer Society. Available at http://www.cancer.org/acs/groups/content/@nho/documents/document/2009casesdeathssitestatepdf.pdf, Accessed October 8, 2010.

[2]The Florida Senate, Interim Report 2010-219, September 2009.

[3]When referring to a grant within this report, the year refers to the fiscal year in which the grant begins. For example, a 2010 grant generally begins July 1, 2010, and ends June 30 of the year of completion.

[4]The grants considered for the Florida Research Challenge Grant were NIH Research Challenge grant applications called RC1's. More information about this NIH grant type is available at http://grants.nih.gov/grants/funding/challenge_award/.

[5]Hurley, Daniel. "Tapping State College Research and Development Capacity in Support of State Economic Development." American Association of State Colleges and Universities, A Higher Education Policy Brief, October 2008. Available at http://www.aascu.org/media/pm/pdf/pmoct08.pdf. Accessed September 7, 2010.

[6]Adapted from the National Association of Chronic Disease Directors, 2006 Definition of Health Disparities.

[7]http://www.floridacharts.com/charts/DeathQuery.aspx. Accessed September 15, 2010.

[8]USDA Economic Research Service. Data Sets, "State Fact Sheets: Florida, available at
"Demographic and Economic Profile, Florida, Updated May 2006." Rupri, Rural Policy Research Institute, available at http://www.rupri.org/Forms/Florida.pdf. Accessed on September 20, 2010.

[9]American College of Physicians. Racial and Ethnic Disparities in Health Care, Updated 2010. Philadelphia: American College of Physicians; 2010: Policy Paper. (Available from American College of Physicians, 190 N. Independence Mall West, Philadelphia, PA 19106.)

[10]Florida Department of Health. Florida Mortality Atlas. Available at http://www.floridacharts.com/charts/atlas.aspx. Accessed September 15, 2010.

[11]USDA Economic Research Service. Data Sets, "State Fact Sheets: Florida, available at
"Demographic and Economic Profile, Florida, Updated May 2006." Rupri, Rural Policy Research Institute, available at http://www.rupri.org/Forms/Florida.pdf. Accessed on September 20, 2010.

[12]"Research Networks, Socioeconomic Status and Health." John D. and Catherine T. MacArthur Foundation, available at http://www.macfound.org/site/c.lkLXJ8MQKrH/b.951947/k.11B4/Research_Networks__Socioeconomic_Status_and_Health.htm. Accessed October 11, 2010.

[13]Welcome to Florida's Office of Rural Health, floridashealth.com. Available at http://www.doh.state.fl.us/workforce/ruralhealth/ruralhealthhome.html#Rural%20Health. Accessed September 15, 2010.

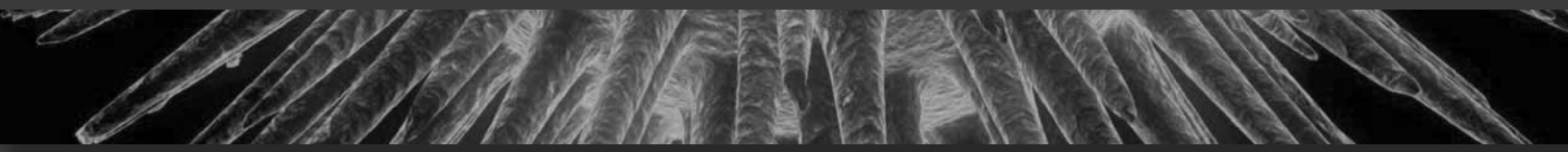
[14]"Rural Health Disparities." Rural Assistance Center. Updated September 28, 2010. Available at http://www.raconline.org/info_guides/disparities/. Accessed October 11, 2010.

[15]"California Breast Cancer Research Program, Advances in Breast Cancer Research," 1999, p. 23.

[16]The number of active grants is dynamic since grants are in the process of completing.

FLORIDA DEPARTMENT OF HEALTH

bankheadcoley
Florida Cancer Research Program



www.floridabiomed.com